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Supplemental Information

Furin: A Potential Therapeutic

Target for COVID-19

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Transparent Methods

Homology Spike protein blast and sequence alignment.

The Spike protein of (GB: QHR63250.1) was downloaded from NCBI nucleotide database. The protein sequence were aligned with whole database using BLASTp to search for homology viral Spike protein (Alogorithm parameters, Max target sequences: 1000, Expect threshold: 10). Multiple-sequence alignment was conducted in BLASTp online and analysis with DNAMAN and Jalview. The evolutionary history was inferred using the Neighbor-Joining method in MEGA 7 software package. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test was determined by 500 replicates. The Spike protein sequence analyses were conducted in snapgene view.

Furin cleavage site prediction

The prediction of furin cleavage sites were carried out in ProP 1.0 Server (http://www.cbs.dtu.dk/services/ProP/).

Compounds database

Approved drug database was from the subset of ZINC database, ZDD (ZINC drug database) containing 2924 compounds (<u>Irwin et al., 2012</u>). Natural products database was constructed by ourselves, containing 1066 chemicals separated from traditional Chinese herbals in own lab and natural-occurring potential antiviral components and derivatives. Antiviral compounds library contains 78 known antiviral drugs and reported antiviral compounds through literature search.

Homology modeling and molecular docking

Corresponding homology models predicted by Fold and Function Assignment System server for each target protein were downloaded from Protein Data Bank (<u>www.rcsb.org</u>). Alignment of two protein sequences and subsequent homology modeling were performed by bioinformatics module of ICM 3.7.3 modeling software on an Intel i7 4960 processor (MolSoft LLC, San Diego, CA). For the structure-based virtual screening, ligands were continuously resiliently made to dock with the target that was represented in potential energy maps by ICM 3.7.3 software, to identify possible drug candidates. 3D

compounds of each database were scored according to the internal coordinate mechanics (Internal Coordinate Mechanics, ICM) (Abagyan et al., 1994). Based on Monte Carlo method, stochastic global optimization procedure and pseudo-Brownian positional/torsional steps, the position of intrinsic molecular was optimized. By visually inspecting, compounds outside the active site, as well as those weakly fitting to the active site were eliminated. The software adopted two kind of scoring system. One is ICM score, which is based on the empirical function of predicted physical interaction, calculated according to seven parameters, including ligand-target hydrogen bonding interactions, internal force-field energy of the ligand, desolvation energy of hydrogen bond donor-acceptor, entropy loss due to conformational differences upon ligand binding, polar and non-polar solvation energychanges upon ligand binding, electrostatic energyand hydrophobic free energy (Neves et al., 2012). Another is mfscore, it is a potential of mean force score and provides an independent score of the strength of ligand-receptor interaction. It is a measure of statistical probability of interaction between the ligand and the receptor. It examines interatomic distances of the docked interaction, and compares that to existing interactions available in PDB (Muegge et al., 1999).

Compounds with Scores less than -30 or mfScores less than -100 (generally represents strong interactions) have priority to be selected. Protein-protein docking procedure was performed according to the ICM-Pro manual.

Expression and purification of furin

The detailed procedures for expression and purification of human furin (UNIPROT ID P09958) refer to previous work with some modifications (<u>Dahms et al., 2018</u>). Briefly, the sequence encoding human furin amino acids 23-574 was cloned into PEGMan vector with N-terminal secretion signal peptide and C-terminal His tag. The expressed plasmid was transfected in HEK293-GnTI cells using polyethylenimine transfection reagent, and the transfected cells were cultured in a 10 cm plate with 10 mL of DMEM (Invitrogen) containing 10% bovine calf serum (HyClone, GE Healthcare) overnight. The medium was changed to 10 mL of freeStyle 293 Expression Media (Thermo Fisher Scientific), and the

cells were cultured for another 72 h. The conditioned medium was collected and centrifuged at 4500 g for 20 min. The supernate protein was dialysis against 25 mM Tris, pH 8.0, 250 mM NaCl, 5 mM CaCl₂ overnight at 20 °C before purification. The secreted furin was purified from the culture media using Ni-NTA agarose (Qiagen) affinity chromatography with gravity flow.

Enzymatic activity and inhibition assays

In brief, the activity of human furin was measured by a continuous kinetic assay, with the substrate Boc-Arg-Arg-Ala-Arg-AMC (GL Biochem) or Boc-Arg-Val-Arg-Arg-AMC (GL Biochem), using wavelengths of 360±40 nm and 460±40 nm for excitation and emission, respectively. Furin was added in assay buffer containing 100 mM HEPES buffer, pH 7.0, 0.2% (v/v) Triton X-100, 2 mM CaCl₂ and 0.1 mg/mL BSA. The assay started by immediately mixing with different concentrations of substrate (0.39-200 μ M). The fluorophore, 7-amino-4-methylcoumarin (AMC) group released from Boc-RRAR-AMC or Boc-RVRR-AMC was monitored in the form of relative fluorescence units as a function of time (RFU/min) using a BioTEK Synergy H1 multimode microplate reader at 37 °C. The IC₅₀ values were calculated by fitted regression equation using the-log plot (GraphPad Prism). Each value was expressed with the means ± SD of three independent tests, each with three replicates.

Supplemental References

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Bink ADDORADI, 1.255 L.L. Bink ADDORADI, 1.267 S.V. gb / ADD SODE, 1.1-037 S.V	gD AAP3309/.1/1-1255 LL	$\mathbf{R} = \frac{g_0}{A1098143.1/1-1202}$ L = \mathbf{R} =	gb ALA49396.1/1-1037 - SV	gb AKN11072.1/1-1037 - SV R	- gb ALJ54488.1/1-1037 - SV R
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B0/AB72979.1/1-1233 LL B0/AB7207.1/1-1233 LL B0/AB72002.1/1-1233 SV B0/AB72002.1/1-1233 SV B0/AB72002.1/1-1233 SV B0/AB72002.1/1-1233 SV B0/AB72002.1/1-1233 SV B0/AB7202.2/1/1-1233 SV B0/AB7207.2/1/1-1233	gb AAV97998.1/1-1255 L	R - gb ANA90027.1/1-1202	gD AH204057.1/1-1037 - SV	refWP 148724438.1/1	- gb AKN11074.1/1-1037 - SV R
Biplantion Biplantion <td>gb ABD72979.1/1-1255 LL</td> <td>R - g0/ALA022//.1/1-1202</td> <td>gb/AID55079.1/1-1037 - SV</td> <td>gb AVN89334.1/1-1037 - SV R</td> <td>- gb ANF29173.1/1-1037 - SV R</td>	gb ABD72979.1/1-1255 LL	R - g0/ALA022//.1/1-1202	gb/AID55079.1/1-1037 - SV	gb AVN89334.1/1-1037 - SV R	- gb ANF29173.1/1-1037 - SV R
B)LAURY 2003.1/1-1335 LL B)LAURY 2003.1/1-135 LL B)LAURY 2003.1/1-135 S V ref(IMP_077068095.1/1-1037 S V B)LAURY 2003.1/1-135 S V ref(IMP_077068095.1/1-1037 S V B)LAURY 2003.1/1-135 S V ref(IMP_077068095.1/1-1037 S V B)LAURY 2003.1/1-1335 S V ref(IMP_077068095.1/1-1037 S V B)LAURY 2003.1/1-1037 S V B)LAURY 2003.1/1-1037 <ths th="" v<=""> B)LAURY 2003.1/1-1037</ths>	gb AAV97000.1/1-1255	gbl 4SO66810 1/1=1202	gb ALJ54517.1/1-1037 - SV 1	gb ATW75479.1/1-1037 - SV R	- gb ASU89955.1/1-1037 - SV R
bpLaw proponul/1-1235 L gbLaw proponul/1-1235 S S gbLaw proponul/1-1235 S	gb ACZ72093.1/1-1255 LL	R - gb AAU93320.1/1-1145	gb AVK87417.1/1-1037 - SV	- ref WP_077698995.1/1 S V R	- gb AJG44080.1/1-1037 - SV R
gplar83672.1/1-1235 LL gplar10378.1/1-133 SV gplar10378.1/1-1037 SV gplar1011.1037 SV gplar10378.1/1-1037 SV gplar111-1037 SV gplar111-1037 SV gplar111-1037 SV gplar111-1037 SV gplar111-1037 SV	gb AAV97990.1/1-1255 L	R - gb ANA96090.1/1-848	gb AMW90853.1/1-1037 - SV	- go ANF29228.1/1-1037 - SV R	- gologersossa.1/1-1037 - 5 V K
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gbl_Att70147.1/1-1255 LL gbl_Att70147.1/1-1255 LL gbl_Att70147.1/1-1255 SV gbl_Att7037 SV gbl_Att70437.1/1-1037 SV gbl_Att70437.1/1-1037 SV gbl_Att704437.1/1-1037 SV gbl_Att7043	gb/ADC35483.1/1-1255	gb ABE77216.1/1-720	gb ALM26400.1/1-1037 - SV	- zb/ASU91010.1/1-1037 - SV P	- gb ODP16195.1/1-1037 - SV R
BDLAMPD (611./1/-1235 L BDLAMPC 201./1/-1037 SV SV SDLAMPC 201./1/-1037 SV SV SDLAMPC 201./1/-1037 SV <th< td=""><td>gb AAT76147.1/1-1255 LL</td><td>ref YP_009072440.1/1-1258 т д</td><td>gb ALL26396.1/1-1037 - SV</td><td>- gb AJG44069.1/1-1037 - SV R</td><td>- gb ALJ54500.1/1-1037 - SV R</td></th<>	gb AAT76147.1/1-1255 LL	ref YP_009072440.1/1-1258 т д	gb ALL26396.1/1-1037 - SV	- gb AJG44069.1/1-1037 - SV R	- gb ALJ54500.1/1-1037 - SV R
Bolabor2008.11/-1235 LL BolaW10044.11/-1219 BolaW10044.11/-1219 BolaW10448.11/-1037 S V S V BolaW1044833.11/-1218 BolaW1044833.11/-1037 S V BolaW104830.11/-1037 S V	gb AAV91631.1/1-1255 L	R - gb ADY17911.1/1-1294 GSR	gb ALA50067.1/1-1037 - S V	gb ALW82742.1/1-1037 - SV R	- gb ANC28678.1/1-1037 - SV R
gplaary yrse.///-1/233	gb ABD72988.1/1-1255 LL	R - SO AWV07048.1/1-1219	gDIAHZ58501.1/1-1037 - SV	gb ALJ54488.1/1-1037 - SV R	- gb ATG84833.1/1-1037 - SV R
Bit All Add Status Bit All	gD AAV97986.1/1-1255 L	R - SUAWV07004.1/1-1030 PPQ	gb AXN92228,1/1-1037 - SV	gb EYE09289.1/1-1037 - S V R	- gb ALA49649.1/1-1037 - SV R
Bits Bits <td>gb/AAS10405.1/1-1255 L</td> <td>R - gb/ADM33558 1/1-1218</td> <td>gb ALA49385.1/1-1037 - SV</td> <td>go ALJ 34433.1/1-103/ - SV K</td> <td>- gD AS199811.1/1-1037 - SV R</td>	gb/AAS10405.1/1-1255 L	R - gb/ADM33558 1/1-1218	gb ALA49385.1/1-1037 - SV	go ALJ 34433.1/1-103/ - SV K	- gD AS199811.1/1-1037 - SV R
ph/arryi072/078/1/1-1235 LL gb/aD/33374/1/1-1218 St gb/aD/33372/1/1-1037 St St gb/aD/33372/1/1-1037 St gb/aD/33372/1/1-1037 St gb/aD/33374/1/1-1273 St gb/aD/33372/1/1-1037 St gb/aD/33372/1/1-1037 St gb/aD/33372/1/1-1037 St gb/aD/33372/1/1-1037 St gb/aD/33372/1/1-1037 St gb/aD/3372/1/1-1037 St gb/aD/3372/1/1-1037 St gb/aD/34/2/2/2/2/1/1-1037 St gb/aD/34/2/2/2/2/1/1-1037 St gb/aD/34/2/2/2/2/2/1/1-1037 St gb/aD/34/2/2/2/2/2/1/1-1037 St gb/aD/34/2/2/2/2/2/2/1/1-1037 St gb/aD/34/2/2/2/2/2/2/2/2/2/2/2/2/2/2/2/2/2/2/	gb ABD72995.1/1-1255 LL	R - gblABN10927.1/1-1218	gb AKIN24830.1/1-1037 - SV 1	gb AKN11074.1/1-1037 - SV R	- gb/AGV08370 1/1-1037 - SV R
gb/aB860959.1/1-1235 LL gb/aDX33182.1/1-1273 Y CLS gb/aDX03182.1/1-1273 Y CLS gb/aDX03182.1/1-1237 Y CLS gb/aDX03182.1/1-1237 <td>gb AGT21078.1/1-1255 LL</td> <td>R - gb ADM33574.1/1-1218</td> <td>gb QDI73610.1/1-1037 - SV</td> <td>gb ANF29173.1/1-1037 - SV R</td> <td>- gb/ASU90329.1/1-1037 - SV R</td>	gb AGT21078.1/1-1255 LL	R - gb ADM33574.1/1-1218	gb QDI73610.1/1-1037 - SV	gb ANF29173.1/1-1037 - SV R	- gb/ASU90329.1/1-1037 - SV R
gb/AZ73742.1/1-1235 LL gb/AZ7342.1/1-1037 SV gb/AZ7422.1/1-1037 SV gb/AZ7422.1/1-1037 SV gb/AZ74122.1/1-1037 SV gb/AZ7412.1/1-1037 SV gb/AZ7412.1/1-	gb ABF68959.1/1-1255 - LL	R - gb ADM33582.1/1-1273	gD ALA49803.1/1-1037 - SV	gb ASU89955.1/1-1037 - SV R	- gb ANF29261.1/1-1037 - SV R
Bole All States	gb ACZ72122.1/1-1255 LL	gb ADM33566.1/1-1273	gb AXP07345.1/1-1037 - SV	gb AJG44080.1/1-1037 - SV R	- gb ASU90340.1/1-1037 - SV R
gb/LABD7064.1/1-1255 LL gb/LBDS060.1/1-1057 SV gb/LDDS0758.1/1-1057 SV gb/LDDS0506.1/1-1057 SV gb/LDDS0507.1/1-1057 SV	2b ARA10473.1/1=1255	gb AWV67040.1/1-1025 PS	gb QBU56412.1/1-1037 - SV	gblQBF80554.1/1-1037 - S V R	- gb AQZ41285.1/1-1037 - SV R
gb/acc231991.1/1-1235 LL gb/acc231991.1/1-1037 S V gb/acc23191.1/1-1037 S V gb/acc2311.1/1-1037 S V	gb AAR07624.1/1-1255 - LL	R - gb ABN10919.1/1-1154 SVS	gb ALJ54450.1/1-1037 - SV	g0/411005/8.1/1-1037 - SV R g6/491805271/1-1027 - SV R	- go AIDS 5090.1/1-1037 - SV R
Bolk #M43807.1/1-1235 LL Bolk ZBC00132071.1/1-1232 AT A Stress Bolk ZBC00132071.1/1-1037 Stress <th< td=""><td>gb ACZ71991.1/1-1255 LL</td><td>R - gb QEH60463.1/1-1061 ATS</td><td>gb ANF29239.1/1-1037 - SV</td><td>gb(DDP161951/1-1037 - SV</td><td>- 80/AQZ41282.1/1-1037 - 5 V R - 80/AJX80261 1/1-1027 - S V R</td></th<>	gb ACZ71991.1/1-1255 LL	R - gb QEH60463.1/1-1061 ATS	gb ANF29239.1/1-1037 - SV	gb(DDP161951/1-1037 - SV	- 80/AQZ41282.1/1-1037 - 5 V R - 80/AJX80261 1/1-1027 - S V R
BOLARTSSTI4.1/1-1235 LL BOLARTSSTI4.1/1-1235 KL BOLARTSSTI4.1/1-1235 KL BOLARTSSTI4.1/1-1235 SV BOLARTSSTI4.1/1-1235 SV BOLARTSSTI4.1/1-1235 SV BOLARTSSTI4.1/1-1237 SV BOLARTSSTI4.1/1-1037 SV	gb AFM43867.1/1-1255 LL	R - go AAW 30014.1/1-490	g0 ASU90142.1/1-1037 - SV	2blALJ54500.1/1-1037 - SV R	- gh ASLO0175.1/1-1037 - SV R
Bip/Levessed.nl/102 SV S SV S </td <td>gb/AFR58714.1/1-1255 LL</td> <td>abioDE43840 1/1-1052</td> <td>sh 41 440836 1/1-1027 OU</td> <td>gb ANC28678.1/1-1037 - SV B</td> <td>- gb/ALD51904.1/1-1037 - SV R</td>	gb/AFR58714.1/1-1255 LL	abioDE43840 1/1-1052	sh 41 440836 1/1-1027 OU	gb ANC28678.1/1-1037 - SV B	- gb/ALD51904.1/1-1037 - SV R
gb/attionality SIme gb/attionality	gb/AR86775.1/1-1255 - LL	B - gb/ABN10935.1/1-1042	gb AVK87439.1/1-1037 - SV	gb ATG84833.1/1-1037 - SV R	- gb ALS20350.1/1-1037 - SV R
gb/AAP07989.1/1-1255 L gb/AA7030812.1/1-088 V AT gb/AA7030812.1/1-087 S V gb/AAF030812.1/1-1037 S V S V gb/AAF04462.1/1-1037 S V S V gb/AAF04462.1/1-1037 S V S V gb/AL154411-1037 S V S V gb/AL154411-10411-1037 S V S V gb/AL154411-1041-1037 S V S V gb/AL154411-1041-1037 S V S	gb AEA10443.1/1-1255 LL	R - gb AVP25406,1/1-1113	gb ATG84756.1/1-1037 - SV	gb ALA49649.1/1-1037 - SV R	- gb ASU90010.1/1-1037 - SV R
gb/ALC869894/1/-1235 LL - gb/ALC969894/1/-1235 - - gb/ALC94940.1/1-1037 S V - gb/ALC94400.1/1-1037 S V - gb/ALC9410.1/1-1037 S V - -	gb AAV97989.1/1-1255 L	B - gb AOG30812.1/1-988	gb ATY74392.1/1-1037 - SV	golASY99811.1/1-1037 - SV R	- gb AHI48528.1/1-1037 - SV R
[g0]AABU/029.1/1-1233 - LL	gb ACB69894.1/1-1255 LL	ref YP_009273005.1/1-988 VAT	gb AHY21469.1/1-1128 - SV	abl 4(11/08370 1/1-1037 - SV R	- gD ALJ54446.1/1-1037 - SV R
Bolar Cottor 11/1-103/ - S 4	g0 AAR07629.1/1-1255 LL	ref YP 001039962.1/1-1044 R V R	gD ALJ 34 521.1/1-1037 - SV	2 201ASU90329.1/1-1037 - SV P	- apl ALBO8311 1/1-1037 - SV R
<i>vbl4t7NR0324.1/1-1037</i> - SV			PohitO04/01/11-102/ - 2 4	- Ib-	gb/AYJ71470.1/1-1037 - SV R
					gb AVN89324.1/1-1037 - SV R
gb/ALK80291.1/1-1037 \$V					gb ALK80291.1/1-1037 - SV R

Figure S1. Multiple sequence alignment of 1000 Spike proteins(1-486). Related to Figure 1.

487-589	590-692	693-796	797-899	900-1000
gblQBF80521.1/1-1037 PR - SV R	gb AMQ23498.1/1-929 - R - R S R	- gb AA006124.1/1-930 - R	- R S R - 1 gb ANZ78838.1/1-936 -	R - R S R - pdb/6NB3/A/1-984 PA - SV G -
gb AWU59321.1/1-1037 PR - SV R gb OBM11737.1/1-1037 PR - SV R	- gb ABI93999.2/1-929 - K - K S K - gb AGO98885.1/1-911 - R - R S R	- gb AID16631.1/1-893 PR - dbilBAM156561/1-00 - P	- E T Y - gb AIL49513.1/1-936 -	R - R S R - gb AXP11690.1/1-929 - R - R S R -
gb AH148737.1/1-1037 'PR - SV R	- gb AZS64221.1/1-929 - R - R S R	- gblABP87990.1/1-906 - R	- RQ R - 1	B - K S
gb AVN89365.1/1-1037 PR - SV R	- gb AV115011.1/1-929 - R - R S R	- gb AIX10758.1/1-935 - R	- R S R - 1 gb AILA0520 1/1-036 -	R-RSR- ph/4/2/008875///-0// -R-RSR-
gb AH148616.1/1-1037 PR - SV R	- gb/AGO98881.1/1-929 - R - R S R	gb ALX10757.1/1-935 - R	- R S R - 1 gb ARKD8679.1/1-912 -	R - R S R - gb AMQ23488.1/1-911 - R - R S R -
gb/BYD89444.1/1-1037 PR - SV R	- gb ABD18928.1/1-929 - R - R S R	gblAIX10760.1/1-935 - R	-RS	R - R S R gb AZS64226.1/1-929 - R - R S R -
gb ANF29272.1/1-1037 PR - SV R	- gb ABD18912.1/1-929 - R - R S R	gb AIL49492.1/1-935 - R	- R S R - 1 80 AIL49507.1/1-936	B-RSR-
gb/ALX27228.1/1-1037 PR - SV R	- gb/AIKI8010.1/1-1030 GB - K A L spl090AR5.1/1-929 - R - R S R	gb AIL49484.1/1-935 - R	- R S R - 1 gb/AON78704.1/1-936 -	R - R S R
gb/ALA49462.1/1-1037 XR - SV R	- gb ABP38279.1/1-929 - R - R S R	gb AIKI 80/9.1/1-894 K R	ref NP_045300.1/1-914 R	R - AD R - gb AIX10761.1/1-936 - R - R S R -
gb ALA49473.1/1-1037 PR - SV R	- gb AXP11688.1/1-929 - R - R S R	- gblAYR18652.1/1-89K R	-DLN-	gb ACN89705.1/1-928 RSR-
gb/QDP16206.1/1-1037 PR - SV R	- gb AAX38490.1/1-929 - R - R S R	gb AYR18625.1/1-89K R	- DL N - gb AVR40344.1/1-912 -	R - R S R - gb/AIL49521.1/1-1147 R - R S R -
gb/ANI69922.1/1-1037 PR - SV R	- gb QBG67077.1/1-929 - R - R S I	- gb ABS87264.1/1-89.H R	- AR R - gb AXX83333.1/1-1147	R - R S R - gb/AVV04341.1/1-1133 gb/AUF40275.1/1-1133R R
gb AN169878.1/1-1037 PR SV	- gb/QBG67074.1/1-929 - R - R S R eb/OBG67076.1/1-929 - R - R S R	- gb AIL49489.1/1-935-	- R S gb AIL49499.1/1-936	gb ACN89722.1/1-1175 PA
gb ALK80251.1/1-1037 gb AMW00843 1/1-1013 PR - SV R	- gb AZS64230.1/1-929 - R - R S R	- gh ATT 40403 1/1-031- R	- R.S R - gb ARK08051.1/1-912 H	R - SV S - gb ANZ78835.1/1-1147 R - RS R -
gb ALJ54502.1/1-1037 PR - SV R	- gb AGO98873.1/1-911 - R - R S R	- gblAAX84791.1/1-93 - R	- R.S R - gb AIL49526.1/1-936	R - R S R - 1 gb/ACN89763.1/1-1175 - R - R A R -
gb APB87325.1/1-1027 PR SV	- gb ATR18399.1/1-893 GR - K A L gb ABP38295.1/1-929 - R - R S R	gb AIL49488.1/1-935	B AIL49543.1/1-936	R - R S R - gb/AQN/8004.1/1-930 - R - R S R -
gb AHL18090.1/1-1036 .PR - SV R	- gb AG098889.1/1-911 R R - E I T T G Y R	_ gb ATP66750.1/1-89	- R S R	R - R S R - gb ANZ78837.1/1-1147 - R - R S R
gb/AKN24812.1/1-1037	- gb ABD18910.1/1-929 - R - R S R	- gb AAX85669.1/1-93K R	- DL N - gb/ALL49531.1/1-936 -	R-RSR- gb AIL49544.1/1-936 - R-RSR-
gb APB87331.1/1-1023 .PR - SV R	- gb/AGO988888.1/1-938 R - E I T T G Y R	- gb AYR18643.1/1-89K	-DLN- gb AIL49518.1/1-936	R - R S R - gb ALX10759.1/1-930 - R - R S R -
gb APB87337.1/1-1013 . PR - SV R	- gb AGO98877.1/1-911 - R - R S R	- gbLAZU96327.1/1-93 - R	-RS	R-RSR- gb/AIV41873.1/1-936 . R.RSR-
gb/gCC20713.1/1-1023 DT NA	- gb/ABG89288.1/1-929 - R - R S R	gb AIX10753.1/1-935	- R S R - gb AU49502.1/1-936	R - R S R - gb QBP84713.1/1-936 SR - RA I -
gb AF011507.1/1-1232 . R . R A	- gb/AGO98876.1/1-911 - R - R S R	gb ANZ78847.1/1-935 - R	- R S R - gb AIL49536.1/1-936	R - R S R - gb AQN78680.1/1-936 - R - R S R -
gb AAB30950.1/1-1232 - R - R A R	- gb AAX38497.1/1-929 - R - R S R	= zb OBG03776.1/1-93;	- R S R - gb AIL49501.1/1-936	R - R S
sp P11225.1/1-1232 - R A R	- gb/QGW57588.1/1-929 - R - R A I - gb/ACT11010.1/1-020 - R - R S R	ref YP_009555241.1/1	- R S R - gb/ARB07433.1/1-930	R - R S R - I gb AOL02453.1/1-936 - R - R S R -
ref YP_009513010.1/1-1 VN - NT F	- gb AGO98886.1/1-911 - R - R S R	- sp QOZME7.1/1-891 R	- KR R - gb AIL49508.1/1-936 -	R - R S R - gblQEG03794.1/1-936 - R - R S R -
gb AGC51116.1/1-994 DP - LT B	-: gb ABD18936.1/1-929 - R - R S R	- gblANZ78841.1/1-935 -	- R S R - gb AIL49542.1/1-936	R - R S R - 1 gb ATN37888.1/1-908 KR - AH R -
gb AAD45229.1/1-1220 . R . R A R	- gb/AGO98872.1/1-991 - R - R S R	gb QEG03803.1/1-93.	- R S R - gb AIL49505.1/1-936	R - R S R - I gb AON78672.1/1-903 - R - R S R -
gb AVV62537.1/1-901 TT-RSS	- gb AXX83351.1/1-935 - R - R S R	_ gb AXX83369.1/1-935	- R S B - gb/ATN39872.1/1-912 -	R - R S R - 1 gb/AIL49503.1/1-936 - R - R S R -
gb ABN10848.1/1-939 SY - SA	gb/AGO98861.1/1-911 - R - R S R	- go ABD/5513.1/1-891 R.R.	- KR R - gb AIL49539.1/1-936	R - R S R - gb AAB27260.2/1-935 - R - R S R -
gb AGF04924.1/1-939 :SY - SA	gb ALG38241.1/1-917 - 8 - R S 8	- gb AAM55464.1/1-73(H	- AR R - gb AAX84792.1/1-936	R - R S R - 1 ph AIL40 500 1/1-036 - R - R A I -
ref YP_001039953.1/1-93(SY - SA	sp[P25194.1/1-918 - R - R S R	- gb AIL49486.1/1-935 - R	- R S R - pb AXX83381.1/1-930	R - R S R - 1 gb AGT17749.1/1-914 RR - AH R -
gb/AG098871.1/1-911 - R S R	gb AHA50776.1/1-911 - R - R S R gb A75642201/1-020 - R - R S R	- dbj BAS18856.1/1-90(- abi 448010151/1-035	- RQ R - gb AIL49516.1/1-936	R - R S R - gb/QBG03814.1/1-936 - R S R -
gb AV11 5053.1/1-929	dbj BAF75631.1/1-918 - R - R S R	- gblAXX83309.1/1-935	- R S R - gb AIV41831.1/1-936	emb CAA79896.1/1-935 R - RS R
gb ANA96039.1/1-933 sb ABN108661/1-930 :SY - SA	ref\WP_148724042.1/1	- gb AZS52618.1/1-891 R	-KRR- gb/AIL49509.1/1-936	R - R S R - 1 all 49511.1/1-930 - R - R S R
gb QAY30020.1/1-738 - B - R S R	emb CCE89338.1/1-929- R - R S R gb AZS64232.1/1-906 - R - R S R	gb ABD75505.1/1-891 R.R.	- KR R - BOARDAN	R - R S R - gb ARB07414.1/1-936 - R - R S R -
gb AVII 5052.1/1-929 - R - R S R	emb CCE89339.1/1-92 - R - R S R	gb AIL49485.1/1-935	-DLN- gb/AIL49509.1/1-936	R - R S R - gb AIX10762.1/1-1110 - R - R S R -
pdb/5X59/A/1-984 'PR - SV S	. gb AZS64231.1/1-929 - R - R S R	- dbj\BAJ52885.1/1-90(-RO	R - K S
gb ABD18916.1/1-929 - R - R S R	gb/AZS64224.1/1-929 - R - R S R	gb AIX10756.1/1-935 - R	- R S R - sp Q8JSP8.1/1-899 -	R - R S R - gb/AHA83608.1/1-730 HB - A R R
gb/ABD18908.1/1-929 - R - R S R	gb ACF21936.1/1-911 - R - R S R	sp Q14EB0.1/1-883 R	KR. gb/ARKD8635.1/1-936	R-RS B- gb AWB14621.1/1-916 HR-ARR-
gb ABD18917.1/1-929 - R - R S R	- emblCCE89340.1/1-92 - R - R S R	dbj BAS18866.1/1-906 _ R	- RQ R - sp Q8BB25.1/1-1133	R-RSR- gb/444870631/1-919 HR-ARR-
gb AAX38492.1/1-929 - R - R S R	· sp P25191.1/1-929 - R - R S R	gblAA067205.1/1-906	- RA I - go ALAY 529.1/1-930	R - R S R - sp Q91KD1.1/1-919 - R - R S R -
gb/AFE48827.1/1-911 - R - R S R	- emb CAA83661.1/1-91 - R - R S R - eb AMI04717.1/1-020 - R - S R R	gb AGT17758.1/1-883 R	-KR	gb AIX10763.1/1-1110 - R - R S R -
gb/ACG75895.1/1-929 - R - R S R	gb ATP66744.1/1-907: AK - RA T	gb ABD75545.1/1-883 R	- KR R - gb AAF69344.1/1-914	R - R S R - gb ANZ / 8843.1/1-930 - R - R S R
gb/ACB30200.1/1-929 - R.S R.S R.S	gb ANJ04728.1/1-929 - R - S R R	- gblAAT84362.1/1-931	- KR R - g0/AAX84/93.1/1-930 - pc - gb/AVR40342.1/1-936	R - R S R - gb/ARC95227.1/1-901 AH - R A R -
gb/AMQ23493.1/1-911 - R - R S R	2b)OGW57586.1/1-92 - R - R S R	gb AIL49494.1/1-935	-RS	gb ADI59790.1/1-898 SS-RRK-
gb AV11 5000.1/1-911 - R - R S R	sp F15777.1/1-929 - R - R S R	- gb AIX10748.1/1-931 - R	- R S R - golAN2/8830.1/1-930 -	R - R S R - gb ARU07577.1/1-728 - H - R A R -
gb/ADP21335.1/1-929 - R - R S R	sp[P25190.1/1-929 - R - SV R chl 47P66773 1/1-803 A P PY	- gblAIL49496.1/1-935	- RA I - abj BBA20970.1/1-114/ pg abj ANZ78839.1/1-1110	R. R.S
gb ADP21336.1/1-929 - R - R S R	dbj BAE96086.1/1-924 - R - R S R	_ gb ASB17086.1/1-737 R	gb QBP84731.1/1-936	R-RS
gb/ABD18930.1/1-929 - B - R S R	gb QGW57589.1/1-92 - R - R S R	- dbj BAN18703.1/1-900 - R	- RQ R - gb APU51936.1/1-912 -	R - R S R - dbj BAKI 8575.1/1-898 S S - K K K -
gb ACJ35486.1/1-1101 - R - R S R	gb ACL12990.1/1-929 - R - R S R	- gb AYR18670.1/1-893 v	- KR gD AQN/8/08.1/1-930 -	2 - R S R - gb/ADD/3009.1/1-728 HR - AR R -
gb/ABD18913.1/1-929 - R - R S R	gb ACB30201.1/1-929 - R - R S R	- sp P36334.1/1-931	- R S gb AYC76638.1/1-936 -	RA H. ref YP_003029848.1/1-05 S - RR K
gb AGO98883.1/1-911 - R - R S R	. dbj BAJ04696.1/1-732 AR - RA R	- gb AIL49490.1/1-935	- R S R - gb AAR92026.1/1-914 -	R - R S R . gb AGT17777.1/1-728
gb[ABP73030.1/1-911 - R - R S R gb[ABP38313.1/1-929 - R - R S R	gb/ATP66756.1/1-112:K R - R A L	- gb QEY10649.1/1-878	- RA I - gb AEN19366.1/1-936 -	gb/ARU07577.1/1-728 - H - R.A R -
gb ABD18914.1/1-929 - R - R S R	gb ABG78748.1/1-929 - R - R S R	- dbj\BBA20982.1/1-935	- R S R - gblAIL49512.1/1-1147 -	R-RSR. gb/AFD97607.1/1-898 KR-DLN-
gb AAX38491.1/1-929 - K - R S K	emb CAA83000.1/1-94 - R - R S R gh ACL03318.1/1-011 - P - R S R	- gb ARC95219.1/1-109.R.R.		R-ARR. ref YP_009/13025.1/1-155-KKK-
gb/ACJ66977.1/1-929 - R - R S R	dbj BAG48179.1/1-931 - R - R S R	- gb ARC95211.1/1-113	- R S gb AAA87062.1/1-733 -	dbj BAK18575.1/1-898 SS-RRK-
gb AAX38489.1/1-929 - R - R S R	gblABD18932.1/1-929 - R - R S R	- gb AGT51630.1/1-114	- R.S	R - R S R . gb/ABD75609.1/1-728 : S S - R R K -
gb AFB48817.1/1-911 - R - KA 1 - gb ABP38253.1/1-929 - R - R S R	zb ACN89743.1/1-733 R R - AR R	- gb ARC95203.1/1-112. - gb AAC59467.1/1-000 R.R.	gb AQN78744.1/1-1148	R-RSR. gb/ADN03339.1/1-728 HB - AR R -
gb AAX38494.1/1-929 - R S R	gb ABD18935.1/1-917 - R - R S R	- gb AGT51501.1/1-936 R.R.	BS	gblAGT17777.1/1-728 SS-RRK
pao(3W9H(A/1-979 PA - SV G pb)AGO98859.1/1-929	golAQ120498.1/1-911 - R - R S R gblACL03310.1/1-911 - P S	gb AAY68297.1/1-113.	- SF T - ph 4N 104074 1/1-020	B-RS
gblQBG67078.1/1-929 - R - R S R	gb AGT51541.1/1-110 - R - R S R	- 20/AGT51700.1/1-930	- R S R - gb AGO98860.1/1-911 -	R - R S R - dbj BAA23719.1/1-888 R R -
g0 ABD18934.1/1-929 - R - R S R phACT10983.1/1-1101 - R S R	- sp P25193.2/1-929 - R - R S R	gb AGT51600.1/1-114	- K S ref NP_150077.1/1-929 -	gb AAR92027.1/1-1161: SS - RR K
gb ACJ66990.1/1-929 - B - R S R	gb ABD18933.1/1-897 - R - R S R	gb AGT51441.1/1-936	- R S R - gb/ABP38243.1/1-929 -	R - R S R - gb ABD75529.1/1-728 : S S - R R K -
gb ABP38236.1/1-929 - R - R S R	gb ATP16757.1/1-110: - R - R S R	- gblAGT51650.1/1-936 - R	- R A V - gb AM023500.1/1-911 -	R-RSR- gb/AGW27836.1/1-728
gb ACJ66946.1/1-929 - R - R S R	gb ALX10752.1/1-1103 - R - R S R gb ACT51431.1/1-110 - R - R S R	gb AGT51760.1/1-936	- RS R - gb ABD18915.1/1-929 -	R-RSR- gb ABD75497.1/1-728 -H-RAR-
gb ASU90450.1/1-641 PR - SV R	gb AGT51402.1/1-110 R - R S R	gb AGT51620.1/1-936	- R S R	R - K S R - gb AAF69334.1/1-911 S S - RR K -
201AV201119.1/1-929 - R S R 201AF25499.1/1-929 - R S R	gb AGT51610.1/1-110 R - R S R	gb AGT31511.1/1-936 - R	- R S R - gb/ACF21935.1/1-929	R - R S R - gb/ABD75593.1/1-728 SS - RR K -
sp P25192.1/1-929 - R - R S R	gb ACL93320.1/1-911 - R - R S R	gb ANZ78845.1/1-114 - R	- R S R - gb AFE48805.1/1-911 -	R - R A I - gb AGW27872.1/1-728 S - R R R
gb QGW37585.1/1-929 - R - R S R sp Q9Q4Q81/1-929 - P S R	gb ABM66810.1/1-929 - R - R S R	- gb ARA15421.1/1-912 - R	- K S ref YP_005454245.1/1-91 -	R - K A I - dbj BBA20983.1/1-728 - B - K A V -
gb/ABP38306.1/1-929 - R - R S R	golAGT51451.1/1-110 R - R S R gblAGT51740.1/1-110 B - B -	gb AIL49497.1/1-936 - R	- R S R - gblAGO98878.1/1-911 -	R - R S R - gb/ABD75553.1/1-728 SS - RR K -
gb AAX38495.1/1-929 - R - R S R	gb AGT51461.1/1-110	gb AEN19358.1/1-936 - R	- R S gb AGO98864.1/1-900 -	R - R S R - gb AMN88694.1/1-728 S S - RR K -
gb/AZS64223.1/1-929 - R S R	gb/ATT09449.1/1-1131 - R - R S R	- gb ATP66733.1/1-948 T	- R S	R - R S R - gb[AAR92028.1/1-116] - M - K A H - ph R S R
gblQBG67079.1/1-929 - R - R S R	gb/AVR18661.1/1-894. K	- gb AGT51481.1/1-114 - R	- R S R - gb/ABD18931.1/1-929	R - R S R - gb/AMW90836.1/1-842 PR - SV R -
gb QEY10673.1/1-929 - R - R S R gb AM(023489.1/1-911 - R - R S R	gb AHN64774.1/1-956	. gb QEY10657.1/1-860 - R	- RA V - gb/ABD18929.1/1-929	R - R S R - gb AAF05704.1/1-906 HR - AR R -
gb/AGO98867.1/1-911 - R - R S R	gb/ALX10749.1/1-1105 - R - R S R	- gb AIX10751.1/1-936 - R	- R S gb AZU96312.1/1-929 -	R - R S R - gb/AGT51491.1/1-936 - R - R S R -
gb/AZS64222.1/1-1101 - E - R S R	gb AHN64783.1/1-112 . R.S	- go ALL49528.1/1-930 - 20 AON78776.1/1-031 -	- R.S R gb/QGY72123.1/1-929	R - R S R - gb/AHI48733.1/1-846 'P R - S V R
gb/ABI93999.2/1-929 - R - R S R	gb ALA50080.1/1-112 . R - R S R	· gb AIL49538.1/1-936 - R	- KA I - gb 0BG67073.1/1-929	R - R S R - gb AAC56567.1/1-898 - H - R A R -
gb AGO98885.1/1-911 - R - R S R	gb/AGT51412.1/1-110	gb AGT51790.1/1-936 -	AH gb AMQ23490.1/1-911	R - R S R - gb/AGZ48795.1/1-243
g0/ALS04221.1/1-929 - R S R gb/AV115011.1/1-929 - R S R	gb QDH43726.1/1-93; SR - RA I	sp/F11224.2/1-914 R	- AH R - gb AMQ23487.1/1-911	B R S B gb AGZ48785.1/1-243
gb AVZ61109.1/1-929 - R - R S R	gb/AVQ05264.1/1-935.SR - RA I	gb ANZ78849.1/1-114 - R	- R S	R-RSR- gb AGZ48787.1/1-243
g0 AGO98881.1/1-911 - R - R S R gb ABD18928.1/1-929 - R - R S R	gb AIX10755.1/1-110: - R.S R	gb ACN89723.1/1-116 R	- R S R - gb AGO98865.1/1-911 -	R - R S R -
		26/ANZ78834.1/1-114 -	- R S B - gb AXP11698.1/1-929	R - R S R -
			SUAL038240.1/1-917	

Figure S2. Multiple sequence alignment of 1000 Spike proteins(487-1000). Related to Figure 1.



Figure S3. Result of furin cleavage site pridiction of Spike protein in SARS-CoV-2, which predicted by online method ProP 1.0 Server. Related to Table 1.



Fig S4 Protein-protein docking calculation model of SARS-CoV-2 spike RBD (light blue) with human ACE2 (yellow), original RBD conformation was shown in orange. The calculated free energy is -50.13 Kcal/mol. Related to Figure 3.



Fig S5 Comparison of SARS-CoV-2 spike RBD (orange) and SARS spike RBD (yellow). The complex with ACE2 (left part, yellow) was shown. The homology model of SARS-CoV-2 spike RBD built from SARS spike RBD was shown as blue. Related to Figure 3.



Figure S6. Expression levels of Furin, ACE2 and TMPRSS2 in various tissues. The data is from pubmed. Related to Figure 2B.

No.	Drug Name	Structure	Pharmacological
			functions
1	Aminopterin	$NH_2 \qquad \qquad$	Anti-tumor
2	Folic acid		Vitamin B9, necessary material for the growth and reproduction of body cells
3	Sulfoxone	HN OF OF	Antibacterial effect
4	Silybin		Hepatoprotective effect
5	Diminazene	H ₂ N NH NH H ₂ N N ² N NH ₂ N ² N NH ₂	Insecticidal effect
6	Fludarabine phosphate		Anti-tumor
7	L-Arginine	H ₂ N H O H ₂ N H O H H	Nutritional supplement
8	Hydroxystilbamidin e		Antifungal effect
9	Methotrexate	$H_2N \xrightarrow{NH_2} N \xrightarrow{H_2} N \xrightarrow{H_2} O \xrightarrow{H_1} O \xrightarrow{H_2} O H_$	Antineoplastic, antirheumatic effects

Table S1Potential furin inhibitors from ZINC drug database, related to Figure 4

10	L dopa	HO O OH	Treatment of
10	L-dopa	H ₂ N OH	Parkinson's disease
11	lrinotecan		Anti-tumor
12	Cefoperazone		Antibacterial effect
13	Folinic acid		Folic acid supplement
	Glycerol	<u>ОН</u> О с <u>т</u> с с	Intermediate for
14	3-phosphate	HO POH	serine synthesis
15	Valganciclovir	$ \begin{array}{c} $	Antivirus
16	Fosaprepitant		Treatment of nausea and vomiting induced by chemotherapy
17	Lomefloxacin	OH O	Antibacterial effect
18	Glutathione		Hepatoprotective effect
19	Famotidine	$H_{2N} \xrightarrow{NH_{2}} N \xrightarrow{NH_{2}}$	Treatment of gastrohelcosis
20	Imatinib		Anti-tumor
21	Chenodeoxycholic acid		Dissolving gallstones

No.	Drug Name	Structure	Pharmacological functions	Source
1	(-)-Epigallocatechin gallate		Antioxidation, anti-tumor, treatment of depression	Camellia sinensis
2	Theaflavin 3,3'-di- <i>O</i> -gallate	$HO \xrightarrow{OH} (H) (H) \xrightarrow{OH} (H) \xrightarrow{OH} (H) (H) (H) (H) (H) (H) (H) (H) (H) (H)$	Antioxidant effect, anti-tumor, anti-virus	Camellia sinensis
3	Biorobin	HO + O + O + O + O + O + O + O + O + O +	Anti-virus	Ficus benjamina
4	14-deoxy-11,12- didehydroandrographiside	HO" Y', OH OH OH	Anti-virus, anti-inflammato ry effect	Andrographis paniculata
5	(1 <i>S</i> ,2 <i>R</i> ,4a <i>S</i> ,5 <i>R</i> ,8a <i>S</i>)-1-formam ido-1,4a-dimethyl-6- methylene-5-((<i>E</i>)-2-(2-oxo-2, 5- dihydrofuran- 3-yl)ethenyl) decahydronaphthalen-2-yl 5-((<i>R</i>)-1,2-dithiolan-3-yl) pentanoate	$ \begin{array}{c} & & & \\ & & & \\ & & \\ & \\ & \\ & \\ & \\ $	Anti-virus, anti-inflammato ry effect	Andrographoli de derivatives
6	28,308-dihydroxy-3,4-seco-fr iedelolactone-27-lactone		Anti-virus	Viola diffusa

Table S2 Potential furin inhibitors from in-house natural product database, related to Figure 5

7	Phyllaemblicin G7	$HO_{HO} \xrightarrow{HO}_{HO} \xrightarrow$	Anti-virus	Phyllanthus emblica
8	Andrographolide	HO' GH2OH	Anti-virus, anti-inflammato ry effect	Andrographis paniculata
9	14-deoxy-11,12- didehydroandrographolide	HO" CH ₂ OH	Anti-virus, anti-inflammato ry effect	Andrographis paniculata
10	(1 <i>S</i> ,2 <i>R</i> ,4a <i>S</i> ,5 <i>R</i> ,8a <i>S</i>)-1-formam ido-1,4a-dimethyl-6-methyle ne-5-((<i>E</i>)-2-(2-oxo-2,5- dihydrofuran-3-yl)ethenyl) decahydronaphthalen-2-yl 2-aminoacetate		Anti-virus, anti-inflammato ry effect	Andrographoli de derivatives
11	2-[[2-O-(6-deoxy-α-L-manno pyranosyl)-β-D-xylopyranosyl]oxy]-1,8-dihydroxy-6-ethoxy -9 <i>H</i> -xanthen-9-one		Anti-virus, anti-inflammato ry effect	Swertia kouitchensis
12	Kouitchenside J		Anti-virus, anti-inflammato ry effect	Swertia kouitchensis
13	Stigmast-5-en-3-ol	HO	Antioxidant effect	Spatholobus suberectus dunn
14	Kouitchenside F		Anti-virus, anti-inflammato ry effect	Swertia kouitchensis

Table S3

Potential furi	n inhihitors from	the commor	antiviral c	drugs database	related to	h Figure 6
Potentiarium			i antivilai t	ulugs ualabase	, relateu ti	Jigule o

No	Drug Name	Structure	Pharmacological
NO.	Drug Name	Structure	functions
1	Suramin		DNA topoisomerase
_	Carannin	HO'S I VO	ll inhibitor
			Human
2	Indinavir		immunodeficiency
2	mamavii		virus Protease (HIV
			PR), anti-malaria
			Hepatitis C virus
2	Pocoprovir		Serine protease
5	Boceprevii		NS3/4A (HCV
			NS3/4A) Modulator
		H ₂ N	HIV-1, HBV
4	Tenofovir		nucleotide reverse
-	alafenamide	O ^{-P} O	transcriptase
			inhibitor
5	Tenofovir		HIV, HBV nucleotide
5	disoproxil		reverse transcriptase
		$ \begin{array}{c} N \\ H_2 N \end{array} \\ \end{array} $	inhibitor
	Acycloguanosine	$\begin{array}{c} O & O \\ HO - P - O - P - O - P - O \\ \end{array}$	Thymidine kinase of
6	triphosphate		herpesvirus

			Hepatitis C virus
7	Telanrevir		Serine protease
	relapievii		NS3/4A (HCV
		∕ o ⊥	NS3/4A) Modulator
		_	Human
Q	Dolutogravir		immunodeficiency
0	Dolutegravii	F F O OH O	virus Integrase (HIV
			IN)
		F_F	1.C-C chemokine
	Maraviroc		receptor type 5
9		ONHN	(CCR5)
		Ň,	2.CCR5 messenger
		∨ \/ // \ N−N	RNA(CCR5 mRNA)
		$\langle \rangle$	Inhibitor of
10	Cobicistat		cytochrome P450 3A
			(CYP3A) enzymes
			Nucleoside analogue
	Stavudino	o _≫ H _≫ o	reverse transcriptase
11	triphocobato		inhibitor used in the
	tripnosphate	HO-Y-O-Y-O-Y-O' \= OH OH OH	treatment of HIV
			infection

Compounds name	In vitro furin protease inhibition percentage at	IC50 (μM)
	100µM(%)	
Aminopterin	72	>30
Folic acid	<30	>30
Sulfoxone	<30	>30
Silybin	74	>30
Diminazene	95	5.42 ±0.11
Fludarabine phosphate	<30	>30
L-Arginine	<30	>30
Hydroxystilbamidine	<30	>30
Methotrexate	73	>30
L-dopa	<30	>30
Irinotecan	<30	>30
Cefoperazone	<30	>30
Folinic acid	44	>30
Glycerol 3-phosphate	<30	>30
Valganciclovir	<30	>30
Fosaprepitant	<30	>30
Lomefloxacin	40	>30
Glutathione	<30	>30
Famotidine	<30	>30
Imatinib	58	>30
Chenodeoxycholic acid	<30	>30
Suramin	<30	>30
Indinavir	<30	>30
Boceprevir	<30	>30
Tenofovir alafenamide	<30	>30
Tenofovir disoproxil	38	>30
Acycloguanosine		
triphosphate	<30	>30
Telaprevir	<30	>30
Dolutegravir	<30	>30
Maraviroc	<30	>30
Cobicistat	<30	>30
Stavudine triphosphate	<30	>30
(-)-Epigallocatechin gallate		
	<30	>30

Table S4. In vitro furin inhibitory effects of screening hits. Related to Figure 7.

Theaflavin 3 3'-di-O-gallate	<30	>30
Biorobin	<30	>30
14-deoxy-11,12- didabydroandrographicida	<20	\20
Phyllaemblicin G7	<30	>30 >30
Andrographolide	<30	>30
14-deoxy-11,12- didehydroandro grapholide	<30	>30
Kouitchenside J	<30	>30
Stigmast-5-en-3-ol	<30	>30
Kouitchenside F	<30	>30