

## Supporting Information for

### Original Article

# D3Targets-2019-nCoV: a webserver for predicting drug targets and for multi-target and multi-site based virtual screening against COVID-19

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Received 1 March 2020; received in revised form 23 March 2020; accepted 25 March 2020

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**Table S1.** The coming or ongoing clinical studies against the SARS-CoV-2 from Chinese Clinical Trial Registry<sup>a</sup>.

No.	Registration number	Date of Registration	Intervention
1.	ChiCTR2000030333	2020-02-28	Conventional standard treatment + Pirfenidone
2.	ChiCTR2000030329	2020-02-28	Umbilical cord blood CIK cells; Umbilical cord blood NK cells
3.	ChiCTR2000030314	2020-02-28	Traditional Chinese medicine Ma-Xing-Shi-Gan-Tang and Sheng-Jiang-San
4.	ChiCTR2000030312	2020-02-28	Anti-SARS-CoV-2 virus inactivated plasma
5.	ChiCTR2000030300	2020-02-28	Mesenchymal stem cells therapy
6.	ChiCTR2000030288	2020-02-27	TCM formula and general treatment based on "Diagnosis and Treatment Program for COVID-19" (trial version 6th)
7.	ChiCTR2000030265	2020-02-26	oXiris CRRT treatment
8.	ChiCTR2000030261	2020-02-26	Aerosol inhalation of exosomes
9.	ChiCTR2000030260	2020-02-26	Enteral nutrition emulsion, tpf-t
10.	ChiCTR2000030259	2020-02-26	Danorevir sodium tablets/ritonavir
11.	ChiCTR2000030255	2020-02-26	Jing-Yin Granule
12.	ChiCTR2000030254	2020-02-26	Farpiravir tablets; Abidole tablets
13.	ChiCTR2000030224	2020-02-26	Injecting Mesenchymal stem cells
14.	ChiCTR2000030215	2020-02-25	Routine treatment + Kanguan No. 1; Routine treatment + Kanguan No. 2; Routine treatment + Kanguan No. 3
15.	ChiCTR2000030196	2020-02-25	Conventional therapy + tocilizumab
16.	ChiCTR2000030187	2020-02-24	Lopinavir and Ritonavir Tablets
17.	ChiCTR2000030179	2020-02-24	Routine treatment + plasma treatment
18.	ChiCTR2000030173	2020-02-24	Umbilical cord mesenchymal stem cells
19.	ChiCTR2000030170	2020-02-24	Routine standard therapy + Jacketinib hydrochloride tablets
20.	ChiCTR2000030165	2020-02-24	Conventional treatment and ozonated autohemotherapy
21.	ChiCTR2000030117	2020-02-23	Xiyanping injection + conventional treatment; Lopinavir /Ritonavir tablets, alpha-interferon
22.	ChiCTR2000030116	2020-02-23	Different stem cell doses
23.	ChiCTR2000030113	2020-02-23	Keep ritonavir/ritonavir treatment; Favipiravir
24.	ChiCTR2000030089	2020-02-22	Conventional treatment and adalimumab
25.	ChiCTR2000030088	2020-02-22	Iv injection of Wharton's Jelly mesenchymal stem cells
26.	ChiCTR2000030082	2020-02-22	Dihydroartemisinin piperazine tablets combined with antiviral treatment
27.	ChiCTR2000030058	2020-02-22	Oral leflunomide
28.	ChiCTR2000030054	2020-02-22	Hydroxychloroquine sulfate; chloroquine phosphate
29.	ChiCTR2000030046	2020-02-21	Anti-2019-nCoV virus inactivated plasma
30.	ChiCTR2000030043	2020-02-21	Conventional treatment and Shenfu injection
31.	ChiCTR2000030041	2020-02-21	FNC
32.	ChiCTR2000030039	2020-02-21	Conventional therapy with Infusion of convalescent

			plasma
33.	ChiCTR2000030034	2020-02-21	TCM + Routine treatment of Western Medicine
34.	ChiCTR2000030033	2020-02-21	Oral antiviral oral solution (Xiangxue Pharmaceutical); Oral "Wu-Zhi-Fang-Guan-Fang" decoction
35.	ChiCTR2000030029	2020-02-21	Suramin (IV.)
36.	ChiCTR2000030027	2020-02-20	Western medicine routine treatment plan plus TCM syndrome differentiation treatment
37.	ChiCTR2000030020	2020-02-20	Mesenchymal stem cells therapy
38.	ChiCTR2000030010	2020-02-19	Anti-SARS-CoV-2 virus inactivated plasma
39.	ChiCTR2000030003	2020-02-19	Traditional Chinese Medicine prescription No. 1 and 2; Gankeshuangqing capsule; Shuanghuanglian oral liquid
40.	ChiCTR2000030002	2020-02-19	Conventional therapy and Tranilast
41.	ChiCTR2000030001	2020-02-19	Basic treatment combined Triazavirin
42.	ChiCTR2000030000	2020-02-19	Ganovo/ritonavir oral; Pegasys injection; Novaferon intramuscular injection + Spray inhalation; Coriolus oral
43.	ChiCTR2000029990	2020-02-18	Mesenchymal stem cells
44.	ChiCTR2000029989	2020-02-18	Recombinant Human Interferon $\alpha$ 1b Eye Drops
45.	ChiCTR2000029988	2020-02-18	Chloroquine Phosphate
46.	ChiCTR2000029974	2020-02-18	Atic treatment medicines
47.	ChiCTR2000029972	2020-02-17	Ultra short wave Electrotherapy
48.	ChiCTR2000029956	2020-02-17	Health Guidance + Guixi Regulating Lung Gong Method + Shenling Baizhu Powder + Moxibustion Treatment
49.	ChiCTR2000029947	2020-02-16	Traditional Chinese medicine compound granules + western medicine symptomatic treatment
50.	ChiCTR2000029939	2020-02-16	Conventional treatment combined with Chloroquine Phosphate.
51.	ChiCTR2000029935	2020-02-16	Treated with conventional treatment combined with Chloroquine Phosphate
52.	ChiCTR2000029895	2020-02-16	Routine treatment + GD31
53.	ChiCTR2000029868	2020-02-15	Oral hydroxychloroquine sulfate tablets
54.	ChiCTR2000029855	2020-02-15	Traditional Chinese medicine clear lung prescription and compound houttuynia mixture treatment
55.	ChiCTR2000029853	2020-02-15	Oral Azvudine tablets
56.	ChiCTR2000029851	2020-02-15	Conventional therapy and ALA
57.	ChiCTR2000029850	2020-02-15	Standardized comprehensive treatment combined with convalescent plasma treatment
58.	ChiCTR2000029849	2020-02-15	Regulating intestinal flora + conventional treatment
59.	ChiCTR2000029822	2020-02-14	Honeysuckle decoction
60.	ChiCTR2000029819	2020-02-14	Conventional treatment + take Ba-Bao-Dan
61.	ChiCTR2000029818	2020-02-14	Conventional treatment followed by Intravenous infusion of Umbilical Cord Blood Plasma preparations
62.	ChiCTR2000029817	2020-02-14	NK cells and mesenchymal stem
63.	ChiCTR2000029816	2020-02-14	Conventional treatment followed by Intravenous infusion of Cord Blood Mesenchymal Stem Cells preparations

64.	ChiCTR2000029814	2020-02-14	Integrated Traditional Chinese and Western Medicine
65.	ChiCTR2000029813	2020-02-14	Conventional Treatment & Tanreqing Capsules
66.	ChiCTR2000029812	2020-02-14	Conventional treatment followed by Intravenous infusion of Umbilical Cord Blood Mononuclear Cells preparations
67.	ChiCTR2000029811	2020-02-14	Conventional treatment + Anti-aging Active Freeze-dried Powder Granules
68.	ChiCTR2000029806	2020-02-14	Thymosin for injection; Camrelizumab
69.	ChiCTR2000029803	2020-02-14	Hydroxychloroquine; Abidol hydrochloride
70.	ChiCTR2000029790	2020-02-13	Western medicine basic treatment combined with traditional Chinese medicine
71.	ChiCTR2000029789	2020-02-13	TCM based on symptomatic treatment
72.	ChiCTR2000029788	2020-02-13	Western medicine routine treatment plan plus TCM syndrome differentiation treatment
73.	ChiCTR2000029781	2020-02-13	Routine treatment and Kangbingdu granules
74.	ChiCTR2000029780	2020-02-13	Routine treatment and Shenqi Fuzheng Injection
75.	ChiCTR2000029778	2020-02-13	Herbal medicine and conventional treatment; QFPD seccion and conventional treatment; SFJD capsuale and conventional treatment
76.	ChiCTR2000029777	2020-02-13	Truncation and Torsion Formula and Routine treatment of Western Medicine
77.	ChiCTR2000029776	2020-02-13	Polyinosinic-Polycytidylic Acid Injection and conventional therapy
78.	ChiCTR2000029769	2020-02-13	Routine treatment + Babaodan capsule
79.	ChiCTR2000029768	2020-02-13	Diammonium Glycyrrhizinate Enteric-coated Capsules, Vitamin C tablets and clinical standard antiviral treatment
80.	ChiCTR2000029765	2020-02-13	Conventional therapy + tocilizumab
81.	ChiCTR2000029763	2020-02-12	TCM and general treatment
82.	ChiCTR2000029761	2020-02-12	Hydroxychloroquine and conventional therapy
83.	ChiCTR2000029757	2020-02-12	Conventional treatment and convalescent plasma therapy
84.	ChiCTR2000029756	2020-02-12	Xiyanping injection; alpha-interferon
85.	ChiCTR2000029747	2020-02-11	Traditional Chinese Medicine
86.	ChiCTR2000029742	2020-02-11	Normal Treatment plus Sodium Aescinate for Injection; Normal treatment plus hormonotherapy
87.	ChiCTR2000029741	2020-02-11	Chloroquine Phosphate; Lopinavir/Ritonavir
88.	ChiCTR2000029739	2020-02-11	Hydrogen-Oxygen Nebulizer
89.	ChiCTR2000029656	2020-02-09	Standard treatment and methylprednisolone for injection
90.	ChiCTR2000029639	2020-02-08	Psychological intervention or drug intervention
91.	ChiCTR2000029636	2020-02-08	Conventional standardized treatment and vMIP atomized inhalation
92.	ChiCTR2000029609	2020-02-06	Chloroquine phosphate plus Lopinavir/ritonavir
93.	ChiCTR2000029603	2020-02-06	Conventional standardized treatment and ASC09/Ritonavir; Conventional standardized treatment and Lopinavir/Ritonavir
94.	ChiCTR2000029600	2020-02-06	Alpha-Interferon atomization; Lopinavir and Ritonavir +

			alpha-Interferon atomization; Favipiravir + alpha-Interferon atomization
95.	ChiCTR2000029589	2020-02-05	Reduning injection combined with basic western medical therapies
96.	ChiCTR2000029580	2020-02-05	Ruxolitinib combined with mesenchymal stem cell
97.	ChiCTR2000029578	2020-02-05	Integrated Traditional Chinese and Western Medicine
98.	ChiCTR2000029573	2020-02-04	Arbidol Tablets; Novaferon injection + Arbidol Tablets; Lopinavir/litonavir
99.	ChiCTR2000029569	2020-02-04	Conventional treatment combined with umbilical cord mesenchymal stem cell conditioned medium group
100.	ChiCTR2000029559	2020-02-04	Hydroxychloroquine
101.	ChiCTR2000029558	2020-02-04	Chinese medicine treatment combined with western medicine treatment
102.	ChiCTR2000029550	2020-02-04	Compound Yinchai granules, Qingqiao antiviral granules
103.	ChiCTR2000029548	2020-02-04	BaloxavirMarboxil; Favipiravir; Lopinavir-Ritonavir
104.	ChiCTR2000029544	2020-02-03	Baloxavir Marboxil tablets; favipiravir tablets
105.	ChiCTR2000029542	2020-02-03	Chloroquine + conventional management
106.	ChiCTR2000029541	2020-02-03	DRV/c + Conventional treatment containing thymosin; LPV/r + Conventional treatment containing thymosin
107.	ChiCTR2000029539	2020-02-03	Conventional standardized treatment and Lopinavir-Ritonavir
108.	ChiCTR2000029518	2020-02-03	TCM clinical prescription combined with the western medicine treatment
109.	ChiCTR2000029496	2020-02-03	Recombinant cytokine gene-derived protein injection
110.	ChiCTR2000029493	2020-02-02	Traditional Chinese Medicine + basic western medical therapies
111.	ChiCTR2000029487	2020-02-02	Oral Gubiao Jiedu Ling Chinese medicine (Traditional Chinese Medicine)
112.	ChiCTR2000029468	2020-02-02	Lopinavir/litonavir (LPV/r) + emtricitabine (FTC)/ Tenofovir alafenamide Fumarate tablets (TAF) in combination
113.	ChiCTR2000029461	2020-02-02	TCM decoctions + basic conventional therapy
114.	ChiCTR2000029439	2020-02-01	TCM standard decoctions + basic western medical therapies
115.	ChiCTR2000029438	2020-02-01	Conventional medicine + TCM
116.	ChiCTR2000029436	2020-02-01	TCM syndrome differentiation treatment + Western medicine treatment
117.	ChiCTR2000029435	2020-02-01	Traditional Chinese medicine
118.	ChiCTR2000029434	2020-02-01	Lian-Hua Qing-Wen Capsule/Granule (TCM) + Routine treatment
119.	ChiCTR2000029432	2020-02-01	Tanreqing Injection (TCM)
120.	ChiCTR2000029431	2020-02-01	Critical Treatment in Critical Period + Ankylosaurus + M1 (type I macrophage) suppression therapy
121.	ChiCTR2000029418	2020-01-30	Combined Treatment of Chinese medicine and western

			medicine
122.	ChiCTR2000029400	2020-01-29	Traditional Chinese medicine treatment
123.	ChiCTR2000029387	2020-01-28	Ribavirin + Interferon alpha-1b; lopinavir / ritonavir + interferon alpha-1b; Ribavirin + LPV/r + Interferon alpha-1b
124.	ChiCTR2000029386	2020-01-28	Adjunctive Corticosteroid Therapy
125.	ChiCTR2000029381	2020-01-27	Xuebijing Injection (TCM)
126.	ChiCTR2000029308	2020-01-23	Lopinavir-ritonavir tablets + interferon- $\alpha$ 2b

<sup>a</sup>Access to <http://www.chictr.org.cn/enIndex.aspx> on 2020-02-29.

**Table S2.** The biological functions of each protein target against the SARS-CoV-2.

Target full name	Target abbreviation	Function	Ref.
Host translation inhibitor nsp1	Nsp1	Nsp1 can facilitate efficient viral gene expression and evasion from host immune response by suppressing host gene expression.	1, 2
Non-structural protein 2	Nsp2	Nsp2 may be involved in the disruption of intracellular host signaling during viral infections.	3
Papain-like proteinase	PLP/PLpro	PLP is responsible for the cleavage of nsp 1, 2 and 3. And PLP can deubiquitinate or deISGylate host cell proteins, resulting in the immune suppression of host cells.	4, 5
ADP ribose phosphatase	ADRP		
Non-structural protein 4	Nsp4	Nsp4 participates in the assembly of virally-induced cytoplasmic double-membrane vesicles, which is necessary for viral replication.	6
3C-like proteinase	3CLpro/Mpro	3CLpro can cleave the virus-encoded polyproteins, which is important for polyprotein maturation.	7
Non-structural protein 6	Nsp6	Nsp6 can limit autophagosome expansion, which may favor coronavirus infection.	8
Non-structural protein 7	Nsp7	Nsp7 can form a hexadecamer with nsp8 that may participate in viral replication by acting as a primase.	9
Non-structural protein 8	Nsp8	Nsp8 can form a hexadecamer with nsp7 that may participate in viral replication by acting as a primase.	9
Non-structural protein 9	Nsp9	Nsp9 is essential for efficient viral	10

		growth and may participate in viral replication.	
Non-structural protein 10	Nsp10	Nsp10 plays a pivotal role in viral transcription.	11
RNA-dependent RNA polymerase	RdRp	RdRp is responsible for replication and transcription of the viral RNA genome.	12
Helicase	/	Helicase plays a vital role in catalyzing the unwinding of duplex oligonucleotides into single strands in an NTP-dependent manner.	13
Guanine-N7 methyltransferase	N7-MTase	N7-MTase is a bifunctional enzyme able to methylate the viral RNA cap and excise erroneous mutagenic nucleotides.	11,14
Uridylate-specific endoribonuclease	NendoU	NendoU is a Mn <sup>2+</sup> -dependent, uridylate-specific enzyme, which leaves 2'-3'-cyclic phosphates 5' to the cleaved bond.	15
2'-O-methyltransferase	2'-O-Mtase	2'-O-Mtase can mediate mRNA cap 2'-O-ribose methylation to the 5'-cap structure of viral mRNAs which is essential for evasion from host immune response.	16,17
ORF7a protein	/	ORF7a can induce apoptosis via a caspase-dependent pathway.	18
Spike protein	S protein	S protein comprises two functional subunits responsible for binding to the host cell receptor (S1 subunit) and fusion of the viral and cellular membranes (S2 subunit).	19, 20
Spike protein-S2 subunit	S protein-S2 subunit	SARS-CoV-2 S protein-S2 subunit is crucial for mediating virus fusion and entry.	21
Spike protein-heptad repeat 1	S-HR1	SARS-CoV-2 S-HR1 plays an important role of mediating virus fusion and entry.	21
Envelope protein	E protein	E protein plays a central role in virus morphogenesis and assembly, as well as the induction of apoptosis.	22,23
Nucleocapsid phosphoprotein	N protein	N protein plays a fundamental role during virion assembly through its interactions with the viral genome and membrane protein M. Besides, it can enhance the efficiency of subgenomic viral RNA transcription as well as viral replication.	24,25

AP2-associated protein kinase 1	AAK1	AAK1 could promote endocytosis, which is involved in viral entry.	26
C-type lectin domain family 4 member M	CLEC4M	CLEC4M can mediate infection by coronavirus.	27
Cyclophilin A	CypA	Cyclophilin A is required for coronavirus replication.	28
Disintegrin and metalloproteinase domain-containing protein 17	ADAM17	ADAM17 plays a role in the proteolytic processing of ACE2.	29
Tyrosine-protein kinase ABL2	ABL2	ABL2 is required for coronavirus replication.	30
Eukaryotic initiation factor 4A-I	eIF4A	EIF4a is involved in protein translation.	31
Dihydroorotate dehydrogenase	DHODH	DHODH is required for coronavirus replication.	32
Furin	Furin	Furin is responsible for cutting the S protein of SARS-CoV-2, which is involved in viral entry.	33
Angiotensin converting enzyme 2	ACE2	ACE2 is the receptor of S protein of SARS-CoV-2.	34
Cathepsin L	CTSL	CTSL activates coronavirus membrane fusion.	35
Transmembrane protease serine 2	TMPRSS2	TMPRSS2 activation induces virus-cell membrane fusion at the cell surface.	36
Glycogen synthase kinase-3 beta	GSK3 $\beta$	GSK3 $\beta$ regulates the phosphorylation of SARS-CoV nucleocapsid protein and viral replication.	37
Heterogeneous nuclear ribonucleoprotein A1	HNRNPA1	HNRNPA1 can bind to the N protein of SARS-CoV, which may be involved in the regulation of coronavirus RNA synthesis.	38
Calnexin	/	Calnexin strictly monitors the maturation of S protein by its direct binding, resulting in conferring infectivity on SARS-CoV.	39
Caveolin-2	CAV2	CAV2 may be involved in replication and transmission of the virus by acting on cell membranes.	40
Mitogen-activated protein kinase 8	JNK1	Persistent SARS-CoV infection needs JNK and PI3k/Akt signaling pathways.	41
Mitogen-activated protein kinase 9	JNK2	JNK2 is required for persistent viral infection.	41
Mitogen-activated protein kinase 10	JNK3	JNK3 is required for persistent viral infection.	41



kinase 10		infection.	
RAC-alpha serine/threonine-protein kinase	AKT1	Persistent SARS-CoV infection needs JNK and PI3k/Akt signaling pathways.	41
RAC-beta serine/threonine-protein kinase	AKT2	AKT2 is required for persistent viral infection.	41
RAC-gamma serine/threonine-protein kinase	AKT3	AKT3 is required for persistent viral infection.	41
cGMP-specific 3',5'-cyclic phosphodiesterase	PDE5	PDEs is responsible for the degradation of cAMP, which may aggravate the virus-induced pulmonary fibrosis.	42

**Table S3.** Scoring function weights and terms.

Weight	Term
-0.035579	gauss1
-0.005156	gauss2
0.840245	Repulsion
-0.035069	Hydrophobic
-0.587439	Hydrogen bonding
1.923	Number of active rotatable bonds between heavy atoms in the ligand
-0.3	gaussian potential between magnesium and oxygen

The conformation-independent function  $g$  can be described as follows.

$$c_{inter} = weight * term \quad (1)$$

$$g(c_{inter}) = \frac{c_{inter}}{1+wN_{rot}} \quad (2)$$

where  $N_{rot}$  is the number of active rotatable bonds between heavy atoms in the ligand and  $w$  is the associated weight.

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