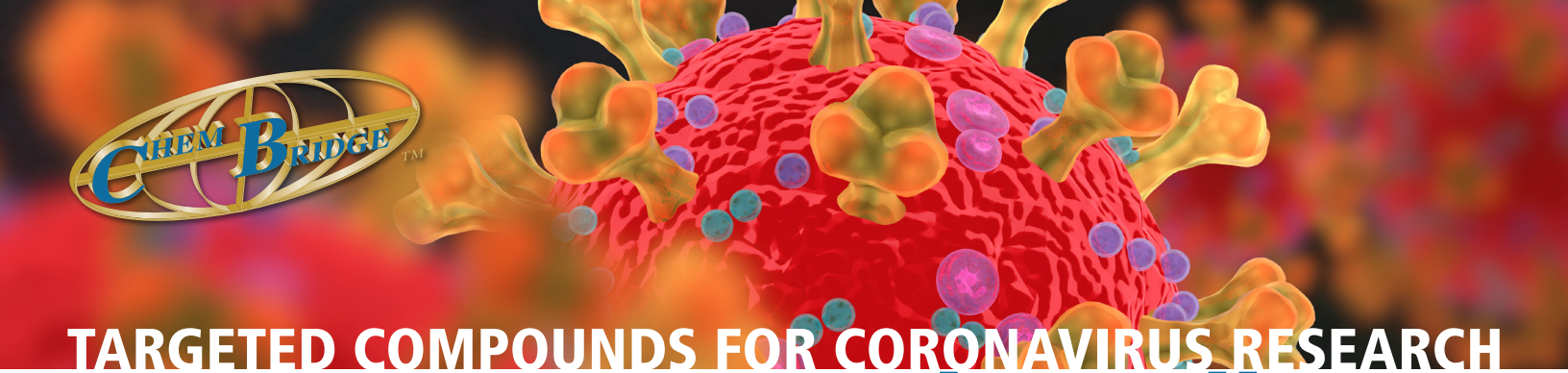


TARGETED COMPOUNDS FOR CORONAVIRUS RESEARCH

Coronavirus Library

Highlights

- Generated in collaboration with a leading academic group
- High quality, PAINS free, lead-like and drug-like, small molecule compounds
- For SARS-CoV-2 and other coronavirus research
- More than 15,000 compounds available covering 17 targets
- Purchase the full library or custom select a subset

Introduction

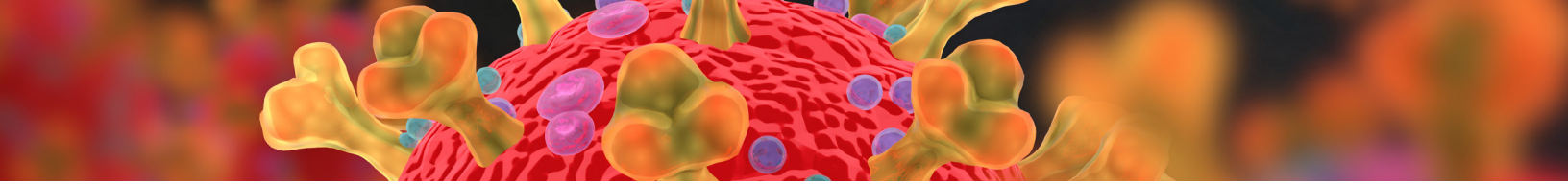
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), previously known as 2019 novel coronavirus (2019-nCoV), has spread rapidly across the globe, creating an unparalleled global health burden and spurring a deepening economic crisis. As of June 2020, more than 6 months into the outbreak, there were no approved vaccines or small-molecule drugs available which were specifically developed for COVID-19. Developing drugs that target multiple points in the viral life cycle could serve as a strategy to tackle the current as well as future coronavirus pandemics.

In August 2020, ChemBridge released the new Coronavirus Library, which offers more than 15,000 compounds with potential to interact with SARS-CoV-2 viral targets or the host target ACE2. Compounds in the Coronavirus Library were selected in collaboration with the Wagner Lab at Harvard using the Virtual Flow methodology developed and published by the Wagner Lab. Details on the Virtual Flow methodology are published in Gorgulla, C., Boeszoermenyi, A., Wang, Z. et al. “An open-source drug discovery platform enables ultra-large virtual screens” Nature 580, 663–668 (2020).

Methodology

ChemBridge’s stock of more than 1.3 million compounds were prepared and docked against each of 40 different target sites on 17 different potential viral and host targets using the Virtual Flow screening platform. Top ranked compounds were further filtered to ensure that the Coronavirus Library included only high quality, lead-like or drug-like compounds free of undesirable chemical functionalities and free of PAINS structural alerts. The compound count per target ranges from 1,000 to 5,000 with 1,000 to 2,000 compounds per site screened.

Structures from ChemBridge stock were prepared with VirtualFlow for Ligand Preparation (VFLP)[1]. For each virtual screen a single target structure was used, and the protein was held rigid. QuickVina-W[2] was used to perform a blind docking procedure for the HR1 domain of the spike protein, the RNA binding interface of the nucleoprotein, the RNA binding site of nsp12, as well as for nsp7 and ORF7a. For all the other site specific docking routines, QuickVina 2[3] was used. Both docking programs are based on AutoDock Vina[4]. The receptor structures were prepared with AutoDockTools[5] from the PDB format to the PDBQT format. The proteins targeted are listed on the on the reverse.



Targets

Protein	Alternname Name(s)	Site(s) Docked
Spike	S-protein	Spike RBD–ACE2 interface, HR1 domain
TMPRSS2	Transmembrane protease serine 2	Active site
ORF7a	Protein 7a	Blind docking
Phosphatase	(macro) X domain	Closed active site, open active site
PLpro	Papain-like protease	Active site, accessory pocket, DUB binding site
Mpro	Main protease	Active site, dimerization site, alpha-helix 5 attachment site
nsp7	Replicase polyprotein 1ab	Blind docking of nsp8 and nsp12 binding interfaces
nsp8	Primase complex	nsp7 binding interface, nsp12 binding interface
nsp9	Replicase	Dimerization interface
nsp10	N/A	nsp14 binding interface, nsp16 binding interface
nsp12	RNA dependent RNA-polymerase	RNA binding interface, nucleotide binding site, nsp8 binding interface, nsp7 binding interface
nsp13	Helicase	RNA binding interface, active site
nsp14	Exoribonuclease or N7 methyltransferase	nsp10 binding interface, ExoN active site, N7-MT active site
nsp15	Endoribonuclease	Active site
nsp16	2′-O methyltransferase	2′-O MT active site, nsp10 binding interface
Nucleoprotein	Ribonucleocapsid protein	NTD RNA binding site, NTD oligomerization site, CTD dimerization interface, CTD oligomerization site
ACE2	Angiotensin-converting enzyme 2	Spike RBD binding region, dynamic pocket 1 near spike RBD, dynamic pocket 2 near spike RBD

Format

- Custom select from more than 15,000 Coronavirus Library compounds or purchase all available compounds.
- The “Target” field in the structure file indicates the potential protein target(s).
- Available in 96-well or 384-well format including acoustic compatible plates.
- Minimum order amount of 1 micromole with amounts as low as 0.25 micromole available for orders of 2,000 or more compounds.
- Compounds are available dry or as DMSO solutions.

For more information or a file of compound structures, please contact sales@chembridge.com

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1. Gorgulla, C., Boeszoermenyi, A., Wang, Z. et al. An open-source drug discovery platform enables ultra-large virtual screens. Nature 580, 663–668 (2020).

2. Protein-Ligand Blind Docking Using QuickVina-W With Inter-Process Spatio-Temporal Integration. Nafisa M. Hassan, Amr A. Alhossary, Yuguang Mu and Chee-Keong Kwoh. Nature Scientific Reports 7(1) (2017). DOI:10.1038/s41598-017-15571-7

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5. Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S. and Olson, A. J. (2009) Autodock4 and AutoDockTools4: automated docking with selective receptor flexiblity. J. Computational Chemistry 2009, 16: 2785-91.

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