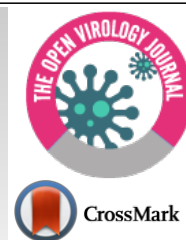




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A Summary of Viral Targets and Recently Released PDB IDs of SARS-CoV-2

Rohit Bhatia^{1,*}, Raj K. Narang¹ and Ravindra K. Rawal²

¹Department of Pharmaceutical Chemistry & Pharmaceutics, ISF College of Pharmacy, Moga, Punjab-142001, India

²Department of Chemistry, Maharishi Markandeshwar (Deemed to be University), Mullana-133207, Haryana, India

Drug discovery and development against coronavirus disease 2019 (COVID-19) is the utmost need and the most challenging task of the hour. Many research groups from different countries are working continuously in this direction, and till 8th March 2020, a total of 382 clinical trials have been registered on the WHO's International Clinical Trials Registry Platform [1]. There is an urgent need to identify specific targets to design promising therapeutic agents against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19. Analysis of SARS-CoV-2 reveals seven major target proteins that can be considered for drug design against the virus. These include the spike, envelope, membrane, nucleocapsid, protease, hemagglutinin esterase and helicase [2, 3]. Beyond these, several Non Structural Proteins (NSPs) can also be evaluated as targets for drug development [4]. There are only a few Protein Data Bank (PDB) IDs available related to SARS-CoV-2 in the RCSB database. Table 1 summarizes recently released PDB IDs (from 5.2.2020 to 25.3.2020) for various SARS-CoV-2 targets [5].

The SARS-CoV-2 genome encodes a relatively large number of proteins [6]. The PL proteinase and the 3CL protease cleave two polyproteins to release different types of NSPs. Hence the proteases represent a relevant target for designing drugs against SARS-CoV-2. The spike (S) protein helps the virus to enter inside the host and also activates the immune response of the host against the virus through the

interaction mediated by its specific segments [7]. Thus, the S protein represents an ideal target for therapeutic drug development. The envelope protein is the smallest protein of SARS-CoV-2 and plays a significant role in morphogenesis of virus particles [8]. It is also reported that the oligomerization of these proteins leads to the formation of specific ion-channels whose role is still unclear. Beyond this, the envelope protein helps in viral assembly and budding, hence its significant as a drug target [9]. Membrane proteins maintain the shape of a viral envelope [10] and also sensitize the host against the virus [11]. These proteins can also be considered as significant targets for drug development. The nucleocapsid proteins have a structure comprising arm, central linker and tail domains [12]. The main function of these proteins is to form ribonucleoprotein complexes. It also regulates replication, transcription of viral RNA and in the host cells, inhibits protein translation leading to disruption in the host cell metabolism [13, 14]. Therefore, targeting this protein can lead to blockbuster therapeutic agents for COVID-19 treatment. Hemagglutinin esterase has been established as a marker for the evolution of SARS-CoV-2 or some influenza infections and has the capacity to act as lectins or receptor destroying enzymes [15]. The Helicase enzyme is also an interesting target, but its inhibitors are associated with some toxicity and specificity issues [16].

COVID-19 pandemic has now become a destructive ailment globally. Therefore the utmost need of the hour is to develop therapeutic candidates or vaccines against it. The targets explained in this summary may be of some aid to design novel molecules by employing drug discovery strategies such as artificial intelligence or CADD tools.

* Address correspondence to this author at the Department of Pharmaceutical Chemistry & Pharmaceutics, ISF College of Pharmacy, Moga, Punjab-142001, India; E-mail: bhatiarohit5678@gmail.com

Table 1. Recently Released Targets in RCSB Database with PDB Ids related to COVID-19 [5].

Target	PDB Ids	Release Date	Web Links
Protease	5RE4, 5RE5, 5RE6, 5RE7, 5RE8, 5RE9, 5REA, 5REB, 5REC, 5RED, 5REE, 5REF, 5REG, 5REH, 5REI, 5REJ, 5REK, 5REL, 5REM, 5REN, 5REO, 5REP, 5RER, 5RES, 5RET, 5REU, 5REV, 5REW, 5REX, 5REY, 5REZ, 5RF0, 5RF1, 5RF2, 5RF3, 5RF4, 5RF5, 5RF6, 5RF7, 5RF8, 5RF9, 5RFA, 5RFB, 5RFC, 5RFD, 5RFE, 5RFF, 5RFG, 5RFH, 5RFI, 5RFJ, 5RFK, 5RFL, 5RFM, 5RFN, 5RFO, 5RFP, 5RFQ, 5RFR, 5RFS, 5RFT, 5RFU, 5RFV, 5RFW, 5RFX, 5RFY, 5RFZ, 5RG0, 6W63	25.03.2020	http://www.rcsb.org/structure/5RE4 (Same link for all, just change the code of ID)
S protein RBD	6M17, 6VW1	11.3.2020, 4.3.2020	https://www.rcsb.org/structure/6M17 , https://www.rcsb.org/structure/6VW1
Spike glycoprotein	6LXT, 6VSB	26.2.2020	https://www.rcsb.org/structure/6LXT , https://www.rcsb.org/structure/6VSB
Non structural polyprotein (NSP)	6LU7, 6M03	5.2.2020, 11.3.2020	https://www.rcsb.org/structure/6LU7 , https://www.rcsb.org/structure/6M03
SARS CoV Protease with unliganded active site	6Y84, 6YB7	11.3.2020, 25.3.2020	https://www.rcsb.org/structure/6Y84 , https://www.rcsb.org/structure/6YB7
COVID-19 protease in complex with Z1367324110	5R7Z, 5R80, 5R81, 5R82, 5R83, 5R84	11.3.2020	https://www.rcsb.org/structure/5R7Z , https://www.rcsb.org/structure/5R81 , https://www.rcsb.org/structure/5R82 , https://www.rcsb.org/structure/5R83 , https://www.rcsb.org/structure/5R84

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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