

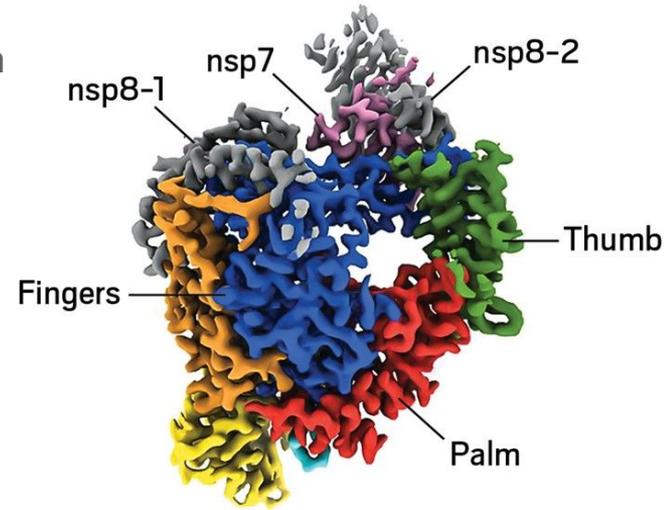
RNA Dependent RNA Polymerase (RdRp) of SARS-CoV-2

Sophia Sunkin

A dark blue diagonal gradient bar that starts from the bottom left corner and extends towards the top right corner, covering the lower half of the slide.

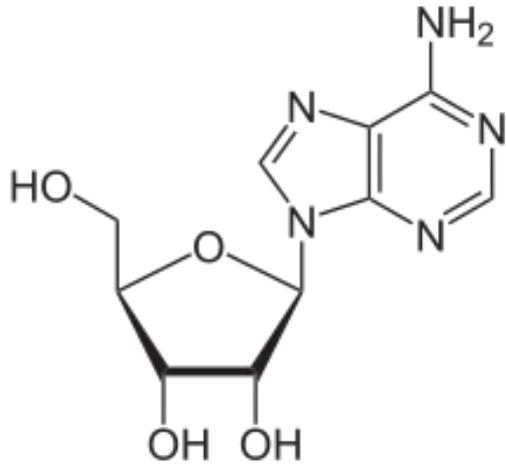
What is RdRp?

- ❑ RdRp (also known as nsp12) is a key part of the SARS-CoV-2 replication machinery, as it catalyzes replication of RNA from an RNA template
 - ❑ RdRp is a nonstructural protein i.e. it does not exist in the viral structure and is encoded in the viral genome solely for replication
 - ❑ Ribosomes produce the proteins for the replication machinery using the instructions encoded in the viral genome
- ❑ RdRp is part of the nsp12-nsp7-nsp8 complex
 - ❑ On its own, nsp12 cannot function and nsp7 and nsp8 are both cofactors
 - ❑ nsp7 and nsp8 both serve to suppress the host genome

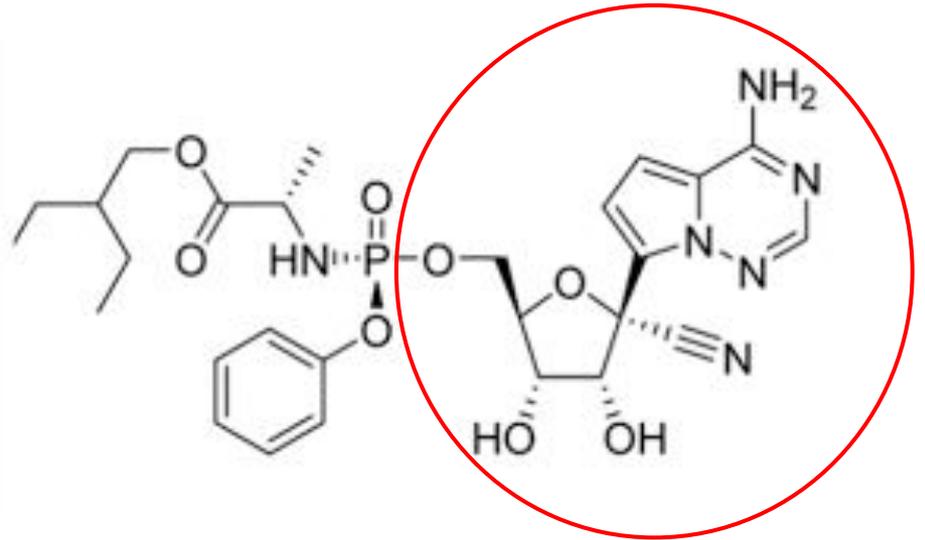


Remdesivir

- ❑ Remdesivir targets the RdRp replication process of the viral genome
- ❑ It strongly resembles the nucleotide adenosine, causing the RNA replicase to incorporate it; this essentially 'caps' the RNA strand being synthesized and replication of viral RNA is prevented
 - ❑ Remdesivir does not interfere with the activity and replication of cells and only inhibits viral replication
 - ❑ However, it is not always entirely effective, as intact viral RNA copies may still be able to escape the cell and infect other cells. If paired with another antiviral drug, treatment could become a lot more effective



Adenosine



Remdesivir

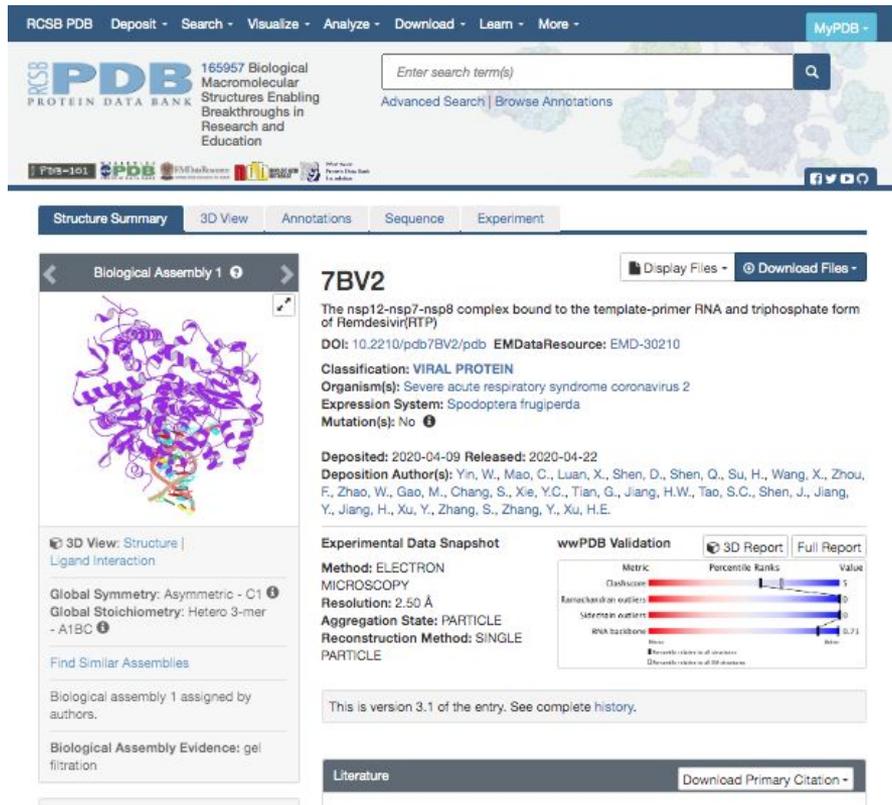
Adenosine and Remdesivir resemblance comparison

Obtaining PDB codes from the Protein Data Bank

The web address for the Protein Data Bank is <https://www.rcsb.org/>.

In order to view proteins on PyMol, you can do one of two things:

1. Find the desired protein in the Protein Data Bank and copy its protein ID. Then, type “fetch” and desired ID into PyMol.
2. Download the PDB file directly from the data bank and open it in PyMol.



The screenshot displays the RCSB PDB website interface. At the top, there is a navigation bar with links for Deposit, Search, Visualize, Analyze, Download, Learn, and More. A search bar is present with the text "Enter search term(s)". Below the search bar, there are tabs for Structure Summary, 3D View, Annotations, Sequence, and Experiment. The main content area shows the entry for 7BV2, which is the nsp12-nsp7-nsp8 complex bound to the template-primer RNA and triphosphate form of Remdesivir(RTP). The entry includes a 3D view of the protein structure, a table of experimental data, and a wwPDB Validation chart. The wwPDB Validation chart shows metrics for Ramachandran outliers, Sites in outliers, and RNA backbone, with values of 0, 0, and 0.71 respectively. The entry is version 3.1, and there is a link to download the primary citation.

RCSB PDB Deposit - Search - Visualize - Analyze - Download - Learn - More - MyPDB -

165957 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education

Enter search term(s)

Advanced Search | Browse Annotations

PDB-101 PDB EM Data Resource

Structure Summary 3D View Annotations Sequence Experiment

Biological Assembly 1

7BV2

The nsp12-nsp7-nsp8 complex bound to the template-primer RNA and triphosphate form of Remdesivir(RTP)

DOI: 10.2210/pdb7BV2/pdb EMDDataResource: EMD-30210

Classification: VIRAL PROTEIN

Organism(s): Severe acute respiratory syndrome coronavirus 2

Expression System: Spodoptera frugiperda

Mutation(s): No

Deposited: 2020-04-09 Released: 2020-04-22

Deposition Author(s): Yin, W., Mao, C., Luan, X., Shen, D., Shen, Q., Su, H., Wang, X., Zhou, F., Zhao, W., Gao, M., Chang, S., Xie, Y.C., Tian, G., Jiang, H.W., Tao, S.C., Shen, J., Jiang, Y., Jiang, H., Xu, Y., Zhang, S., Zhang, Y., Xu, H.E.

Experimental Data Snapshot

Method: ELECTRON MICROSCOPY

Resolution: 2.50 Å

Aggregation State: PARTICLE

Reconstruction Method: SINGLE PARTICLE

wwPDB Validation

Metric	Percentile Ranks	Value
Ramachandran outliers	100	0
Sites in outliers	100	0
RNA backbone	100	0.71

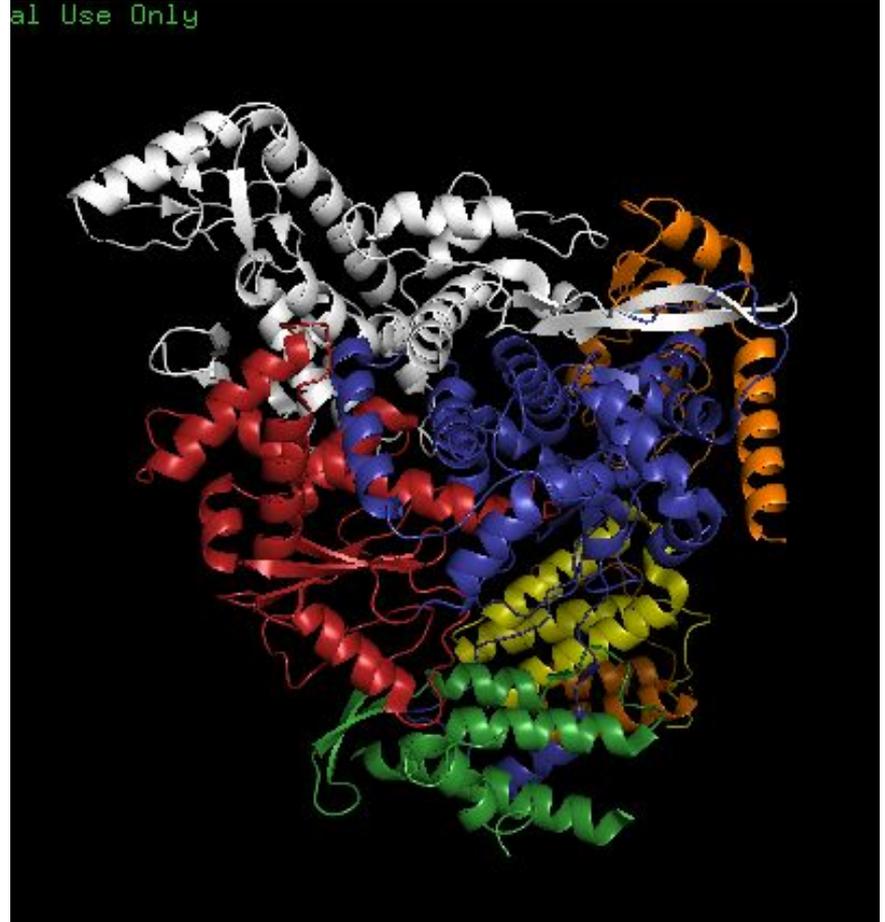
This is version 3.1 of the entry. See complete history.

Literature Download Primary Citation -

SARS-CoV-2 RNA-dependent RNA polymerase in complex with cofactors (6M71)

Key:

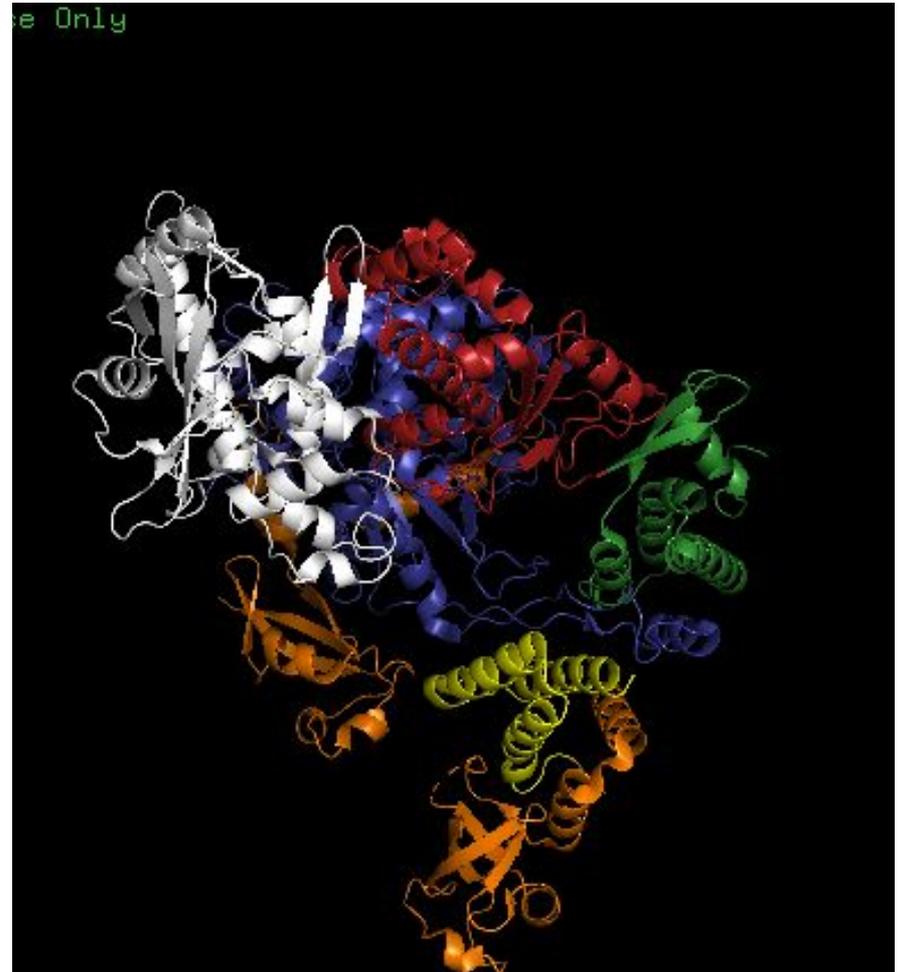
- Nsp12
 - Beta Hairpin, NiRAN, and interface - White
 - Fingers - Blue
 - Palm - Red
 - Thumb - Green
- Nsp7 - Yellow
- Nsp8 - Orange



SARS-CoV-2 RNA-dependent RNA polymerase in complex with cofactors in reduced condition (7BTF)

Key:

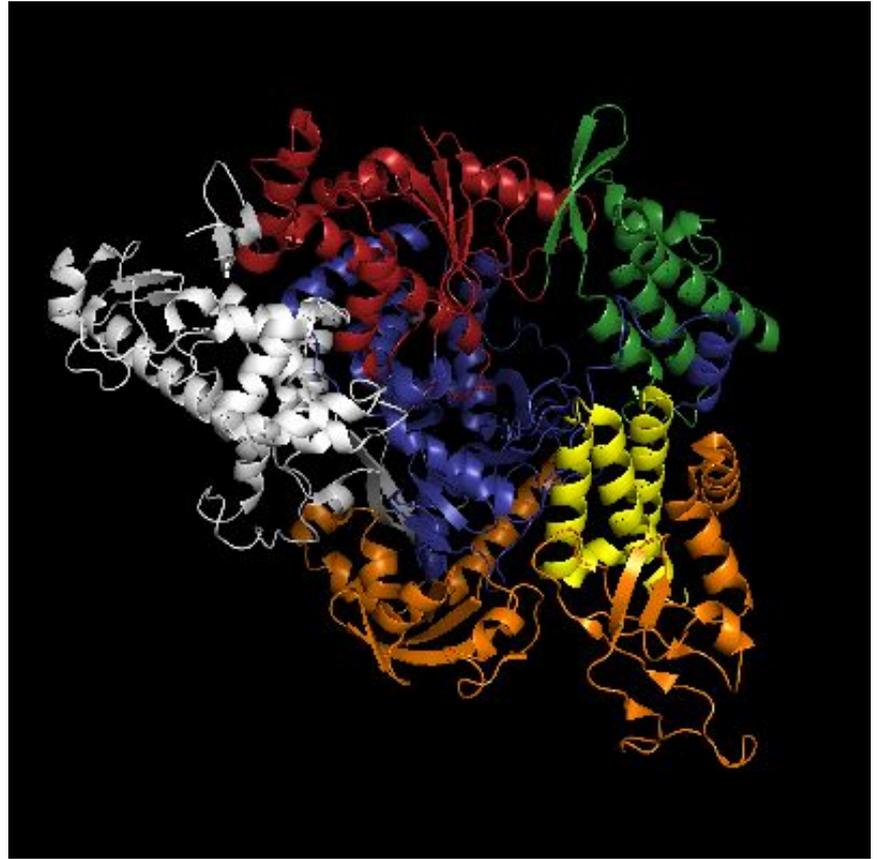
- Nsp12
 - Beta Hairpin, NiRAN, and interface - White
 - Fingers - Blue
 - Palm - Red
 - Thumb - Green
- Nsp7 - Yellow
- Nsp8 - Orange



Cryo-EM structure of the apo nsp12-nsp7-nsp8 complex (7BV1)

Key:

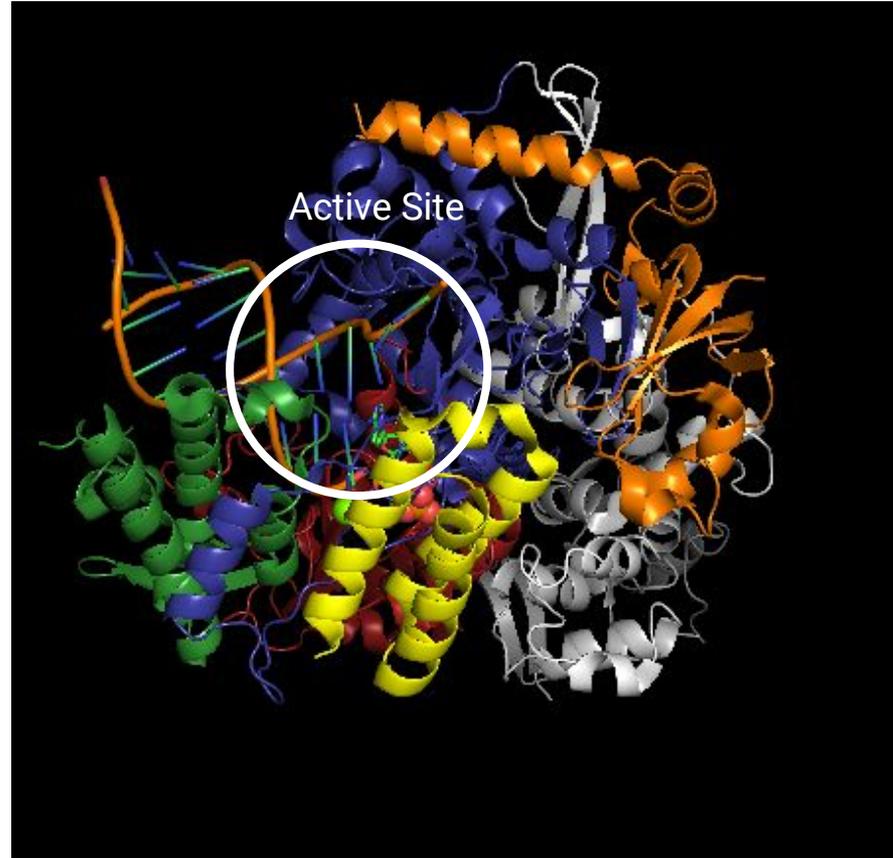
- Nsp12
 - Beta Hairpin, NiRAN, and interface - White
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 - Thumb - Green
- Nsp7 - Yellow
- Nsp8 - Orange



The nsp12-nsp7-nsp8 complex bound to the template-primer RNA and triphosphate form of Remdesivir(RTP) (7BV2)

Key:

- Nsp12
 - Beta Hairpin, NiRAN, and interface - White
 - Fingers - Blue
 - Palm - Red
 - Thumb - Green
- Nsp7 - Yellow
- Nsp8 - Orange



COVID-19 RNA-dependent RNA polymerase pre-translocated catalytic complex (7C2K)

Key:

- Nsp12
 - Beta Hairpin, NiRAN, and interface - White
 - Fingers - Blue
 - Palm - Red
 - Thumb - Green
- Nsp7 - Yellow
- Nsp8 - Orange

