Molecular Dynamics of SARS-CoV-2 Nsp1 Structural Changes Associated with Variant Mutations

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Abstract

SARS-CoV-2 non-structural protein 1 (Nsp1) is a virulence factor that inhibits the translation of host mRNAs and interact with viral RNA. Despite the relevance of Nsp1, few studies have been conducted to understand the effect of mutations on Nsp1 structure and function. Here, we provide a molecular dynamics simulation of SARS-CoV-2 Nsp1, wild type and variants. We found that SARS-CoV-2 Nsp1 has a more R_g value than SARS-CoV-1 Nsp1, with indicate an effect on the folding protein. This result suggest that SARS-CoV-2 Nsp1 can more easily approach the active site of the ribosome compared to SARS-CoV-1 Nsp1. In addition, we found that the C-terminal of the SARS-CoV-2 Nsp1, in particular residues 164 to 170, are more flexible than other regions of SARS-CoV-2 Nsp1 and SARS-CoV-1 Nsp1, confirming the role of this region in the interaction with the 40S subunit. Moreover, multiple deletion mutations have been found in the N/C-terminal of the SARS-CoV-2 Nsp1, which seems the effect of SARS-CoV-2 Nsp1 multiple deletions is greater than that of substitutions. Among all deletions, D156-158 and D80-90 may destabilize the protein structure and possibly increase the virulence of the SARS-CoV-2. Overall, our findings reinforce the importance of studying Nsp1 conformational changes in new variants and its effect on virulence of SARS-CoV-2.

1. Introduction

The 5'-end of SARS-CoV-2 genome includes more than two-thirds of RNA genome that comprises two large open reading frames (ORFs/ORF1ab) [1]. ORF1ab proteolytically processed by two virally encoded proteinases (PLpro and M^{Pro}) to produce 16 non-structural proteins (NSP1 to NSP16) [2][3]. Non-structure protein 1 (Nsp1) is encoded by the gene closest to the 5'-end of the SARS-CoV-2 genome, being also known as leader protein [4, 5]. NSP1 has identical physical features and biological activity with other β -coronaviruses, however, it seems Nsp1 is not highly conserved among the lineage of viruses [5, 6]. Nsp1 has 180 amino acids (aa) forming two unstructured domains and one domain working as an interconnecting region between the two unstructured domains [7]. The crystal structure of SARS-CoV-2 Nsp1 revealed a six-stranded and capped β -barrel motif similar to SARS-CoV Nsp1 [8]. Based on previous studies, the interaction between the helical hairpin at the C-terminal domain of Nsp1 and the host 40S subunit of ribosome prohibits the entry of mRNA into the host ribosome [9]. Therefore, Nsp1 leads to translational shutoff of proteins from host mRNAs by binding the 40S ribosome of the host cell [9–11]. The C-terminal domain of Nsp1 has two helices [10] that are inserted into the entrance area of the ribosomal mRNA channel, probably contributing to the translational blockage [9, 10]. In fact, Nsp1 leads to an endonucleolytic cleavage near the 5' UTR of host mRNA (capped mRNA) when binding to ribosome [12]. Moreover, Nsp1 inhibits all cellular antiviral defense mechanisms such as Type I interferon (IFN-I) response, which leads to the shutoff of the response of the innate immune system [10, 13]. Nsp1 directly binds to SARS-CoV-2 stem-loop 1 (SL1) of 5-UTR RNA, which it seems this interaction can increase viral gene replication in the host cells by recruiting the host 40S ribosome at that region [5]. Examination of the physical properties of the SARS-CoV-2 Nsp1 has shown that has a positive surface charge [14]. Despite the existence of a structural model of the Nsp1 [9, 15], few studied have been conducted on the dynamic

aspects of this protein and how mutations may be change its conformation and function. Here, we used molecular dynamic (MD) to further investigate the structure of Nsp1 in SARS-CoV-2 and SARS-CoV-1 and determined the effect of mutations on Nsp1 stability. These observations highlight the relevance of understanding how mutations effect the Nsp1 inhibition of immune response and binding to the ribosome.

2. Computational Methods

2.1. Sequence and structure alignment

The sequences of wild type (Polyprotein1ab) NSP1 proteins isolated from the SARS-CoV-2 and SARS-CoV-1 viruses were retrieved from UniProtKB (<http://www.uniprot.org/>), under the identifier numbers of P0DTD1 and P0C6X7, respectively. To investigation of interaction between NSP1 and ribosome, structure of complex (PDB code: 7K5I) was downloaded from RCSB and a complete model of complex retrieved from SARS-CoV-2 3D (<https://sars3d.com/>). The automated sequence alignment was performed using the EMBOSS Needleman–Wunsch method [16, 17]. This tool indicates the percentage of identity and similarity between both nsp1. I-TASSER server [18] was utilized to build the 3D structure of both NSP1, which is an online server for automated protein structure prediction. The best model was selected based on its C-score and the quality of the predicted structure was confirmed by PROCHECK [19, 20] and ProSA [21], which calculate an overall quality score for 3D structures. The local environment of amino acids was investigated through the WHAT IF coarse packing quality control, which should stay above 5 [22]. Mutations were also predicted with the use of the Dynamut mutation prediction. In the end, H++ server was used to predict the protonation of histidine residues at 7.4 pH [23]. UCSF Chimera (1.14) is a program that was used to visualization and analysis of structures [24].

2.2. Nsp1 complexes, mutations and calculation of binding energy

SARS-CoV-2 Nsp1 mutations (substitutions, insertions, and deletions) were retrieved from the CoV-GLUE database [25]. PRODIGY web server [26] was used to predict the binding affinity, number and type of intermolecular contacts within the 5.5 Å distance cut off of Nsp1-ribosome complex from it 3D structure. The identified substitutions in the Nsp1 C-terminal (helix-turn-helix) were examined in the DynaMut [27] web server to determine their effects on protein stability. The effect of mutations in protein stability and the estimation of change in the folding free energy upon the mutation ($DDG^{\text{Destablizing}}$) [27, 28] and vibrational entropy energy (DDS^{Vis}) was predicted using the DynaMut tool [27]. MutaBind2 [29] was used to evaluate the effects of mutations on Nsp1-ribosome interactions. This server computed changes in binding affinity upon single mutations (DDG^{Binding}).

2.3. Molecular dynamics simulation

The molecular dynamics (MD) simulation were carried out using the GROMACS (2020.2). A water box was created with at least 1 nm (10 Å) distances from the protein using the SPC water model and applying boundary conditions. The system neutralization was done by adding Na^+ and Cl^- ions at the

concentration of 0.1 M. The MD simulation was carried out to examine the quality of the model structures by investigating their stability via performing 100 ns simulations at a constant temperature 310 K (NVT). Energy minimization was performed in 50,000 steps to avoid any bad contacts generated while solvating the system. Then, the NPT optimization was done for 100 ps. To increase the likelihood of achieving the appropriate structure, the MD simulation was performed for 100 ns using the OPLS force field. The MD simulation was performed in three replicas for SARS-CoV-2 and two for SARS-CoV-1 Nsp1. In addition the MD simulation was carried out for mutant types of SARS-CoV-2 Nsp1. At the end of this process, the GROMACS Tools package were used for the trajectory analysis. In addition, CHARMM-GUI [30] was used to generate inputs of Nsp1-RNA complex for GROMACS and the MD simulation was carried out for ~73 ns using CHARMM force field.

2.4. Network analysis of Nsp1-ribosome complex and intrinsically disordered protein

RING 2.0 [31] was used to represent 2D structure of Nsp1-ribosome complex and it was applied for the identification of covalent and non-covalent bonds between Nsp1 and ribosome subunits, including π - π stacking, Hbond and VDW. The network visualized using Cytoscape. This network represents nodes (e.g. residues) and edges (e.g. bonds between the residue side chains), which are essential factors to network analysis.

Traditional structural studies have shown that proteins need a well-defined structure to perform their function. In contrast, recent structural studies have introduced proteins that have parts that do not form a specific three-dimensional structure and are known as Intrinsically disordered regions (IDRs) [32–34]. Recognition of the natural frequency and functional importance of IDRs and ordered regions of proteins were identified as an essential factor in studying different biological processes [33]. PONDR[®] has been used to investigate IDRs of SARS-CoV-2 Nsp1, which is based on several different predictors such as VL3 and VSL2 [35, 36]. In each of these predictors, the first letter refers to the method of characterization (V: Various) and the second letter refers to the length of the disordered region (S: Short (8 - 9 residues), and L: Long (40 or more residues)).

3. Results

3.1. Sequence and structure alignment

The results of the amino acid sequence alignment revealed that the Nsp1 of SARS-CoV-2 shares 84.4% identity and 91.1% similarity with the Nsp1 of SARS-CoV-1. The tertiary structure of SARS-CoV-2 NSP1 has consisted of regular secondary structural elements arranged sequentially as β 1, α 1, β 2, α 2, β 3, β 4, β 5, β 6, α 3, and α 4, which secondary structure is composed of a mixture of parallel and antiparallel β -strands (Fig. 1). The β -strands consist of residues 14 to 20 (β 1), 51 to 55(β 2), 68 to 73 (β 3), 87 to 91 (β 4), 104 to 109 (β 6), and 117 to 123 (β 6), while β 5, β 1 and β 6 are shorter and β 3 and β 4 are longer than identical β -strands of SARS-CoV-1 Nsp1. Also, NSP1 contains four α -helixes namely α 1 (35 to 49), α 2 (60 to 63), α 3 (153 to 160), and α 4 (164–178) that α 3 and α 4 locate at the C-terminal of protein. Investigation of the

Nsp1-ribosome complex revealed that the $\alpha 3$ and $\alpha 4$ play a key role in forming this complex. In particular, several specific residues (Y154, E155, D156, F157, Q158, E159, N160, W161, T170, L173, M174, L177, N178) in this region were identified as essential residues involved in the interaction with components of the 40S ribosome subunit (U3 and S2). Most of these residues are found in the list of SARS-CoV-2 Nsp1 mutations. Therefore, examining important residues and understanding their position in protein sequence and structure can provide a novel insight into the effect of mutations on protein function. Furthermore, the Nsp1 has only one cysteine at position 51, which is the first amino acid of $\beta 2$. This residue is significant because its neighboring residues may mutate and create an extra cysteine. It is suggested that it may lead to form disulfide bond and increase the stability of the protein structure.

3.2. Analysis of Nsp1 complexes and effect of mutations

The complex structure of the SARS-CoV-2 Nsp1 protein and human ribosomal 40S subunit were analyzed. The binding site of Nsp1 to the ribosome contains 26 residues at Nsp1 C-terminal. Among these residues, 17 residues form a helix-turn-helix (HTH) motif and lead to form Nsp1-ribosome complex. HTH interacts simultaneously with different regions of the ribosome called “head region” including uS3 and “body region” including eS30 and uS5. HTH interacts with uS3 by D152, E155, D156, E159, Q158, and N160 residues, as well as this motif involved in interaction with uS5 by Y154, F157, Q158, W161, T170, L173, L177, N178 residues. R175, E176, and G179 residues of HTH motif play a key role in forming Nsp1-ribosome (eS30) complex. We calculated the binding energy ($\Delta G^{Binding}$) for these interactions, which showed that the interaction between the Nsp1 and uS3 is stronger than the other interactions (Table 1).

Table 1
Binding affinity (ΔG) and dissociation constant (K_d) predicted values for the interaction between SARS-CoV-2 Nsp1 and human ribosome.

Protein-protein complex (Viral Nsp1/ribosome)	ΔG (kcal/mol)	K_d (M) at 37.0 $^{\circ}C$
Nsp1-uS3	-6.9	1.3E-05
Nsp1-uS5	-5.6	1.1E-04
Nsp1-eS30	-4.1	1.2E-03

Substitutions F157S, E159D, L173P and R175H had $\Delta \Delta G^{Destablizing} < 0$ and $\Delta \Delta S^{Vib} > 0$ (Fig. 2), suggesting that they may increase the infectivity of host cells by destabilizing the Nsp1 and increasing its entropy and flexibility. Other mutations may have the opposite effect on Nsp1, such as E159K, T170I, M174K and N178K, which have $\Delta \Delta G^{Destablizing} > 0$ and $\Delta \Delta S^{Vib} < 0$, which stabilize the protein and reduce its entropy (Fig. 2). These substitutions may reduce the rate at which the Nsp1 binds to the host ribosomal subunits and thus reduces the rate of infection.

We identified W161 in the HTH motif as causing a turn in that motif, leading to the helix disruption. This residue can also cause hydrophobic interactions (with F157) and stabilize the protein structure. Several mutations are known for this residue, including W161C, W161S, W161L, and W161R. We found that W161C has $\Delta\Delta G^{\text{Destabilizing}} < -1$, which may lead to instability of the protein structure. Mutation F157S can also affect the formation or loss of this hydrophobic interaction, which in turn probably impacts the stability of the Nsp1 in that region.

Investigation of Nsp1-RNA complex have shown that protein can interact with viral RNA through their residues, which include 41E, 47K, 48D, 49G, 50T, 51C, 72K, 75D, 77R, 82G, 96Q, 97T, 99R, 102E, 112G, 113E and 114I (with Hydrogen bond)/ 122L (Hydrophobic interaction)/ 31F (π -stacking) (Fig. 3a). Several residues at the surface interaction of Nsp1-RNA are known to have mutated. Among the most frequent mutations (Table 2), G112 change to C/S and G49 to C result in $\Delta\Delta G^{\text{Destabilizing}}$ below zero. These results suggested that the mutation of glycine to cysteine and serine could lead to protein instability, increased flexibility of Nsp1 and increase entropy of this protein. These factors can increase the rate at which Nsp1 binds to viral RNA. D75G and L122F mutations also showed negative values for $\Delta\Delta G^{\text{Destabilizing}}$ and $\Delta\Delta S^{\text{Vis}}$, indicating that they affect structure stability and thermodynamics parameters (*i.e.* decrease entropy and protein flexibility). A third group of mutations (D75E and E102K) leads to increase stability, decrease entropy and flexibility of protein, which perhaps reduce protein binding to the viral RNA, thereby reducing infectivity. The last group of mutations includes D48G, which showed positive values for $\Delta\Delta G^{\text{Destabilizing}}$ and $\Delta\Delta S^{\text{Vis}}$. Based on results of calculations by computational tools, this mutation appears to increase stability and entropy of Nsp1.

Figure 3b shows the surface potential of the Nsp1-RNA complex that indicating the Nsp1 binds to viral RNA through its positive residues in that region.

Some mutations also have effects on intra-atomic interactions of Nsp1 that lead to the elimination and formation of interactions such as van der Waals (yellow), weak Hydrogen bond (orange), and hydrophobic interactions (green), polar (light pink), as shown in Fig. 4.

Table 2
Frequency, $\Delta\Delta G^{\text{Destabilizing}}$ and $\Delta\Delta S^{\text{Vib}}$ are achieved for the mutations of Nsp1 N-ter.

Mutation	Frequency	$\Delta\Delta G^{\text{Destabilizing}}$ (kcal/mol)	$\Delta\Delta S^{\text{Vib}}$ (kcal.mol ⁻¹ .K ⁻¹)
G112C	102	-0.800	0.032
G49C	118	-1.765	0.084
G112S	145	-1.060	0.039
D75G	161	-0.244	-0.005
L122F	224	-0.077	-0.811
I114V	232	-0.097	0.058
E102K	321	0.534	-0.185
I114L	403	-0.164	0.072
D75E	990	0.848	-0.265
D48G	1185	0.001	0.089

3.3. MD simulation

Molecular dynamics (MD) simulations were performed for the wild type and mutant types of SARS-CoV-2 Nsp1 and SARS-CoV-1 Nsp1. The RMSD plot indicates that all proteins reached equilibrium after 100 ns and that the SARS-CoV-1 Nsp1 deviation is less than the SARS-CoV-2 Nsp1 (Fig. 5a). We identified four main deletions in Nsp1 at sites 80–90, 156–158, 158–161 and 175–177. The deletions result in different conformations in Nsp1 C-terminal region (Fig. 6). SARS-CoV-2 Nsp1 ($\Delta^{175-177}$) and Nsp1 ($\Delta^{1158-161}$) follow a pattern similar to SARS-CoV-1 Nsp1 and have less fluctuations than other proteins. This result indicates that the Nsp1 has a lower value of RMSD with the 175–177 and 158–161 deletions, so the mutated proteins are more stable than the wild protein and other mutant protein (Fig. 5a). In contrast, $\Delta^{156-158}$ and Δ^{80-90} have higher RMSD values than SARS-CoV-2 Nsp1 wild type, which may indicate increasing protein fluctuations and instability.

The SARS-CoV-1 Nsp1 exhibited a lower R_g values compared to the SARS-CoV-2 Nsp1 (Fig. 5b). The difference between R_g of these two proteins is ~ 0.12 nm. Overall, all models of SARS-CoV-2 Nsp1 had various values of R_g that including Nsp1 ($\Delta^{156-158}$) > Nsp1 (wild) > Nsp1 (Δ^{80-90}) > Nsp1 ($\Delta^{175-177}$) > Nsp1 ($\Delta^{158-161}$). Nsp1 ($\Delta^{156-158}$) has more functional movements due to its higher value of R_g and lesser compactness.

The RMS plot was constructed from the 100 ns data in order to understand the deviation of each Nsp1 (Fig. 5c). The RMSF of the backbone for the SARS-CoV-2 Nsp1 displayed more flexible 164 to 170 residues (Lys, His, Ser, Ser, Gly, Val, and Ter), as compared to the SARS-CoV-1 Nsp1. This region corresponds to the C-terminal of the Nsp1 related to the protein interaction with the ribosome through CT, meaning that its flexibility could be related to its function. As shown in Fig. 5c, the RMSF plot of mutant proteins had more fluctuations compared to wild Nsp1 due to their deleted residues. In order to understand the total motion of Nsp1 structures in the phase space, the first two eigenvectors were projected onto it. The results indicate that the motion features characterized by the two eigenvectors are different in the SARS-CoV-2 and SARS-CoV-1 Nsp1 proteins. SARS-CoV-2 Nsp1 show wider motions than SARS-CoV-1 Nsp1, indicating more conformational changes.

As shown in Fig. 5(d-e), the values of RMSD and R_g resulting from the analysis of Nsp1-RNA trajectories after ~ 73 ns MD simulation are 0.6 nm and 1.5 nm, respectively. The RMSF plot of this complex also showed fluctuations in the site of RNA binding to the protein (Fig. 5f).

3.4. Analysis of Network and IDRs of Nsp1

Critical residues at the interface between the SARS-CoV-2 Nsp1 and ribosome subunits in their complex are indicated in the RIN presented (Fig. 7). Key residues were determined by using stress and betweenness as the two main parameters of the local metrics. High betweenness values represent that the node is a mediator of interactions with other nodes and that is probably a key structural residue, while stress is defined as the number of shortest paths passing through a node. The analysis of NSP1 (C-terminal) network revealed crucial residues including F157, V169, T170, and L173. These amino acids were identified as critical residues at the interface between the SARS-CoV-2 NSP1 and ribosome. Furthermore, these residues were known as amino acids that have mutated.

In addition, Table 3 describes the most important residues of the SARS-CoV-2 involved in the interaction between its Nsp1 and ribosome via H-bonds, van der Waals bonds, and π - π stacking interactions. Among these residues, Δ 158-161, Δ 156-158, Δ 175-177, F157S, E159D, L173P and R175H are critical because their mutations could alter the ability of the Nsp1 to bind to ribosome, which could lead to the loss of efficacy of drugs targeting the Nsp1 or competing with it for ribosome.

Table 3
Representation of interaction between different residues of
the SARS-CoV-2 Nsp1 and ribosome subunits.

Residues of Ribosome	Residues of Nsp1	Interaction
(uS5)	178ASN	VDW
105GLU	177LEU	VDW
106VAL	157PHE	VDW
109ILE	173LEU	VDW
109ILE	161TRP	VDW
122THR	161TRP	PIPISTACK
124PHE	161TRP	VDW
124PHE	154TYR	VDW
147VAL	158GLN	HBOND
147VAL	158GLN	VDW
147VAL	161TRP	VDW
147VAL	177LEU	VDW
151ILE		
(uS3)	155GLU	HBOND
115VAL	152ASP	HBOND
116ARG	155GLU	HBOND
116ARG	155GLU	VDW
116ARG	155GLU	HBOND
143ARG	156ASP	VDW
143ARG	159GLU	VDW
143ARG		
(eS30)	175ARG	VDW
52LYS		

The VSL2 predictor was used to characterize disordered regions of any length and identified accurately the short disordered regions of SARS-CoV-2 NSP1 at 120–180 positions (Fig. 8). PONDR VL3 predictor was applied to determine SARS-CoV-2 NSP1 tendency for disorder. This predictor identified regions of interest at positions 150–180 (Fig. 8). The regions identified as disorder regions are approximately

related to the C-terminal protein. It is also suggested that the occurrence of mutations in this region may increase these disorders in the protein. Structural studies revealed that IDRs of virus structure influence viral genome (RNA) adaptive capacity, host-virus interactions, virus-host range, cross-species transmission, and host tropism [37–41]. In antigen selection, IDRs are significantly considered because these disordered regions may induce an undesirable immune response (weak or even completely non-immune responses)[42].

Discussion

The COVID-19 epidemic is spreading as an unsolvable problem worldwide. Despite the efforts of researchers, many details on SARS-CoV-2 biology remain unknown. Our study focused on the Nsp1 structure and stability by using different computational tools. We found that SARS-CoV-2 Nsp1 has a reduced compactness in comparison with SARS-CoV-1 Nsp1. In addition, we found that the C-terminal of the SARS-CoV-2 Nsp1 is more flexible than other regions of SARS-CoV-2 Nsp1 and SARS-CoV-1 Nsp1, confirming the role of this region in the interaction with the 40S subunit.

Interestingly, a previous study suggested that when SARS-CoV-2 5'-UTR bind to Nsp1 N-terminal, the covalently linked Nsp1 C-terminal is not able to bind the 40S subunit [43]. The authors suggest that this may be due to a steric factor in which Nsp1 C-terminal is unable to approach the 40S subunit to form the Nsp1-ribosome complex. Several mutations in the Nsp1 N-terminal may change the affinity of Nsp1 binding to the 5'-UTR of SARS-CoV-2, perhaps making it more effective in using the host ribosome for translation of viral proteins.

Clinical data showed that D500-532 in Nsp1 N-terminal correlated with lower viral load and lower serum IFN- β that indicating its clinical significance [44]. Therefore, mutations can have a major effect on pathogenicity of SARS-CoV-2. According to the results of MD simulation analysis, it can be suggested that mutations, especially deletion mutations, can play a vital role in protein structure and function. For example, based on MD analysis, D156-158 maybe increase the rate of binding of Nsp1 to ribosome subunit and mutations D158-161 and D175-177 may affect protein binding to the ribosome and reduce pathogenicity of the virus. Moreover, substitution mutations such as M174K/T170I mutations and E159D, R175H, L173P and F157S in the HLH motif of Nsp1 C-terminal could alter the thermodynamics parameters that may affect the interactions of the Nsp1-ribosome complex and rate of infectivity of SARS-CoV-2. Hence, investigation the results of *in silico* studies and comparing them with experimental data can show the association of mutations with the immune system response as well as the function of the virus in the host cell.

Conclusion

Among 795 Nsp1 substitutions, 69 belonged to the HTH motif in the C-terminal region. In this article, out of 69 mutations, only 11 substitutions with a frequency above 10 were examined and it was revealed that these mutations affect the thermodynamic parameters of the interaction between the protein and the

ribosome. The effect of HTH mutations may increase the pathogenicity of SARS-CoV-2 and in turn, increase the inhibition of host protein translation. Important mutations were identified as important mutations in the Nsp1 N-terminal that may affect the affinity binding of viral RNA to this protein. Therefore, findings suggest that Nsp1 should be considered as an important virulence factor because more mutations in the binding motif of Nsp1 may have drastic consequences.

Declarations

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Figures

Figure 1

Structure and sequence alignment between SARS-CoV-2 NSP1 and SARS-CoV-1 NSP1 ; Red box indicates the region that interacts with the ribosome.

Figure 2

Representation of effect of Nsp1 (HTH motif) mutations on thermodynamics parameters including $\Delta\Delta G^{\text{Destabilizing}}$, $\Delta\Delta S^{\text{Vib}}$, and $\Delta\Delta G^{\text{binding}}$.

Figure 3

(a) RNA-protein complex and RNA-binding residues and (b) Surface potential of Nsp1-RNA complex are represented.

Figure 4

Effect of mutations on interatomic interactions of Nsp1. (a) D48G, (b) E102K, (c) M174K and (d) T170I.

Figure 5

MD simulation analysis. (a)RMSD, (b) Rg, and (c) RMSF of the SARS-CoV-2 and SARS-CoV-1 NSP. (d-f) Analysis of Nsp1-RNA complex.

Figure 6

(a) Sequence logo of SARS-CoV-2 Nsp1 C-terminal (160-180 residues), and (b) representation of superimposed structures of Nsp1 mutants that indicate regions including deletions.

Figure 7

2D and 3D representation of Nsp1-ribosome complex and interface interaction between viral protein and human ribosome.

Figure 8

Representation of IDRs of SARS-CoV-2 NSP1 by using PONDR.

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