

Interfering with mRNA methylation by the 2'O-Methyltransferase (NSP16) from SARS-CoV-2 to tackle the COVID-19 disease

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Table S1. Protein Data Bank ID codes of human betacoronavirus NSP16/NSP10 complexes with ligands and/or RNA.

	Code	mRNA binding groove	Cofactor/Inhibitor binding site	Ions
<i>SARS-CoV</i> Nsp16/10 complex	2XYQ	----	SAH	Cl/Mg/Na/Zn
	2XYR	----	SFG	Cl/Mg/Na/Zn
	2XYV	----	SAH	Cl/Mg/Na/Zn
	3R24	----	SAM	Zn
<i>MERS-CoV</i> Nsp16/10 complex	5YN5	---	---	Zn
	5YN6	----	SAM	Zn
	5YN8	----	SAH	Zn
	5YNB	----	SFG	Zn
	5YNF	m7GpppA	----	Zn
	5YNI	m7GpppG	SAM	Zn
	5YNJ	m7GpppG	----	Zn
	5YNN	m7GpppG	SFG	Zn
	5YNO	m7GpppA	SAH	Zn
	5YNP	m7GpppA	SFG	Zn
5YNQ	m7GpppG	SAH	Zn	
<i>SARS-CoV-2</i> Nsp16/10 complex	6W4H	----	SAM	SO ₃ , Zn
	6W61	----	SAM	Cl/Zn
	6W75 (dimer)	----	SAM	Na/Zn
	6WJT (dimer)	----	SAH	Na/Zn
	6WKQ(dimer)	----	SFG	Na/Zn
	6WKS	m7GpppA	SAM	Zn
	6WQ3	m7GpppA	SAH	SO ₄ /Zn
	6WVN	M7GpppA	SAM	Cl/SO ₄ /Zn
	6YZ1	----	SFG	Zn

	7C2J	----	SAM	Zn
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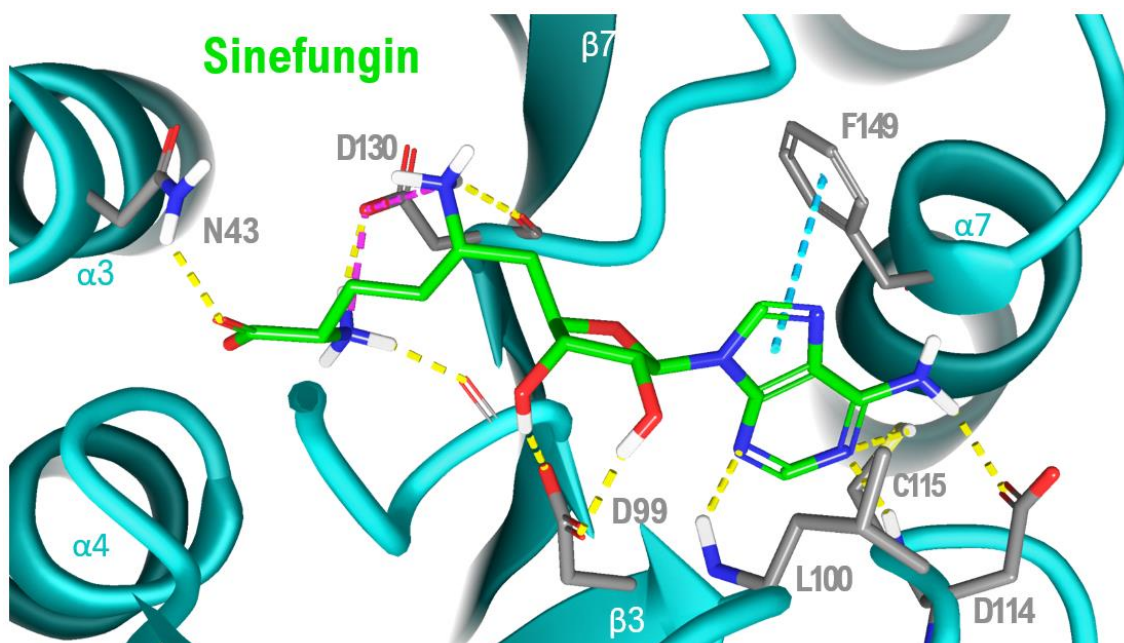


Figure S1. Molecular docking of SFG to NSP16. Yellow dashed lines represent hydrogen bonds, magenta dashed lines represent salt bridges and blue dashed lines show aromatic stacking; non-polar hydrogens are not shown for the sake of clarity. Direct interacting residues are displayed as grey tubes and SFG is shown in green.

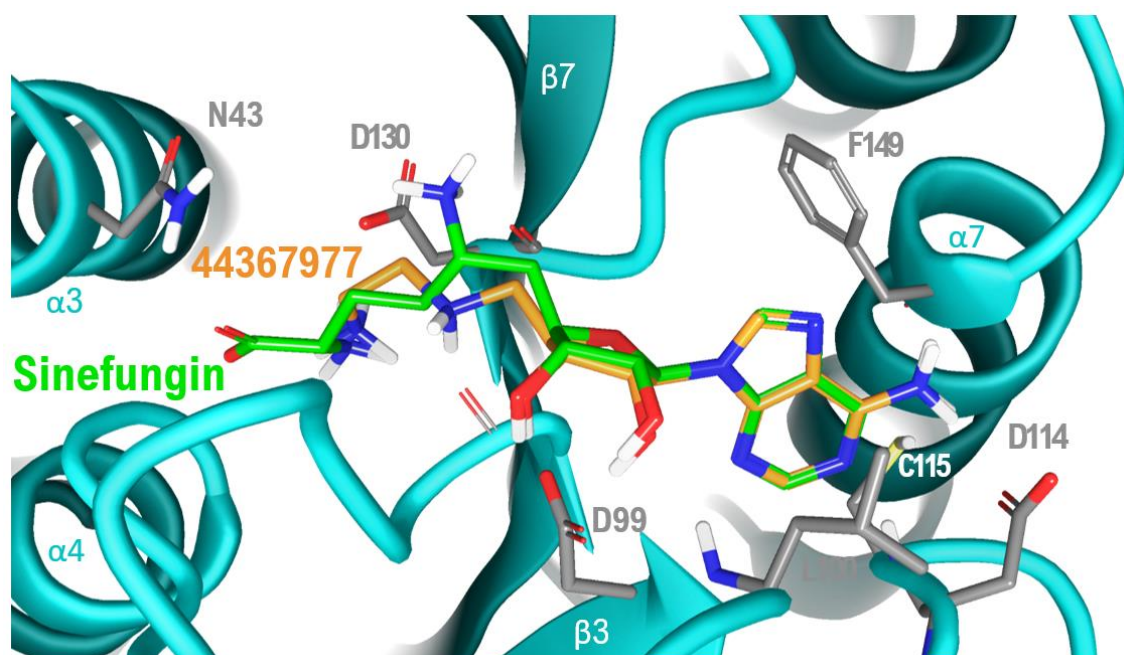


Figure S2. Structure of the 44367977/NSP16 complex with SFG superimposed. 44367977 is displayed in orange and SFG in green.

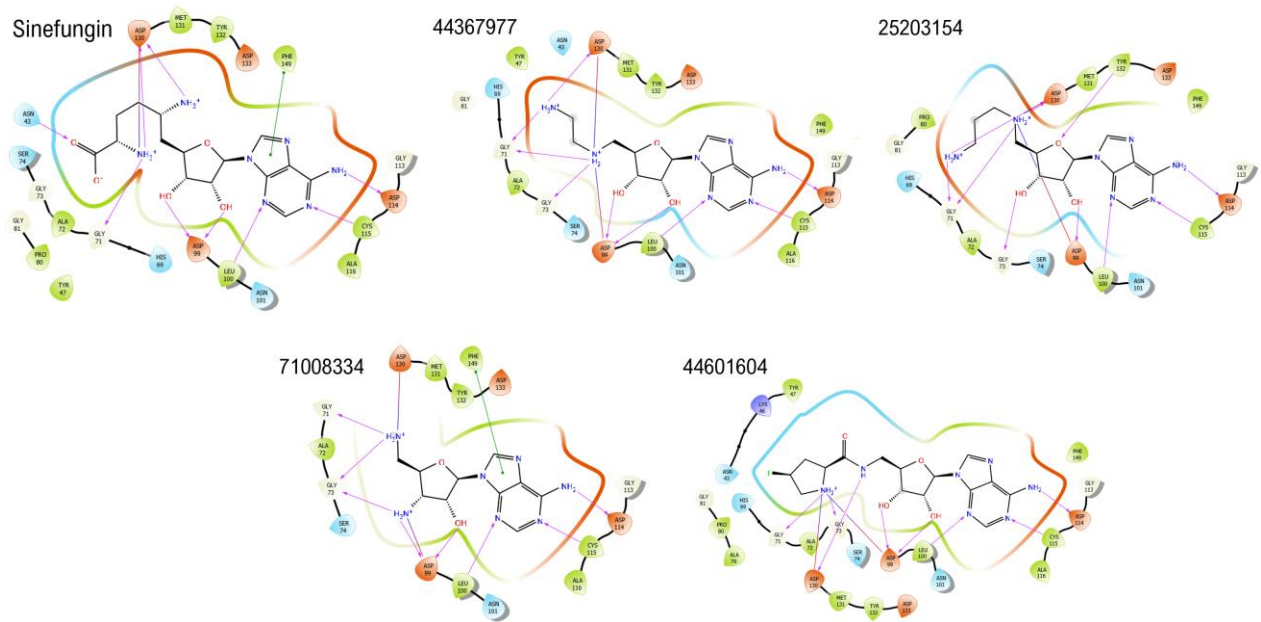


Figure S3. Ligand interaction diagrams of NSP16 with SFG, 44367977, 25203154, 71008334 and 44601604.

Table S2. PubChem indexed biological assays data of SFG and the newly identified molecules.

Compd	BioAssay Results				
	Activity	Target Name	BioAssay Name	BioAssay AID	Substance SID
44367977	-	-	-	-	-
25203154	-	-	-	-	-
71008334	-	-	-	-	-
14728195	-	-	-	-	-
25200440	-	-	-	-	-
66856272	-	-	-	-	-
44601596*	Inconclusive	DNA dC->dU-editing enzyme APOBEC-3F isoform a (Homo sapiens)	qHTS for Inhibitors of Vif-A3F Interactions: qHTS	602313	24783750
44601604*	Inconclusive	thioredoxin reductase (Norway rat)	qHTS Assay for Inhibitors of Mammalian Selenoprotein Thioredoxin Reductase 1 (TrxR1): qHTS	588453	87336325
	Inconclusive		qHTS assay for MDR1-selective chemotherapeutics: Primary screen using the drug-selected MDR subline cells KB-V1	1347076	87336325
66855668	-	-	-	-	-
57126779	-	-	-	-	-
54016655	-	-	-	-	-
57324736	-	-	-	-	-
117805851	-	-	-	-	-
91397803	-	-	-	-	-
71444955	-	-	-	-	-
	Active	Histone-lysine N-methyltransferase EHMT1 (Homo sapiens)	Inhibition of EHMT1 (unknown origin)	1461885	104240365

SFG*	Active		Inhibition of EHMT2 (unknown origin)	1461884	104240365
	Active	Chain A, Structure of Adenine-n6-dna-methyltransferase Taqi (Thermus aquaticus)	Experimentally measured binding affinity data (Kd) for protein-ligand complexes derived from PDB	977611	46391461
	Active	interferon gamma precursor (Homo sapiens)	<i>Toxoplasma gondii</i> at dose in the presence of IFN- γ	1259418	375178464
	Active	Protein arginine N-methyltransferase 1 (Homo sapiens)	Inhibition of GST-fused human recombinant PRMT1 after 90 min by SDS-PAGE based scintillation counting	476872	104240365
	Active		Antimicrobial activity against <i>Leishmania donovani</i>	496828	104240365
	Active	interferon gamma precursor (Homo sapiens)	<i>Toxoplasma gondii</i> at dose in the absence of IFN- γ	1259420	375178464
	Active		Inhibition of <i>Haemophilus influenzae</i> TrmD using S-[methyl-3H] adenosyl-L-methionine as substrate assessed as leucine-tRNA methylation after 60 min by scintillation proximity assay	772725	104240365
	Active	Histone-lysine N-methyltransferase SETD7 (Homo sapiens)	Inhibition of GST-fused human recombinant SET7 after 90 min by SDS-PAGE based scintillation counting	476874	104240365
	Active	Chain A, Structure Of Rubisco Lsmt Bound To Sinefungin And Monomethyllysine (pea)	Experimentally measured binding affinity data (Kd) for protein-ligand complexes derived from PDB	977611	46394220
	Active	Thiopurine S-methyltransferase (Homo sapiens)	Binding affinity to thiopurine methyltransferase (unknown origin) by NMR analysis	1179566	104240365
	Active		Inhibition of <i>Escherichia coli</i> TrmD using S-[methyl-3H] adenosyl-L-methionine as substrate assessed as leucine-tRNA methylation after 60 min by scintillation proximity assay	772727	104240365
	Active	Chain A, The Structure of the Rna Methyltransferase Ermc': Implications For The Reaction Mechanism (Bacillus subtilis)	Experimentally measured binding affinity data (Ki) for protein-ligand complexes derived from PDB	977610	46392974
Active	Histone-lysine N-	Inhibition of recombinant human His6-SUMO	1390742	104240365	

		methyltransferase, H3 lysine-79 specific (<i>Homo sapiens</i>)	tagged DOT1L (1 to 416 residues) expressed in <i>Escherichia coli</i> BL21(DE3) using oligonucleosome as substrate measured after 30 mins in presence of SAM by AlphaLISA assay		
	Active	Protein-L-isoaspartate(D-aspartate) O-methyltransferase (<i>Homo sapiens</i>)	Kinetic constant was measured for Protein Methylase II of <i>Leishmania donovani</i> promastigotes using supernatant (S12) fraction	164156	104240365
	Active	Chain A, The Structure of the Rrna Methyltransferase Ermc': Implications For The Reaction Mechanism (<i>Bacillus subtilis</i>)	Experimentally measured binding affinity data derived from PDB	1811	46392974
	Active	Chain A, Structure Of Adenine-n6-dna-methyltransferase Taqi (<i>Thermus aquaticus</i>)	Experimentally measured binding affinity data derived from PDB	1811	46391461
	Active	Histone-lysine N-methyltransferase SETD7 (<i>Homo sapiens</i>)	Inhibition of human SET7/9	772713	104240365
	Active		Displacement of [3H]-SAM from biotinylated Dengue virus 3 methyltransferase expressed in <i>Escherichia coli</i> at 20 uM preincubated for 20 min followed by [3H]-SAM addition measured after 15 min by scintillation counting analysis	1226489	104240365
	Active	Histone-lysine N-methyltransferase EHMT1 (<i>Homo sapiens</i>)	Inhibition of EHMT1 (unknown origin) preincubated for 5 min followed by SAM and biotinylated H3K9 peptide addition measured after 120 min by HTRF assay	1461878	104240365
	Active		Inhibition of EHMT2 (unknown origin) preincubated for 15 min followed by SAM and biotinylated H3K9 peptide addition measured after 30 min by TR-FRET assay	1461879	104240365
<p>*Full details of reported biological results can be found here: 44601596: https://pubchem.ncbi.nlm.nih.gov/compound/44601596#section=BioAssay-Results&fullscreen=true 44601604: https://pubchem.ncbi.nlm.nih.gov/compound/44601604#section=BioAssay-Results&fullscreen=true SFG: https://pubchem.ncbi.nlm.nih.gov/compound/65482#section=BioAssay-Results&fullscreen=true</p>					

