Two Ligand-Binding Sites on SARS-CoV-2 Non-Structural Protein 1 Revealed by Fragment-Based X-ray Screening

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Table S1: Representative crystallisation conditions and images of three types of SARS-CoV-2 nsp1$_{10\text{-}126}$ crystals. All crystals grew at 18°C at protein concentrations between 15 and 27 mg/mL.

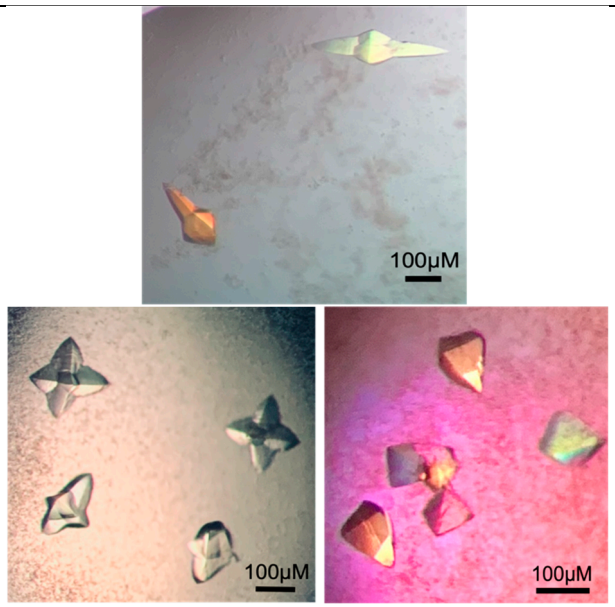
Commercial screens	**Crystallisation condition**	**Crystal images**
Index™	0.1 HEPES pH 7.5, 25% w/v PEG3350	
Morpheus®	0.12 M Ethylene glycol, 0.1 M Imidazole, 0.1 M MES monohydrate acid pH 6.5, 20% v/v Ethylene glycol, 10% w/v PEG8000	
JCSG-*plus*™	0.2 M Ammonium formate, 20% w/v PEG3350	

Table S2. Data collection, data processing, and model refinement statistics for five nsp1$_{10\text{-}126}$-fragment complexes from SARS-CoV-2. Data in parenthesis correspond to the highest resolution shell.

	Nsp1-11C6	**Nsp1-10B6**	**Nsp1-5E11**
PDB ID	8AZ9	8AYS	8ASQ
Wavelength [Å]	0.9655	0.9655	0.9655
Resolution range [Å]	35.63 - 1.42 (1.471 - 1.42)	35.51 - 1.37 (1.419 - 1.37)	32.58 - 1.15 (1.191 - 1.15)
Space group	$P4_32_12$	$P4_32_12$	$P4_32_12$
Unit cell parameters (Å, °)	*a*=*b*=36.817, *c*=141.205, α=β=γ=90	*a*=*b*=36.6882, *c*=140.98, α=β=γ=90	*a*=*b*=36.705, *c*=141.491, α=β=γ=90
Total reflections	136107 (14061)	192589 (3956)	313412 (27576)
Unique reflections	19225 (1872)	19842 (1315)	35543 (3461)
Multiplicity	7.1 (7.5)	9.7 (3.0)	8.8 (8.0)
Completeness [%]	99.46 (99.57)	93.33 (63.87)	96.69 (100.00)
Mean I/sigma(I)	20.46 (2.85)	23.83 (1.21)	9.77 (0.95)
Wilson B-factor (Å^2)	18.20	13.88	14.28
R-meas [%]	5.202 (67.27)	5.332 (19.74)	9.982 (131.60)
$CC_{1/2}$	0.999 (0.838)	0.999 (0.938)	0.997 (0.560)
R_{cryst}/R_{free} [%]	15.04 (20.81) / 14.67 (18.00)	14.55 (17.30) / 15.53 (16.06)	20.16 (30.74) / 25.19 (34.72)
Total no. of non-hydrogen atoms (protein)	1094	1082	960
No. of protein/ligand/solvent atoms	959 / 26/ 120	941 / 21/ 128	876 / 28/ 70
Average B-factor/protein/ligands/solvent	25.90 / 23.66 / 82.69 / 37.31	20.86 / 18.85 / 46.03 / 33.09	23.93 / 22.61 / 60.46 / 33.04
RMSD (bonds, angles)	0.012 / 1.33	0.012 / 1.26	0.012 / 1.34
Ramachandran favoured/allowed/outliers/rotamer outliers [%]	97.32 / 2.68 / 0.00 / 1.87	97.32 / 2.68 / 0.00 / 0.00	99.10 / 0.90 / 0.00 / 1.06
Clashscore	7.63	9.36	3.92

Continuation Table S2. Data collection, data processing, and model refinement statistics for five nsp1$_{10\text{-}126}$-fragment complexes from SARS-CoV-2. Data in parenthesis correspond to the highest resolution shell.

	Nsp1-8E6	**Nsp1-7H2**
PDB ID	8AZ8	8AYW
Wavelength [Å]	0.9655	0.9655
Resolution range [Å]	35.34 - 1.18 (1.222 - 1.18)	35.5 - 1.10 (1.139 - 1.10)
Space group	$P4_32_12$	$P4_32_12$
Unit cell parameters (Å, °)	a=b=36.643, c=141.366, α=β=γ=90	a=b=36.524, c=141.988, α=β=γ=90
Total reflections	297661 (30739)	458335 (28515)
Unique reflections	30502 (3207)	40253 (3891)
Multiplicity	9.8 (9.6)	11.4 (7.3)
Completeness [%]	92.79 (100.00)	99.89 (99.01)
Mean I/sigma(I)	18.77 (2.19)	15.90 (1.32)
Wilson B-factor (Å²)	15.64	13.51
R-meas [%]	5.976 (97.11)	7.452 (130.9)
$CC_{1/2}$	0.998 (0.795)	0.998 (0.589)
R_{cryst}/R_{free} [%]	16.65 (19.89) / 20.81 (25.73)	17.04 (26.77) / 19.09 (27.97)
Total no. of non-hydrogen atoms (protein)	970	1032
No. of protein/ligand/solvent atoms	878 / 24 / 81	919 / 20 / 103
Average B-factor/protein/ligands/solvent	24.22 / 22.96 / 54.47 / 33.70	23.42 / 22.01 / 56.28 / 32.75
RMSD (bonds, angles)	0.012 / 1.40	0.012 / 1.36
Ramachandran favoured/allowed/outliers/rotamer outliers [%]	96.49 / 3.51 / 0.0 / 0.0	94.74 / 5.26 / 0.0 / 1.0
Clashscore	1.69	5.89