Supplementary Information

Artificial Intelligence-Aiding Lab-on-a-Chip Workforce Designed Oral [3.1.0] Bi and [4.2.0] Tricyclic Catalytic Interceptors Inhibiting Multiple SARS-CoV-2 Protomers Assisted by Double-Shell Deep Learnings

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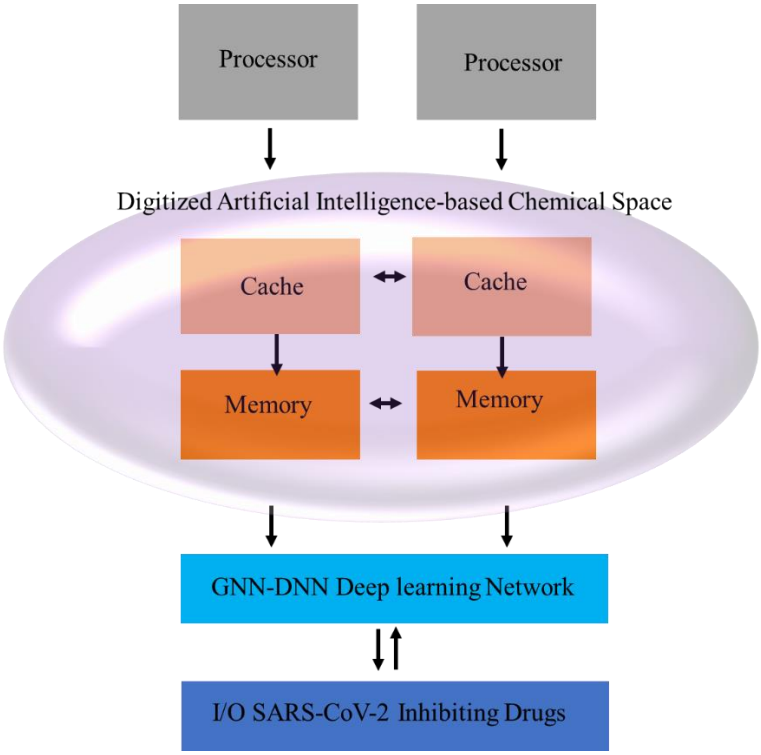


Dual-core processors allow cache coherency circuitry to operate at a higher clock rate, providing better performance in finding an inhibitor in the artificial intelligence-based chemical space. In this homogeneous architecture (two identical processors), they break up the overall computations, in which one MCU designs an inhibitor using GNN deep learning and another MCU predicts docking scores. The cache exploitation in the dual core is shared between cores, which increases cache access time, allowing a higher chance to access memory, which enhances execution and performance.

Figure S1. System-level lab onchip with shared memory model

Figure S2. An example of GNN-output of SARS-CoV-2 inhibiting candidates with probabilistic docking fitting percentage.

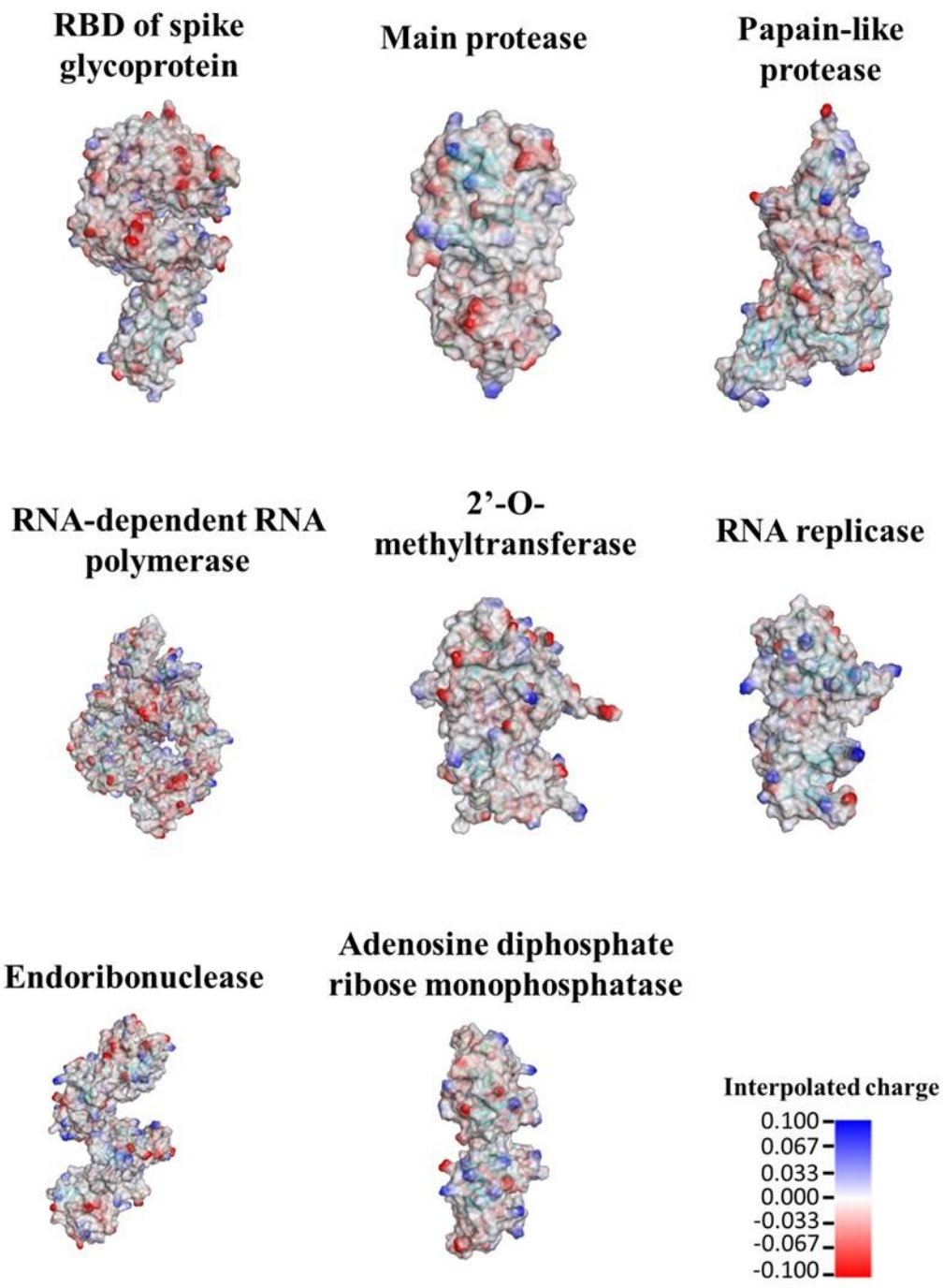


Figure S3. 3D-Interpolated charge representation of different SARS-CoV-2 protein targets.

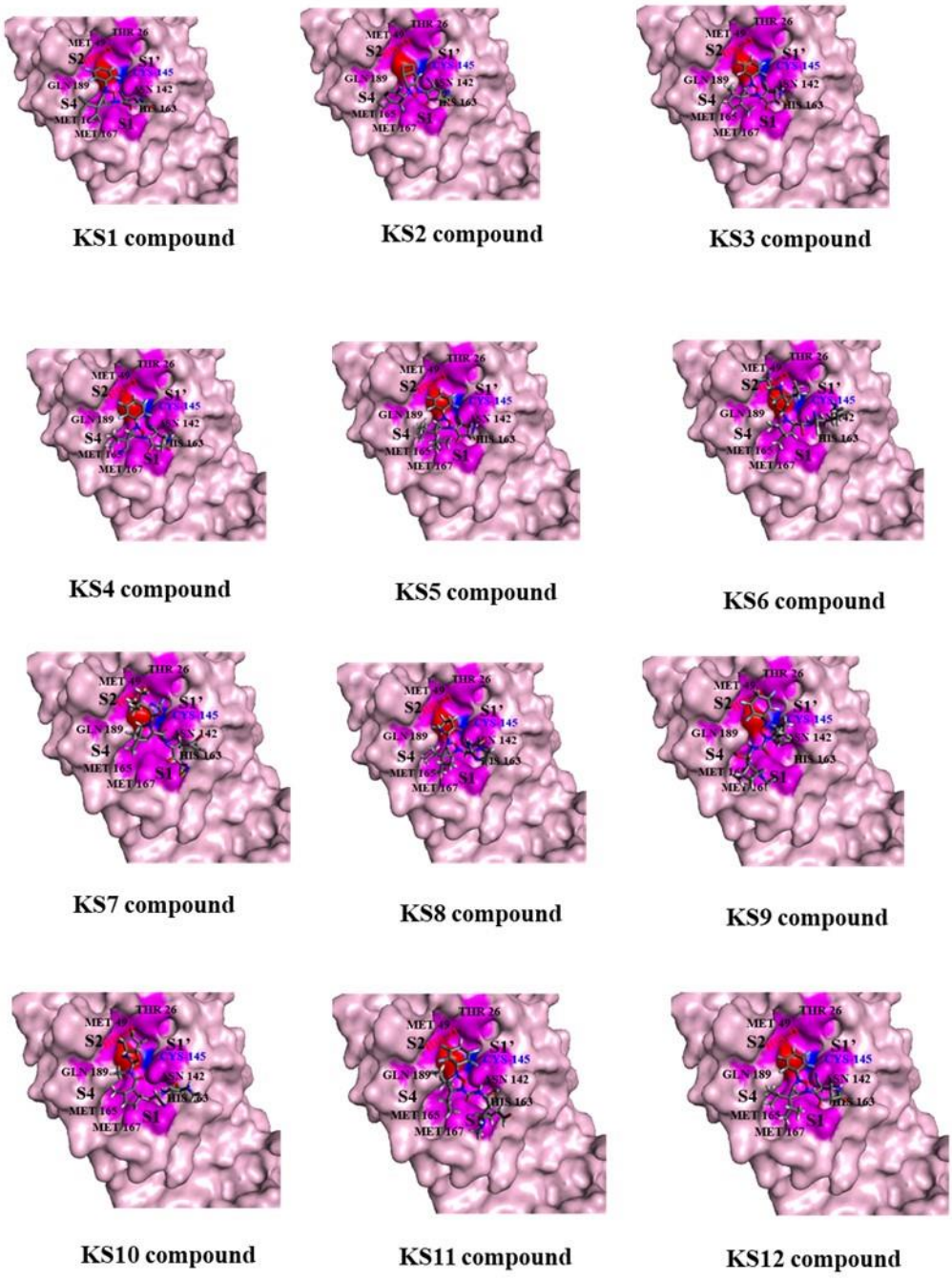
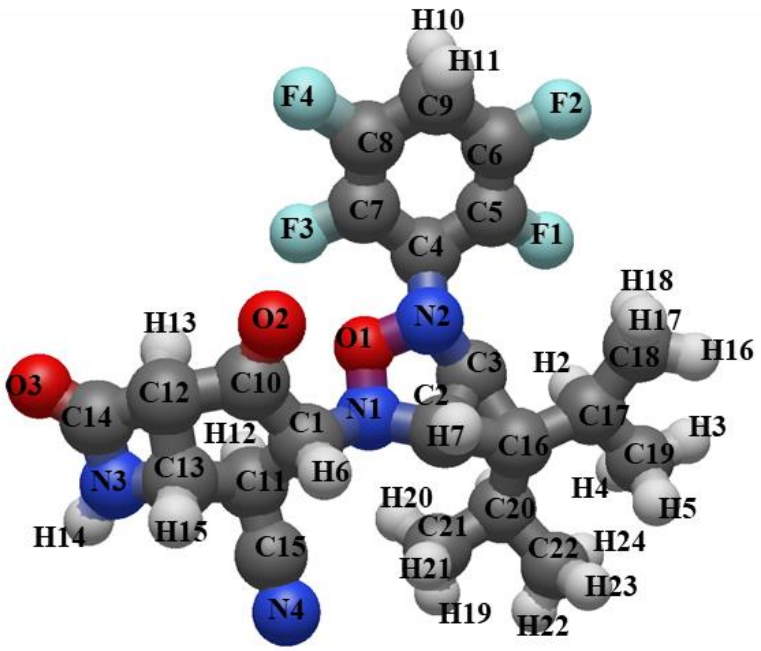


Figure S4. Conformation of **KS** compounds on a selected CYS145 and HIS41 catalytic dyad site of SARS-CoV-2 main protease using METEORITE process.



Nonbonded parameters for all atom types simulated in the molecular dynamic simulation.

Located atom	Atomic number	Mass	σ(nm)	ϵ (kJ/mol)
CR	6	12.011	0.387541	0.23012
NR	7	14.0067	0.329632	0.8368
CR3R	6	12.011	0.333196	0.589944
OR	8	15.9994	0.315378	0.636386
C=C	6	12.011	0.372396	0.284512
F	9	18.9984	0.290433	0.56484
C=O	6	12.011	0.356359	0.46024
CR4R	6	12.011	0.333196	0.589944
NC=O	7	14.0067	0.329632	0.8368
O=C	8	15.9994	0.302905	0.50208
CSP	6	12.011	0.370614	0.284512
NSP	7	14.0067	0.329632	0.8368
HCMM	1	1.0079	0.235197	0.092048
HNCO	1	1.0079	0.040001	0.192464

Bonded parameters for all atom types simulated in the molecular dynamic simulation.

Paired atom		d_{eq} (nm)	k_b (kJ mol^{-1} nm^{-2})
CR	CR	0.338541	0.04184
CR	NR	0.334087	0.187114
CR	CR3R	0.335869	0.157109
CR	OR	0.32696	0.163176
CR	C=C	0.355469	0.109105
CR	F	0.314487	0.15373
CR	C=O	0.34745	0.138768
CR	CR4R	0.335869	0.157109
CR	NC=O	0.334087	0.187114
CR	O=C	0.293997	0.144938
CR	CSP	0.354578	0.109105
CR	NSP	0.334087	0.187114
CR	HCMM	0.286869	0.062059
CR	HNCO	0.189271	0.089737
O=C	NR	0.289542	0.648182
O=C	CR3R	0.291324	0.544242
O=C	OR	0.282415	0.565258
O=C	C=C	0.310924	0.377952
O=C	F	0.269942	0.532536
O=C	C=O	0.302905	0.480705
O=C	CR4R	0.291324	0.544242
O=C	NC=O	0.289542	0.648182
O=C	O=C	0.249452	0.50208
O=C	CSP	0.310033	0.377952
O=C	NSP	0.289542	0.648182
O=C	HCMM	0.242324	0.214978
O=C	HNCO	0.144726	0.310857

Triple-atom angle	k_θ (kJ mol^{-1} rad^{-2})	θ_{eq} (deg)
N-C-C	720.84	105.8370
C-C-F	655.81	119.1000
N-C-O	546.20	127.1520
N-O-N	722.65	109.5000

Dihedral angles	kJ mol^{-1}	ψ
C-C-C-F	12.0416	0
C-C-C-O	78.2910	0
N-C-C-H	-12.0416	180

Figure S5. The atom index in the **KS1** inhibitor with bonded and nonbonded force parameters.

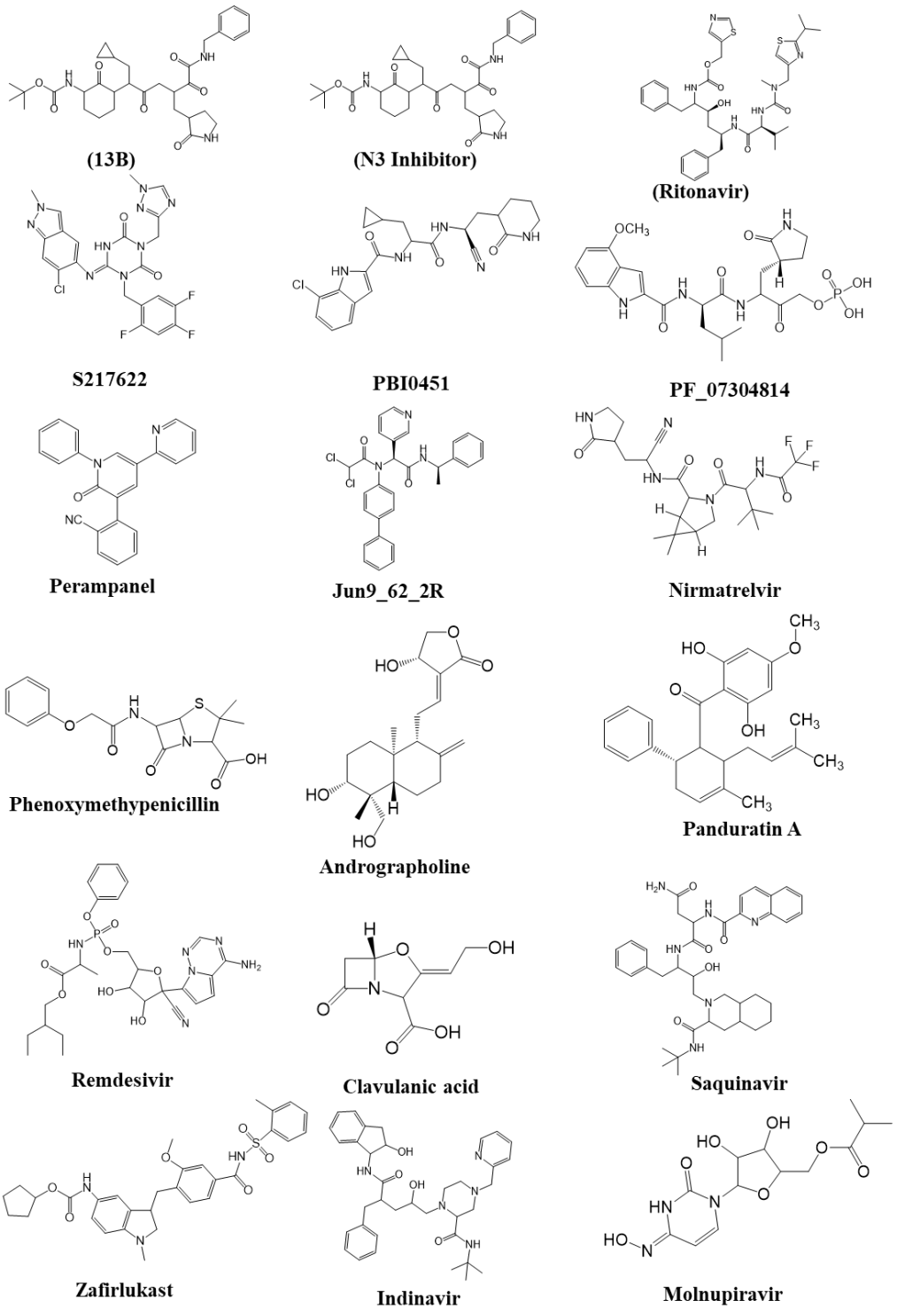


Figure S6. Nomenclature of contemporary SARS-CoV-2 inhibitors used in the study.

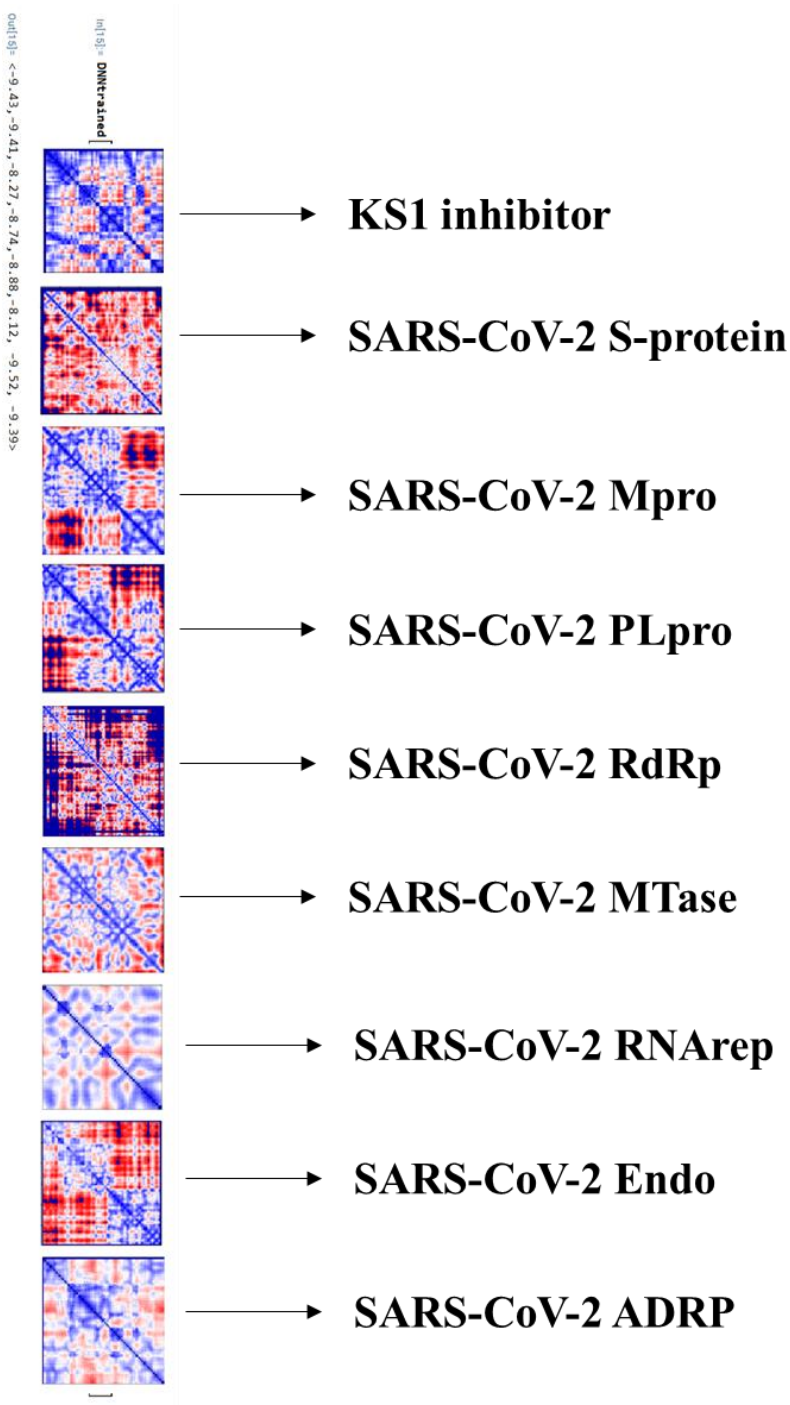


Figure S7. An example of the optimum DNN-output or METEORITE-PROOF score of KS1 compound inhibiting on SARS-CoV-2 s-protein, Mpro, PLpro, RdRp, MTase, RNArep, Endo, and ADRP.

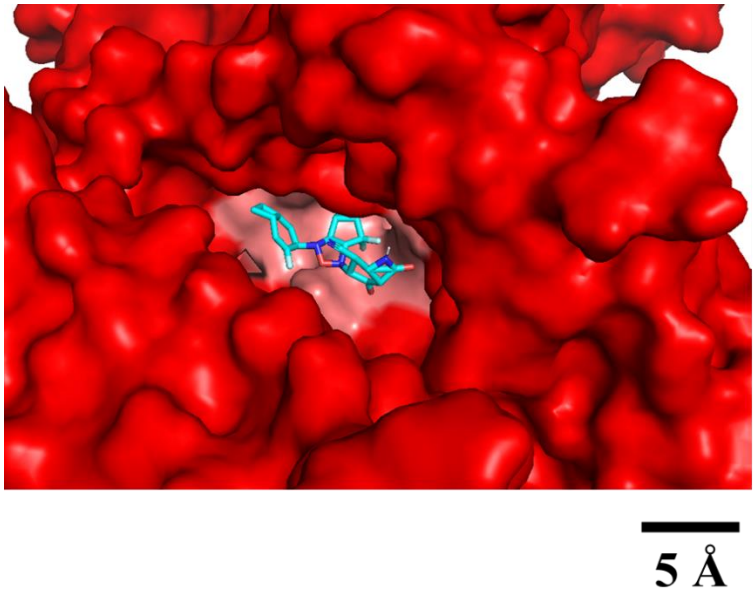
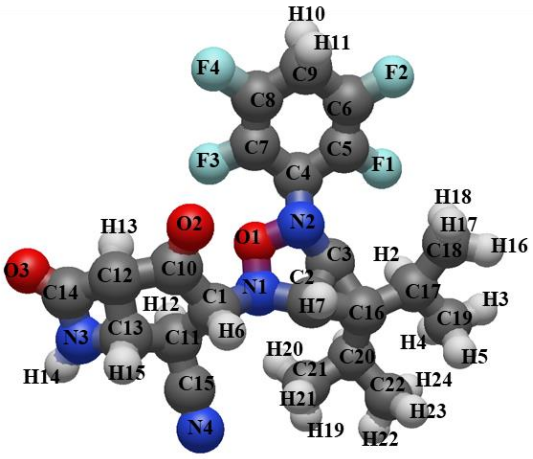


Figure S8. Zoomed-in simulated **KS2** compound transported into a S-protein pocket gate within 5Å radius.



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NC=O	7	14.0067	0.329632	0.8368
O=C	8	15.9994	0.302905	0.50208
CSP	6	12.011	0.370614	0.284512
NSP	7	14.0067	0.329632	0.8368
HCMM	1	1.0079	0.235197	0.092048
HNCO	1	1.0079	0.040001	0.192464

Bonded parameters for all atom types simulated in the molecular dynamic simulation.

Paired atom		d_{eq} (nm)	k_b (kJ mol^{-1} nm^{-2})
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CR	NR	0.334087	0.187114
CR	OR	0.32696	0.163176
CR	C=C	0.355469	0.109105
CR	CE4R	0.354578	0.109105
CR	CR4R	0.335869	0.157109
CR	F	0.314487	0.15373
CR	C=O	0.34745	0.138768
CR	NC=O	0.334087	0.187114
CR	O=C	0.293997	0.144938
CR	CSP	0.354578	0.109105
CR	NSP	0.334087	0.187114
CR	HCMM	0.286869	0.062059
CR	HNCO	0.189271	0.089737
O=C	NR	0.289542	0.648182
O=C	OR	0.282415	0.565258
O=C	C=C	0.310924	0.377952
O=C	CE4R	0.310033	0.377952
O=C	CR4R	0.291324	0.544242
O=C	F	0.269942	0.532536
O=C	C=O	0.302905	0.480705
O=C	NC=O	0.289542	0.648182
O=C	O=C	0.249452	0.50208
O=C	CSP	0.310033	0.377952
O=C	NSP	0.289542	0.648182
O=C	HCMM	0.242324	0.214978
O=C	HNCO	0.144726	0.310857

Triple-atom angle	k_θ (kJ mol^{-1} rad^{-2})	θ_{eq} (deg)
N-C-C	467.91	108.2900
C-C-F	602.21	120.0000
C-C-O	429.38	129.4920
N-O-N	722.65	109.5000

Dihedral angles	kJ mol^{-1}	ψ
C-C-C-F	12.0416	0
C-C-C-O	78.2910	0
C-C-C-C	6.0250	0
N-C-C-H	-12.0416	180

Figure S9. The atom index in the **KS2** inhibitor with bonded and nonbonded force parameters.

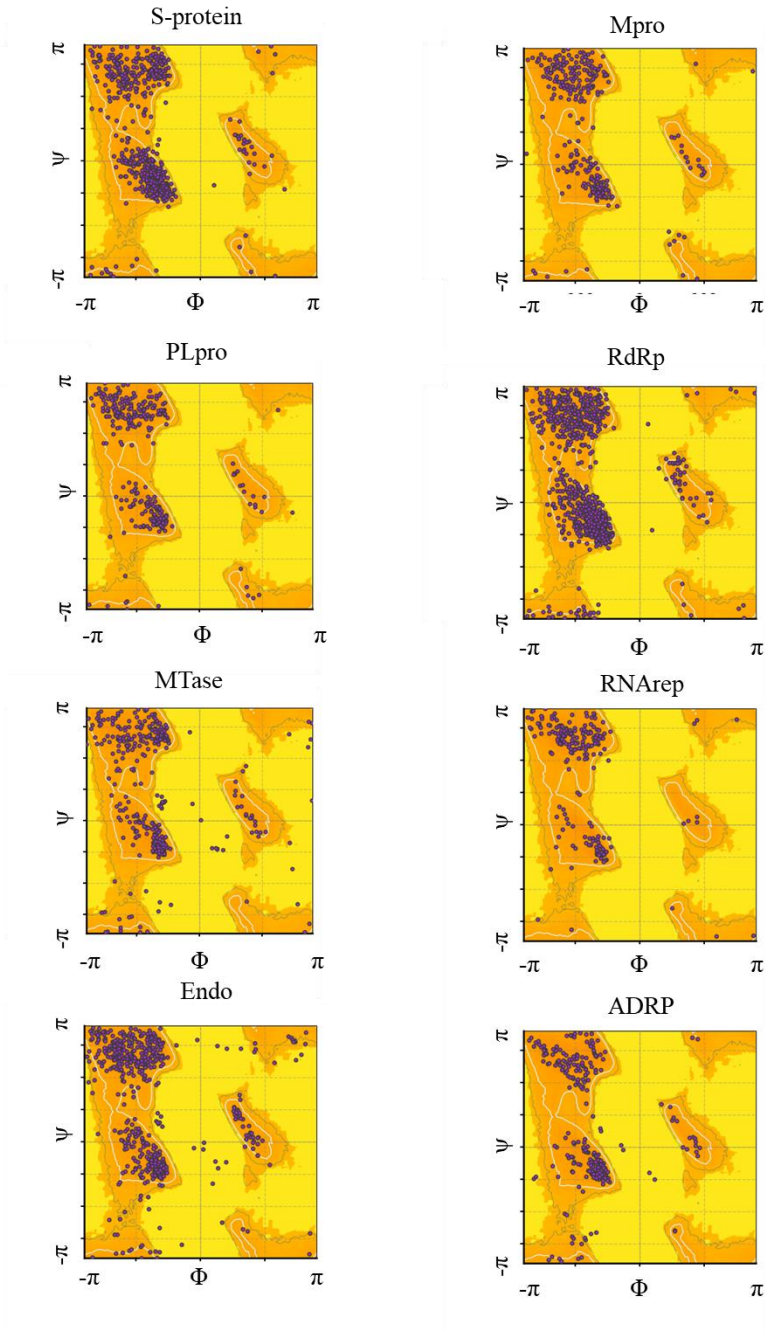

Figure S10. Ramachandran diagram illustrating stereochemical geometry of unligated SARS-CoV-2 complex.

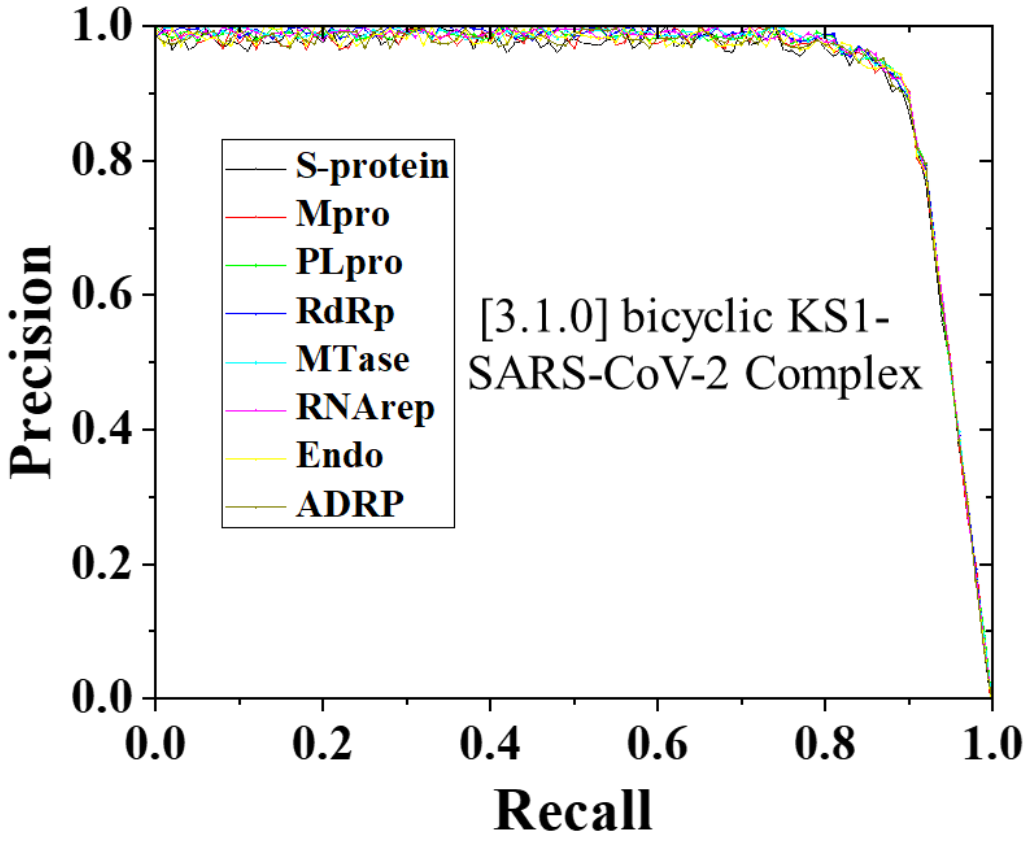

Figure S11. Precision-recall plot during allosteric docking classification of [3.1.0] bicyclic KS1 compound inhibiting protein targets using deep learning process for 200 epochs.

Figure S12. Snapshot of wearable lab onchip in accommodating dual microprocessors.

(KS1 inhibitor)	CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2N C(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F
(KS2 inhibitor)	FC1=CC2CCC2=C(F)C1N1ON(C2C(C#N)C3N C(=O)C3C2=O)C2C1C1CCC1C2(F)F
(KS3 inhibitor)	CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F
(KS4 inhibitor)	CC(C)C1(C#N)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F
(KS5 inhibitor)	CC(C)(C)C1(C2C1N(ON2C1C(C#N)C2NC(=O)C2C 1=O)C1C(F)=C(F)CC(F)=C1F)C(C)(C)C
(KS6 inhibitor)	CC1CC(N(C1C)C1OC2OC(NC22C1C2(C)C)C(F)(F)F)C(=O)NC(CC1CCNC1=O)C#N
(KS7 inhibitor)	[H]C12CN(C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)C)C(=O)C(NC(F)=O)C(C)(C)C
(KS8 inhibitor)	[H]C12N(ON(C3CC(F)C(F)C(F)N3)C1([H])C2(C(C)C)C(C)C)C1C(=O)C(=O)N2CNC(C#N)C12N
(KS9 inhibitor)	CNC1CC(C=O)C1C(O)NC(=O)N1ON(C2C(F)=C(F)C C(F)=C2F)[C@]23CC[C@]12CC3
(KS10 inhibitor)	CCN(C1NC2C(F)C(F)C(F)C2O1)C(=O)C1C(C) CC(C)C1C(=O)C(NC1OC1NC)C#N
(KS11 inhibitor)	CCC1C(CC)N(ON1C1C(F)=C(F)CC(F)=C1F) C(=O)NC(O)C1C(CC1C=O)NC
(KS12 inhibitor)	CC(C)C1(C(C)C)C23CC12N(ON3C1C(C#N)C 2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F

Figure S13: List of main **KS** inhibitors with their SMILES string output in lab onchip.

AI-Designing Drugs	Drug analog
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(C)CC(F)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(F)CC(F)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(F)C2C1=O)C1C(O)=C(F)CC(F)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(F)C2C1=O)C1C(F)=C(O)CC(F)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(F)C2C1=O)C1C(F)=C(O)CC(O)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(C#N)C2NC(F)C2C1=O)C1C(O)=C(O)CC(O)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(F)C2C(NC2=O)C1C#N)C1C(O)=C(F)CC(F)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(F)C2C(NC2=O)C1C#N)C1C(O)=C(F)CC(O)=C1F	KS1
CC(C)C1(C(C)C)C2C1N(ON2C1C(F)C2C(NC2=O)C1C#N)C1C(O)=C(O)CC(F)=C1O	KS1
CC(C)C1(C(C)C)C2C1N(CN2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS1
OC1=C2CCC2C=C(F)C1N1ON(C2C(C#N)C3NC(=O)C3C2=O)C2C1C1CCC1C2(F)F	KS2
OC1=CC2CCC2=C(O)C1N1ON(C2C(C#N)C3NC(=O)C3C2=O)C2C1C1CCC1C2(F)F	KS2
OC1=CC2CCC2=C(O)C1N1ON(C2C(C#N)C3NC(=O)C3C2=O)C2C1C1CCC1C2(F)F	KS2
CC1CC2C=C(F)C(N3ON(C4C(C#N)C5NC(=O)C5C4=O)C4C3C3CCC3C4(F)F)C(O)=C12	KS2
OC1(F)C2CCC2C2C1N(ON2C1C(F)=CC2CCC2=C1F)C1C(C#N)C2NC(=O)C2C1=O	KS2
(O)C2CCC2C2C1N(ON2C1C(F)=CC2CCC2=C1F)C1C(C#N)C2NC(=O)C2C1=O	KS2
FC1C2C(NC2=O)C(C#N)C1N1ON(C2C3CCC3C(F)(F)C12)C1C(F)=CC2CCC2=C1F	KS2
FC1NC2C1C(=O)C(C2C#N)N1ON(C2C3CCC3C(F)(F)C12)C1C(F)=CC2CCC2=C1F	KS2
FC1=CC2CCC2=C(F)C1N1CN(C2C(C#N)C3NC(=O)C3C2=O)C2C1C1CCC1C2(F)F	KS2
FC1=CC2CCC2=C(F)C1N1ON(C2C(C#N)C3=NC(=O)C3C2=O)C2C1C1CCC1C2(F)F	KS2
CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(O)=C(F)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(O)=C(O)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(O)=C(O)CC(O)=C1F	KS3
CC1CCC(F)C11C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(C)CC(F)=C1F	KS3
CC1=C(C)C(N2ON(C3C2C32C(F)CCC2F)C2C(C#N)C3NC(=O)C3C2=O)C(F)=C(F)C1	KS3
CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2NC(F)C2C1=O)C1C(O)=C(F)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(ON2C1C(F)C2C(F)NC2C1C#N)C1C(O)=C(O)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(CN2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(ON2C1C(C=N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS3
CC1CCC(C)C11C2C1N(ON2C1C(C#N)C2=NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1	KS3
CC(C)C1(C#N)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(O)=C(F)CC(F)=C1F	KS4
CC(C)C1(C#N)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(O)=C(F)CC(O)=C1F	KS4
CC(C)C1(C=N)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS4
OC1=C(F)C(N2ON(C3C2C3(C#N)C(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(O)=C(F)C1	KS4
CC(C)C1(C#N)C2C1N(ON2C1C(O)C2C(NC2=O)C1C#N)C1C(F)=C(F)CC(F)=C1F	KS4
CC(C)C1(C#N)C2C1N(ON2C1C(C#N)C2NC(O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS4
CC1=C(F)C(N2ON(C3C2C3(C#N)C(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(C)=C(F)C1	KS4
CC(F)C1(C#N)C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(F)CC(F)=C1F	KS4

CCC1(C2C1N(ON2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F)C(C)=N	KS4
CC(C)C1(C#N)C2C1N(CN2C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(F)CC(F)=C1F	KS4
CC1=C(F)C(N2ON(C3C2C3(C#N)C(C)(C)F)C2C(C#N)C3NC(=O)C3C2=O)C(F)=C(F)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C#N)C(C)(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(F)=C(F)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C#N)C(F)(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(C)=C(F)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C#N)C(F)(F)F)C2C(F)C3C(NC3=O)C2C#N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C=N)C(F)(F)F)C2C(F)C3C(NC3=O)C2C#N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C=N)C(F)(F)F)C2C(F)C3C(NC3=O)C2C=N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(C=N)C(F)(F)F)C2C(F)C3C(=O)N=C3C2C=N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(CF)C(N)(F)F)C2C(F)C3C(=O)N=C3C2C=N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(CF)C(N)(F)F)C2C(F)C3C(=O)N=C3C2C=N)C(C)=C(O)C1	KS5
CC1=C(C)C(N2ON(C3C2C3(CF)C(N)(F)F)C2C(C=N)C3=NC(F)C3C2=O)C(C)=C(O)C1	KS5
CC1=C(F)CC(F)=C(F)C1N1ON(C2C1C2(C(C)(C)C)C(C)(C)F)C1C(C#N)C2NC(=O)C2C1=O	KS6
CC1=C(C)C(N2ON(C3C2C3(C(C)(C)C)C(C)(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(F)=C(F)C1	KS6
CC1=C(C)C(N2ON(C3C2C3(C(C)(C)C)C(F)(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(F)=C(C)C1	KS6
CC1=C(C)C(N2ON(C3C2C3(C(C)(C)F)C(F)(F)F)C2C(C#N)C3NC(=O)C3C2=O)C(C)=C(C)C1	KS6
CC1=C(C)C(N2ON(C3C2C3(C(C)(O)F)C(F)(F)F)C2C(C#N)C3NC(=O)C3C2=C)C(C)=C(C)C1	KS6
CC1=C(C)C(N2ON(C3C2C3(C(C)(O)O)C(F)(F)F)C2C(C#N)C3NC(F)C3C2=C)C(C)=C(C)C1	KS6
CC1=C(C)C(N2CN(C3C2C3(C(O)(O)O)C(F)(F)F)C2C(C#N)C3NC(F)C3C2=C)C(C)=C(C)C1	KS6
CC1=C(C)C(N2CN(C3C2C3(C(C)(F)F)C(O)(O)O)C2C(F)C3C(F)NC3C2C#N)C(C)=C(C)C1	KS6
CC1=C(C)C(N2CN(C3C2C3(C(C)(C)F)C(O)(O)O)C2C(F)C3C(F)NC3C2C#N)C(C)=C(C)C1	KS6
CC1NC2C1C(F)C(C2C#N)N1CN(C2C1C2(C(C)(C)F)C(O)(O)O)C1C(C)=C(C)CC(F)=C1C	KS6
CC1CC(N(C1C)C1OC2CC(NC22C1C2(C)C)C(F)(F)F)C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1CC(N(C1C)C1CC2CC(NC22C1C2(C)C)C(F)(F)F)C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1CC2CC(C3C(F)(F)C23N1)N1C(C)C(C)CC1C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1CC2CC(C3C(C)(F)C23N1)N1C(F)C(C)CC1C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1CC2CC(C3C(C)(C)C23N1)N1C(F)C(F)CC1C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1CC2OC(C3C(C)(C)C23N1)N1C(F)C(F)CC1C(=O)NC(CC1CCNC1=O)C#N	KS7
CC1NC23C(C(OC2O1)N1C(F)C(F)CC1C(=O)NC(CC1CCNC1=O)C#N)C3(C)C	KS7
CC1NC23C(C(OC2O1)N1C(F)C(F)CC1C(O)NC(CC1CCNC1=O)C#N)C3(C)C	KS7
CC1NC23C(C(OC2O1)N1C(F)C(O)CC1C(O)NC(CC1CCNC1F)C#N)C3(C)C	KS7
CC(NC(CC1CCNC1F)C#N)C1CC(O)C(F)N1C1OC2OC(C)NC22C1C2(C)O	KS7
[H]C12CN(C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)C)C(=O)C(NC(C)=O)C(C)(C)F	KS8
[H]C12C(N(CC1(F)C2(C)C)C(=O)C(NC(C)=O)C(C)(C)C)C(=O)NC(C1NC1=O)C(=O)C1NS1	KS8
[H]C12CN(C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1(F)C2(C)C)C(=O)C(NC(C)=O)C(C)(C)C	KS8
[H]C12CN(C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)F)C(=O)C(NC(C)=O)C(C)(C)C	KS8
[H]C12CN(C(C(=O)NC(C(F)C3NS3)C3NC3=O)C1([H])C2(C)O)C(=O)C(NC(C)=O)C(C)(C)C	KS8
[H]C12CN(C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)C)C(=O)C(NC(O)F)C(C)(C)C	KS8
[H]C12CN(C(O)C(NC(O)F)C(C)(C)C)C(C(=O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)C	KS8
[H]C12CN(C(O)C(NC(O)F)C(C)(C)C)C(C(O)NC(C3NC3=O)C(=O)C3NS3)C1([H])C2(C)C	KS8
[H]C12CN(C(O)C(NC(O)F)C(C)(C)C)C(C(O)NC(C3NC3O)C(=O)C3NS3)C1([H])C2(C)C	KS8
[H]C12CN(C(O)C(NC(O)F)C(C)(C)C)C(C(O)NC(C(O)C3NS3)C3NC3O)C1([H])C2(C)C	KS8
[H]C12N(ON(C3CC(C)C(F)C(F)N3)C1([H])C2(C(C)C)C(C)C)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9

[H]C12N(ON(C3CC(F)C(C)C(F)N3)C1([H])C2(C(C)C)C(C)C)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(ON(C3CC(F)C(F)C(C)N3)C1([H])C2(C(C)C)C(C)C)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(ON(C3CC(C)C(F)C(F)N3)C1([H])C2(C(C)C)C(C)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(ON(C3CC(C)C(C)C(F)N3)C1([H])C2(C(C)C)C(F)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(ON(C3CC(C)C(C)C(C)N3)C1([H])C2(C(C)F)C(F)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(CN(C3CC(C)C(C)C(C)N3)C1([H])C2(C(O)F)C(F)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(CN(C3C(=O)C(=O)N4CNC(C#N)C34N)C1(O)C2(C(C)F)C(F)F)C1CC(C)C(C)C(C)N1	KS9
[H]C12N(CN(C3CC(C)C(C)C(C)N3)C1(O)C2(C(C)F)C(F)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
[H]C12N(CN(C3CC(C)C(O)C(C)N3)C1([H])C2(C(C)F)C(F)F)C1C(=O)C(=O)N2CNC(C#N)C12N	KS9
CNC1CC(C=O)C1C(F)NC(=O)N1ON(C2C(O)=C(F)CC(F)=C2F)[C@]23CC[C@]12CC3	KS10
CNC1CC(C=O)C1C(F)NC(=O)N1ON(C2C(O)=C(F)CC(F)=C2F)[C@]23CC[C@]12CC3	KS10
CNC1CC(C=O)C1C(F)NC(=O)N1ON(C2C(F)=C(O)CC(F)=C2F)[C@]23CC[C@]12CC3	KS10
CNC1CC(CO)C1C(F)NC(=O)N1ON(C2C(F)=C(O)CC(F)=C2F)[C@]23CC[C@]12CC3	KS10
CNC1CC(F)C1C(=O)NC(=O)N1ON(C2C(F)=C(O)CC(F)=C2F)[C@]23CC[C@]12CC3	KS10
CNC1CC(C)C1C(=O)NC(O)N1ON(C2C(F)=C(F)CC(F)=C2F)[C@@]23CC[C@@]12CC3	KS10
CNC1CC(C)C1C(O)NC(O)N1ON(C2C(F)=C(F)CC(F)=C2F)[C@@]23CC[C@@]12CC3	KS10
CNC1CC(C)C1C(O)NC(O)N1ON(C2C(F)=C(C)CC(F)=C2F)[C@@]23CC[C@@]12CC3	KS10
CNC1CC(C)C1C(O)NC(O)N1ON(C2C(C)=C(C)CC(F)=C2F)[C@@]23CC[C@@]12CC3	KS10
CNC1CC(F)C1C(O)NC(O)N1ON(C2C(C)=C(C)CC(F)=C2F)[C@@]23CC[C@@]12CC3	KS10
CNC1OC1NC(C#N)C(=O)C1C(C)CC(C)C1C(=O)N(CF)C1NC2C(F)C(F)C(C)C2O1	KS11
CCN(C1NC2C(F)C(F)C(C)C2O1)C(=O)C1C(F)CC(C)C1C(=O)C(NC1OC1NC)C#N	KS11
CCN(C1NC2C(F)C(F)C(C)C2O1)C(=O)C1C(C)CC(F)C1C(=O)C(NC1OC1NC)C#N	KS11
CCN(C1NC2C(F)C(F)C(C)C2O1)C(=O)C1C(C)CC(C)C1C(=O)C(NC1OC1NF)C#N	KS11
CCN(C1NC2C(F)C(F)C(F)C2O1)C(=O)C1C(C)CC(O)C1C(=O)C(NC1CC1NC)C#N	KS11
CCN(C1NC2C(F)C(F)C(F)C2O1)C(=O)C1C(C)CC(O)C1C(=O)C(NC1CC1NC)C#N	KS11
CCNC1CC1NC(C#N)C(=O)C1C(C)CC(C)C1C(=O)N(CO)C1NC2C(F)C(F)C(F)C2O1	KS11
CCNC1CC1NC(C#N)C(=O)C1C(C)CC(C)C1C(=O)N(CO)C1NC2C(F)C(F)C(F)C2O1	KS11
CCN(C1NC2C(O)C(F)C(F)C2O1)C(=O)C1C(O)CC(C)C1C(=O)C(NC1CC1NC)C#N	KS11
CCN(C1NC2C(O)C(F)C(F)C2O1)C(=O)C1C(C)CC(O)C1C(=O)C(NC1CC1NC)C#N	KS11
CCC1C(CC)N(ON1C1C(C)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NC	KS12
CCC1C(CC)N(ON1C1C(F)=C(C)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NC	KS12
CCC1C(CC)N(ON1C1C(F)=C(C)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NC	KS12
CCC1C(CF)N(ON1C(=O)NC(O)C1C(CC1C=O)NC)C1C(C)=C(F)CC(F)=C1F	KS12
CCC1C(CF)N(ON1C1C(C)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NC	KS12
CCC1C(CC)N(ON1C1C(C)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NF	KS12
CCC1C(CC)N(ON1C1C(C)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(CC1C=O)NF	KS12
CCC1C(CC)N(ON1C1C(F)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(CC1=N)C=O	KS12
CCC1C(CC)N(ON1C1C(F)=C(F)CC(F)=C1F)C(=O)NC(O)C1C(N)CC1CO	KS12
CCC1C(CC)N(ON1C(O)NC(O)C1C(N)CC1CO)C1C(F)=C(F)CC(F)=C1F	KS12
CCC1C(CC)N(CN1C(O)NC(O)C1C(N)CC1CO)C1C(F)=C(F)CC(F)=C1F	KS13
CC(C)C1(C(C)C)C23CC12N(ON3C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(C)CC(F)=C1C	KS13
CC(C)C1(C(C)C)C23CC12N(ON3C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(C)CC(F)=C1F	KS13
CC(C)C1(C(C)C)C23CC12N(ON3C1C(C#N)C2NC(=O)C2C1=O)C1C(F)=C(C)CC(F)=C1F	KS13

CC(C)C1(C(C)F)C23CC12N(ON3C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(F)CC(F)=C1F	KS13
CC(F)C1(C(F)F)C23CC12N(ON3C1C(C#N)C2NC(=O)C2C1=O)C1C(C)=C(C)CC(C)=C1F	KS13
CC1=C(C)C(N2ON(C3C(C#N)C4NC(=O)C4C3=O)C34CC23C4(C(F)F)C(F)F)C(C)=C(C)C1	KS13
CC1=C(C)C(N2ON(C3C(C#N)C4NC(O)C4C3=O)C34CC23C4(C(F)F)C(F)F)C(C)=C(C)C1	KS13
CC1=C(C)C(N2ON(C3C(O)C4C(O)NC4C3C#N)C34CC23C4(C(F)F)C(F)F)C(C)=C(C)C1	KS13
CC1=C(C)C(N2ON(C3C(O)C4C(O)N=C4C3C#N)C34CC23C4(C(F)F)C(F)F)C(C)=C(C)C1	KS13

Figure S14: List of main KS inhibiting analogs with their SMILES string output in the lab-on-a-chip.

Video S1: Simulated [3.1.0] bicyclic **KS1** inhibitor (RO5 with less than 10 rotational bonds) bound to allosteric sites of SARS-CoV-2 RNA replicase.

Video S2: Simulated [4.2.0] tricyclic **KS2** inhibitor bound to active dyad of SARS-CoV-2 main protease.

Video S3: Demonstration of lab-on-a-chip activation.