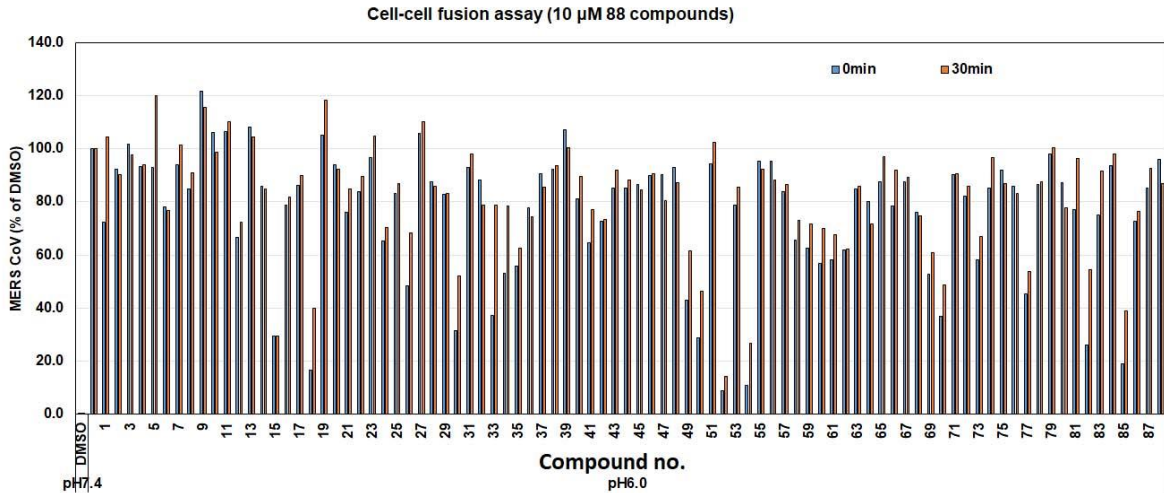
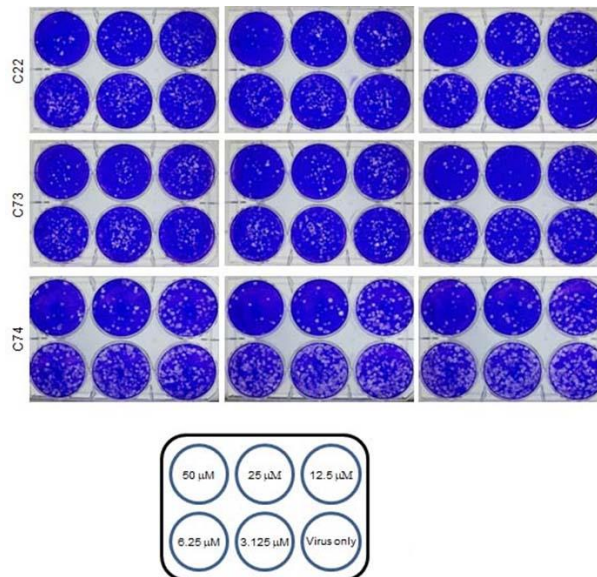


Supplemental Data



Supplementary Fig. 1. Effect of the time of addition of 88 compounds on MERS CoV cell-cell fusion assay. The X-axis represents the compound number. The Y-axis displays the effect of compounds on the DSP (RL) activity normalized to DMSO (control). Compounds were either incubated with MERS CoV spike expression cells for 30 min before addition of CD26/TMPRSS2 expressing cells (orange) or at the time of addition of CD26/TMPRSS2 expression cells (blue).



Supplementary Fig. 2. Inhibitory effect of compounds 22, 73, and 74 on MERS CoV infection in Vero cells. MERS CoV was pre-incubated with two-fold serially diluted compounds 22, 73, or C74 (n=3) for 30 min at 37°C. Vero cells were treated with the mixture of the virus and each compound and incubated for 4 days in DMEM/F12 containing 0.6% oxidoid agar. The plaques were observed by staining with crystal violet and counted.

Supplementary Table 1. The docking scores (of -8.0 or higher) and IDs of 88 compounds arranged by descending order and their corresponding binding pocket.

Compound no	ID	Docking score	Pocket
22	24071746	-8.951	P _{HR2}
74	F2282-0127*	-8.923	P _{HR2}
73	98931397	-8.916	P _{HR2}
75	F2282-0124*	-8.898	P _{HR2}
4	6505627	-8.769	P _{HR2}
76	F2282-0128*	-8.749	P _{HR2}
58	57295921	-8.748	P _{HR2}
77	F2282-0139*	-8.738	P _{HR2}
35	30625545	-8.66	P _{HR2}
78	F2068-0373*	-8.627	P _{HR2}
56	54164606	-8.611	P _{HR2}
49	45992201	-8.569	P _{HR2}
44	43459696	-8.564	P _{HR2}
79	F5788-2664*	-8.55	P _{HR2}
80	F2323-0673*	-8.526	P _{HR2}
18	13211152	-8.521	P _{HR2}
26	25947446	-8.508	P ₁
81	F2375-0556*	-8.506	P ₁
82	F0556-0537*	-8.497	P ₁
46	43697919	-8.494	P _{HR2}
15	10574148	-8.486	P _{HR2}
62	71147511	-8.486	P _{HR2}
21	15188232	-8.466	P _{HR2}
42	41877966	-8.46	P _{HR2}
50	46273925	-8.439	P _{HR2}
72	90291121	-8.439	P _{HR2}
55	53357526	-8.437	P _{HR2}
67	75149556	-8.427	P _{HR2}
17	11141423	-8.426	P _{HR2}
83	F0556-0674*	-8.391	P ₁
43	42864544	-8.382	P _{HR2}
37	31156947	-8.375	P _{HR2}
28	27079003	-8.354	P _{HR2}
84	F2323-1532*	-8.35	P _{HR2}
51	46293002	-8.317	P _{HR2}
32	29174861	-8.309	P _{HR2}
60	66172782	-8.307	P _{HR2}
54	51728554	-8.295	P _{HR2}
63	72092261	-8.293	P _{HR2}
40	41018344	-8.287	P _{HR2}
68	76861747	-8.269	P _{HR2}
39	40027187	-8.266	P _{HR2}
69	78170314	-8.263	P _{HR2}

71	89995246	-8.259	P _{HR2}
9	7782185	-8.239	P _{HR2}
19	13575208	-8.235	P _{HR2}
61	67801543	-8.23	P _{HR2}
70	82523386	-8.224	P _{HR2}
48	45671272	-8.217	P _{HR2}
1	5925757	-8.213	P _{HR2}
27	26680773	-8.193	P _{HR2}
20	13693110	-8.19	P _{HR2}
57	56977994	-8.189	P _{HR2}
31	29141135	-8.181	P _{HR2}
66	74695372	-8.179	P _{HR2}
53	47501212	-8.177	P _{HR2}
24	24715372	-8.171	P ₂
3	6434576	-8.164	P _{HR2}
38	38776116	-8.161	P _{HR2}
47	44235692	-8.159	P _{HR2}
52	46965943	-8.157	P _{HR2}
5	6824099	-8.143	P _{HR2}
14	10066614	-8.137	P _{HR2}
85	F5912-0718*	-8.13	P _{HR2}
30	28880861	-8.12	P _{HR2}
45	43556300	-8.112	P _{HR2}
86	F2323-0674*	-8.108	P _{HR2}
23	24213373	-8.1	P _{HR2}
59	59003854	-8.1	P ₂
25	25722219	-8.099	P _{HR2}
87	F5791-1891*	-8.093	P _{HR2}
64	74110675	-8.088	P _{HR2}
88	F6125-2274*	-8.088	P _{HR2}
65	74576651	-8.077	P _{HR2}
11	7908899	-8.076	P _{HR2}
13	7939034	-8.05	P _{HR2}
34	29401144	-8.037	P _{HR2}
41	41042980	-8.032	P _{HR2}
29	27536983	-8.03	P _{HR2}
33	29194995	-8.029	P _{HR2}
8	7671108	-8.004	P _{HR2}
12	7909919	-8.001	P ₁
2	5941181	-8.001	P ₁
7	7594379	-8.001	P _{HR2}
6	7398628	-8	P _{HR2}
10	7906284	-8	P _{HR2}
16	11095275	-8	P _{HR2}
36	31091692	-8	P _{HR2}

Compounds marked with (*) were supplied by Life Chemicals, the rest of compounds were supplied by Chembridge.

Supplementary Table 2. Effect of the time of addition of 88 compounds on MERS CoV cell-cell fusion assay. Compounds were either incubated with MERS CoV spike expression cells for 30 min before addition of CD26/TMPRSS2 expressing cells or at the time of addition of CD26/TMPRSS2 expression cells.

	0min		30min	
	AVERAG E	%	AVERAG E	%
DMSO	7.96875	0.399593	7.09375	0.359604
DMSO	1994.219	100	1972.656	100
1	1440	72.20873	2059	104.377
2	1840	92.26671	1781	90.28436
3	2032	101.8945	1925	97.58416
4	1861	93.31975	1856	94.08634
5	1856	93.06903	2368	120.0412
6	1557	78.07569	1514	76.74931
7	1877	94.12207	2000	101.3861
8	1691	84.79511	1797	91.09545
9	2427	121.7018	2278	115.4788
10	2117	106.1569	1947	98.69941
11	2123	106.4577	2176	110.3081
12	1328	66.59249	1429	72.4404
13	2155	108.0624	2059	104.377
14	1712	85.84815	1675	84.91089
15	586	29.38494	581	29.45267
16	1568	78.62728	1611	81.66653
17	1717	86.09888	1776	90.03089
18	331	16.59798	784	39.74337
19	2096	105.1038	2331	118.1655
20	1877	94.12207	1819	92.21069
21	1520	76.22032	1675	84.91089
22	1675	83.99279	1765	89.47327
23	1925	96.52903	2069	104.884
24	1301	65.23858	1386	70.26059
25	1659	83.19047	1717	87.04
26	965	48.38988	1344	68.13149
27	2107	105.6554	2171	110.0547
28	1744	87.45279	1691	85.72198
29	1653	82.8896	1643	83.28871
30	629	31.54117	1029	52.16317
31	1851	92.8183	1931	97.88832
32	1760	88.25511	1552	78.67564

33	741	37.15741	1557	78.92911
34	1056	52.95307	1546	78.37149
35	1114	55.86147	1237	62.70733
36	1552	77.82496	1466	74.31604
37	1808	90.66207	1685	85.41782
38	1840	92.26671	1845	93.52871
39	2134	107.0093	1979	100.3216
40	1621	81.28496	1765	89.47327
41	1290	64.68699	1520	77.05347
42	1450	72.71018	1450	73.50495
43	1701	85.29656	1813	91.90653
44	1696	85.04584	1739	88.15525
45	1723	86.39975	1669	84.60673
46	1792	89.85975	1787	90.58851
47	1797	90.11048	1584	80.29782
48	1856	93.06903	1723	87.34416
49	853	42.77364	1216	61.64277
50	570	28.58262	917	46.48554
51	1883	94.42294	2021	102.4507
52	176	8.825511	277	14.04198
53	1573	78.87801	1685	85.41782
54	213	10.68087	528	26.76594
55	1899	95.22526	1819	92.21069
56	1904	95.47599	1744	88.40871
57	1675	83.99279	1707	86.53307
58	1306	65.48931	1440	72.99802
59	1248	62.5809	1413	71.62931
60	1130	56.66379	1381	70.00713
61	1162	58.26843	1333	67.57386
62	1232	61.77858	1226	62.1497
63	1691	84.79511	1691	85.72198
64	1600	80.23192	1413	71.62931
65	1744	87.45279	1915	97.07723
66	1563	78.37656	1813	91.90653
67	1744	87.45279	1760	89.2198
68	1514	75.91945	1477	74.87366
69	1050	52.6522	1200	60.83168
70	736	36.90668	960	48.66535
71	1797	90.11048	1787	90.58851
72	1637	82.08728	1696	85.97545
73	1157	58.01771	1322	67.01624
74	1696	85.04584	1909	96.77307
75	1835	92.01598	1712	86.78653
76	1712	85.84815	1643	83.28871
77	906	45.43132	1061	53.78535

78	1723	86.39975	1728	87.59762
79	1952	97.88294	1984	100.575
80	1739	87.20207	1536	77.86455
81	1536	77.02264	1899	96.26614
82	517	25.92494	1077	54.59644
83	1498	75.11714	1808	91.65307
84	1867	93.62062	1931	97.88832
85	378	18.95479	768	38.93228
86	1450	72.71018	1509	76.49584
87	1701	85.29656	1829	92.71762
88	1915	96.02758	1717	87.04

Supplementary Table 3. In silico pharmacokinetic and other ADME descriptors of 15 compounds (10 compounds from the top docking score + 5 compounds with promising results from cell-cell fusion assay).

molecule	mol_MW ^a	donorHB ^b	accept HB ^c	Human Oral Absorption % ^d	Rule of Five ^e	QLogP o/w ^f	#rotor ^g	QLogS ^h	QLogHERG ⁱ	QLogKp ^j	QPPCa ^k	QLogBB ^l	QPPMDCK ^m	QLogKhsa ⁿ	SASA ^o	FISA ^p	Carcinogenicity in mouse	Carcinogenicity in rat	Ames toxicity test
C22	379.4	2.0	5.7	100.0	0.0	4.1	5.0	-6.3	-6.5	-2.4	514.6	-1.1	436.8	0.6	703.7	135.4	positive	negative	mutagen
C74	462.0	0.0	9.0	89.8	0.0	2.4	5.0	-3.8	-3.6	-2.7	532.6	-0.8	626.0	-0.5	675.3	133.3	negative	negative	non-mutagen
C73	597.7	1.0	7.8	82.5	2.0	6.1	4.0	-9.0	-5.6	-2.4	355.2	-0.8	2391.0	1.1	902.5	130.8	negative	negative	non-mutagen
C75	441.5	0.0	9.0	88.7	0.0	2.2	5.0	-3.6	-3.6	-2.7	532.2	-1.0	253.4	-0.5	683.2	133.4	negative	negative	non-mutagen
C4	358.4	1.0	5.5	100.0	0.0	3.9	5.0	-5.8	-7.1	-2.0	488.5	-1.2	228.1	0.5	681.6	137.8	negative	negative	mutagen
C76	455.6	0.0	9.0	89.5	0.0	2.4	5.0	-3.7	-3.2	-2.9	532.7	-0.9	253.7	-0.4	686.3	133.3	negative	negative	non-mutagen
C58	578.8	0.0	10.3	71.3	2.0	5.7	9.0	-6.6	-9.9	-4.5	114.6	-0.2	58.3	1.0	1038.0	77.0	negative	positive	non-mutagen
C77	457.5	0.0	9.8	87.6	0.0	2.0	6.0	-3.3	-3.8	-2.6	529.2	-1.0	260.7	-0.7	700.2	132.2	negative	negative	non-mutagen
C35	450.6	2.0	6.3	89.8	1.0	5.1	9.0	-7.1	-5.8	-1.9	371.9	-1.4	464.3	0.8	865.7	128.0	negative	negative	mutagen
C78	474.5	0.0	10.0	88.0	0.0	2.7	5.0	-4.8	-5.4	-2.5	342.7	-1.2	388.4	-0.5	790.7	140.7	negative	negative	mutagen
C60	536.7	0.0	9.5	78.1	1.0	4.7	9.0	-4.9	-8.7	-3.9	108.3	0.1	92.4	0.5	975.4	57.5	negative	positive	non-mutagen
C61	498.6	2.0	7.0	95.6	1.0	6.0	8.0	-7.6	-9.1	-2.4	379.0	-0.4	347.0	1.2	899.2	85.9	negative	positive	mutagen
C69	558.6	2.0	9.7	80.2	2.0	5.6	13.0	-8.1	-7.9	-1.6	406.2	-2.1	186.8	0.8	972.8	146.3	negative	positive	non-mutagen
C26	482.6	2.0	10.7	100.0	0.0	3.8	7.0	-6.2	-7.9	-3.4	484.6	-0.3	373.7	0.4	894.4	74.6	positive	positive	mutagen
C33	428.6	2.0	6.5	90.5	1.0	5.2	8.0	-6.7	-8.7	-2.7	368.7	-0.6	186.1	1.0	849.4	87.1	negative	negative	non-mutagen

^aMolecular weight of the molecule, acceptable range < 500. ^bHydrogen bond donor, acceptable range <5. ^cHydrogen bond acceptor, acceptable range <10. ^dOral absorption % in human, >80% is high, <25% is poor. ^eThe number of violations of Lipinski's rule of five, the recommended maximum number is 3. ^fPredicted octanol/water partition coefficient (QLogP o/w) acceptable range <5. ^gNumber of rotatable bonds, acceptable range 0-15. ^hPredicted aqueous solubility (QLogS), acceptable range <0.5. ⁱPredicted IC50 value for blockage of HERG K

+ channels (QPlogHERG) acceptable range <-0.5. ^jPredicted skin permeability (QPlogKp), acceptable range -8.0-1.0. ^kApparent Caco-2 cell permeability, acceptable range <25 poor, >500 great. ^lPredicted brain/blood partition coefficient, acceptable range -3-1.02. ^mPredicted apparent MDCK cell permeability, acceptable range >500 is high, <25 is poor. ⁿbinding to human serum albumin, , acceptable range -1.5-1.5. ^oTotal solvent accessible surface area, acceptable range 300-1000. ^pHydrophilic component of the SASA, acceptable range 7-330.