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Supporting Information

for

Design and selection of peptides to block the SARS-CoV-2 receptor binding domain by molecular docking

Kendra Ramirez-Acosta, Ivan A. Rosales-Fuerte, J. Eduardo Perez-Sanchez, Alfredo Nuñez-Rivera, Josue Juarez and Ruben D. Cadena-Nava

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Additional experimental data

Table S1: Summary of antiviral peptides used for initial docking; their known antiviral activity is listed. Information taken from the Antimicrobial Peptide Database (https://aps.unmc.edu/database/anti).

APD ID	PEPTIDE NAME	ACTIVITY
AP00013	Aurein 1.2	Anti-HIV
AP00023	Antiviral protein Y3	Inhibition of Tobacco Mosaic Virus (TMV)
AP00025	Alloferon 1	Inhibition of Herpes Simplex Virus (HSV)
AP00026	Lactoferricin B	Anti-HIV
AP00028	Tricyclic peptide RP 71955	Anti-HIV
AP00029	Cecropin A(1-8)-Magainin 2(4-12) hybrid peptide (CE-MA)	Anti-HIV
AP00058	Maximin 1	Anti-HIV
AP00060	Maximin 3	Anti-HIV
AP00061	Maximim 4	Anti-HIV
AP00062	Maximin 5	Anti-HIV
AP00074	Brevinin-1	Inhibition of Herpes Simplex Virus (HSV)
AP00094	Temporin A	Active against Channel Catfish Virus (CCV) and Frog Virus 3 (FV3)
AP00095	Temporin B	Inhibition of Herpes Simplex Virus (HSV)
AP00102	Thanatin	Inhibition of Tobacco Mosaic Virus (TMV)
AP00121	RANATUERIN 2P	Active against Channel Catfish Virus (CCV) and Frog Virus 3 (FV3)
AP00139	Cecropin A	Anti-HIV
AP00144	Magainin 2	Anti-HIV
AP00146	Melittin	Inhibition of Herpes Simplex Virus (HSV-1 & HSV-2)
AP00150	Indolicidin	Anti-HIV, Anti-HSV-1, Anti-HSV-2
AP00160	Dermaseptin-S4	Anti-HIV
AP00173	GNCP-2	Neutrophil. Generic antiviral activity is inferred.
AP00174	GNCP-1	Neutrophil. Generic antiviral activity is inferred.
AP00176	human neutrophil peptide-1	Anti-HIV. Active against Zika Virus.
AP00177	human neutrophil peptide-2	Inhibition of Herpes Simplex Virus (HSV-1 & HSV-2)
AP00178	human neutrophil peptide-3	Anti-HIV. Active against pseudo typed viruses expressing SARS-CoV-2 spike proteins.
AP00179	human neutrophil peptide-4	Anti-HIV
AP00180	human defensin 5	Inhibits non-enveloped BK virus infection.
AP00181	human defensin 6	Human defensin. Innate antiviral activity is expected.
AP00187	Rabbit neutrophil peptide 1	Neutrophil. Generic antiviral activity is inferred.
AP00188	Rabbit neutrophil defensin 2	Neutrophil. Generic antiviral activity is inferred.
AP00195	Protegrin 1	Anti-HIV
AP00211	Polyphemusin I	Anti-HIV
AP00212	Polyphemusin II	Anti-HIV
AP00214	Tachyplesin I	Anti-HIV, Anti-HSV-1, Anti-HSV-2
AP00217	Rabbit neutrophil defensin 3a	Neutrophil. Generic antiviral activity is inferred.
AP00218	Protegrin 2	Anti-HIV
AP00219	Protegrin 3	Anti-HIV
AP00220	Protegrin 4	Anti-HIV
AP00221	Protegrin 5	Anti-HIV
AP00222	RatNP-1	Neutrophil. Generic antiviral activity is inferred.
AP00223	RatNP-2	Neutrophil. Generic antiviral activity is inferred.
AP00224	RatNP-3	Neutrophil. Generic antiviral activity is inferred.

AP00225	RatNP-4	Neutrophil. Generic antiviral activity is inferred.
AP00240	Caerin 1.1	Anti-HIV
AP00241	Caerin 1.2	Anti-HIV
AP00242	Caerin 1.3	Anti-HIV
AP00243	Caerin 1.4	Anti-HIV
AP00244	Caerin 1.5	Anti-HIV
AP00245	Caerin 1.6	Anti-HIV
AP00246	Caerin 1.7	Anti-HIV
AP00257	Caerin 4.1	Anti-HIV
AP00272	mBD-1	A fusion construction of mBD-1 and mBD-3 is active against Influenza A Virus (IAV).
AP00274	Circulin A	Anti-HIV
AP00275	Circulin B	Anti-HIV
AP00281	mCRAMP	Inactivates Zika virus (ZIKV).
AP00283	Human beta defensin 3	Anti-HIV
AP00310	LL-37	Anti-HIV, Anti-HSV-1, Anti-HSV-2. Active against Zika virus and Dengue virus type 2.
AP00325	Uperin 3.6	Anti-HIV
AP00327	Uperin 7.1	Anti-HIV
AP00333	Mytilin B	Related to innate antiviral immune response.
AP00345	Caerin 1.10	Anti-HIV
AP00355	Ginkbilobin	Anti-HIV
AP00366	BMAP-27	Anti-HIV
AP00367	BMAP-28	Anti-HSV-1
AP00384	Ponericin L2	Anti-HIV
AP00399	Spinigerin	Anti-HIV
AP00405	RANATUERIN 6	Anti-HIV
AP00408	RANATUERIN 9	Anti-HIV
AP00445	RTD-1	Active against HIV and SARS virus.
AP00446	Alpha-basrubrin	Anti-HIV
AP00449	Alpha-MSH	Anti-HIV
AP00451	hBD-1	Anti-HIV
AP00473	Piscidin 1	Anti-HIV
AP00474	Piscidin 3	Active against Channel Catfish Virus (CCV).
AP00499	Gramicidin A	Anti-HIV
AP00505	human Histatin 5	Anti-HIV
AP00524	Human beta defensin 2 (monomero)	Anti-HIV
AP00549	Plectasin	Active against dengue virus type 2.
AP00553	Sesquin	Anti-HIV
AP00708	GF-17	Anti-HIV
AP00729	Kalata B1	Anti-HIV
AP00730	Kalata B8	Anti-HIV
AP00928	Subtilosin A	Active against HSV-1 and HSV-2.
AP01010	Latarcin 1	Active against dengue virus type 2.
AP01034	Palicourein	Anti-HIV
AP01049	Kalata B2	Anti-HIV
AP01058	Vhl-1	Anti-HIV

AP01065	Cycloviolacin O14	Anti-HIV
AP01136	Tricyclon A	Anti-HIV
AP01208	Retrocyclin-2	Anti-HIV
AP01382	TEWP	Active against Chandipura virus.
AP01406	EP5-1	Active against pseudorabies virus (PRV).
AP01580	Elafin	Anti-HIV, Anti-HSV-1, Anti-HSV-2
AP01654	Caerin 1.19	Anti-HIV
AP02095	SLPI	Anti-HIV
AP02099	RNase 3	Active against respiratory syncytial virus, group B (RSV-B).
AP02130	Antiviral lectin scytovirin	Anti-HIV
AP02131	Cyanovirin-N	Anti-HIV
AP02132	Microcystis viridis lectin	Anti-HIV
AP02133	Griffithsin	Anti-HIV
AP02146	ALFpm3	Active against White Spot Syndrome Virus (WSSV).
AP02337	RNase 2	Active against respiratory syncytial virus (RSV).

Table S2: Molecular docking scores of the 104 peptides using AutoDock Vina. The table shows the biochemical properties and the peptide's organism of origin.

Peptide	Sequence fragment	PDB/ *UNIPRO*	Residues	Sequence	Affinity (kcal/mol)	H bonds/ Residues	Organism of origin
Alpha-Basrubrin	1-20	P83186	20	GADFQECMKEHSQKQHQHQG	-5.2	0.95	*Basella alba*
Human Beta Defensin 3	27-45	1KJ6	19	EEQIGKCSTRGRKCCRRKK	-5.0	0.95	*Homo sapiens*
Sesquin	1-10	P84868	10	KTCENLADTY	-5.6	0.80	*Vigna unguiculata subsp. sesquipedalis*
Indolicidin	1-13	1G89	13	ILPWKWPWWPWRR	-8.0	0.77	*N/A*
BMAP-28	1-18	2NDC	18	GGLRSLGRKILRAWKKYGPIIVPIIRIG	-4.4	0.77	*Bos taurus*
GF-17	1-17	2L5M	17	GFKRIVQRIKDFLRNLV	-5.3	0.76	*synthetic construct*
Cyanovirin-N (70-80)	70-80	2EZM	10	AAECKTRAQQ	-5.3	0.73	*Nostoc ellipsosporum*
Protegrin 5	1-18	2NC7	18	RGGRLCYCRPRFCVCVGR	-7.2	0.72	*Sus scrofa (Porcine)*
MVL (94-110)	94-110	1ZHS	17	GQWRTIVEGVMSVIQIK	-5.0	0.71	*Microcystis viridis*
Temporin B	1-13	6GIL	13	LLPIVGNLLKSLL	-5.6	0.69	*Rana temporaria*
Dermaseptin-S4	1-13	2DD6	13	ALWKTLLKKVLKA	-5.5	0.69	*N/A*
MVL (74-87)	74-87	1ZHS	14	NDEAQKLGPQIAAS	-5.9	0.64	*Microcystis viridis*
MVL (16-34)	16-34	1ZHS	19	AEAQQVGPKIAAAHQGNFT	-5.8	0.63	*Microcystis viridis*
ACE2	21-44	6VYB	24	IEEQAKTFLDKFNHEAEDLFYQSS	-4.6	0.63	*Homo sapiens*
RTD-1	1-18	2LYF	18	GFCRCLCRRGVCRCICTR	-7.1	0.61	*N/A*
Spinigerin	1-25	1ZRV	25	HVDKKVADKVLLLKQLRIMRLLTRL	-5.0	0.6	*N/A*
RNase 3	33-42	2BZZ	10	NYQRRCKNQN	-6.0	0.6	*Homo sapiens*
Protegrin 1	1-18	1PG1	18	RGGRLCYCRRRFCVCVGR	-6.9	0.56	*Sus scrofa*
LL-37 core	17-29	2K6O	13	FKRIVQRIKDFLR	-4.8	0.54	*Homo sapiens*
Latarcin 1	1-26	2PCO	26	SMWSGMWRRKLKKLRNALKKKLKGEK	-4.5	0.54	*N/A*
Gramicidin A	1-15	1MAG	15	VGALAVVVWLWLWLW	-6.4	0.53	*Brevibacillus brevis*
MVL (64-82)	64-82	1ZHS	19	TDVLAGPLWSNDEAQKLGP	-5.0	0.53	*Microcystis viridis*
Piscidin 1	1-22	2JOS	22	FFHHIFRGIVHVGKTIHRLVTG	-5.3	0.5	*N/A*
Human Histatin 5	1-24	P15516	24	DSHAKRHHGYKRKFHEKHHSHRGY	-4.4	0.5	*Homo sapiens*
ALC (51-90)	51-90	2QT4	40	GPTYCWDEAKNPGGPNRCSNSKQCDGARTCSSSGFCQGTA	-5.1	0.5	*Scytonema varium*
MVL (35-42)	35-42	1ZHS	8	GQWTTVVE	-6.1	0.5	*Microcystis viridis*
MVL (60-74)	60-74	1ZHS	15	HEFKTDVLAGPLWSN	-4.6	0.47	*Microcystis viridis*
Tachyplesin 1	1-17	1WO1	17	KWCFRVCYRGICYRRCR	-5.9	0.47	*Tachypleus tridentatu*
Alpha-MSH	1-13	P01190	13	SYSMEHFRWGKP	-5.7	0.46	*Bos taurus*
MVL (10-30)	10-30	1ZHS	20	GPLWSNAEAQQVGPKIAAAH	-6.1	0.45	*Microcystis viridis*
MVL (42-57)	42-57	1ZHS	16	ESAMSVVEVELQVENT	-5.2	0.44	*Microcystis viridis*
Protegrin 2	1-16	2MUH	16	RGGRLCYCRRRFCVCV	-6.5	0.44	*Sus scrofa*
Protegrin 4	1-18	6QKF	18	RGGRLCYCRGWICFCVGR	-7.0	0.44	*Sus scrofa*
Ranatuerin-9	1-14	P82824	14	FLFPLITSFLSKVL	-5.8	0.43	*Lithobates catesbeianus*

Caerin 1.7	1-24	P62548	24	GLFKVLGSVAKHLLPHVAPVIAEK	-5.5	0.42	*Ranoidea xanthomera*
BMAP-27	1-27	2KET	27	GRFKRFRKKFKKLFKKLSPVIPLLHLG	-4.0	0.41	*Bos taurus*
Caerin 1.5	1-25	P56230	25	GLLSVLGSVVKHVIPHVVPVIAEHL	-4.3	0.4	*Ranoidea caerulea*
Retrocyclin-2	1-18	2LZI	18	GICRCICGRRICRCICGR	-7.4	0.39	*N/A*
Caerin 1.6	1-24	P62546	24	GLFSVLGAVAKHVLPHVVPVIAEK	-5.4	0.38	*Ranoidea xanthomera*
Piscidin 3	1-22	2MCX	22	FIHHIFRGIVHAGRSIGRFLTG	-5.7	0.36	*Morone chrysops*
Caerin 4.1	1-23	P56242	23	GLWQKIKSAAGDLASGIVEGIKS	-4.1	0.35	*Ranoidea caerulea*
Uperin 3.6	1-17	P82050	17	GVGDLIRKAVSVIKNIV	-5.0	0.35	*Litoria ewingii*
GNCP-2	1-32	P49112	32	GRRCICTTRTCRFPYRRLGTCLFQNRV YTFCC	-5.5	0.34	*Cavia porcellus*
NCP 2	61-93	P49112	32	GRRCICTTRTCRFPYRRLGTCLFQNRV YTFCC	-5.5	0.34	*Cavia porcellus*
RNase 3 (beta)	38-46	1H1H	9	CKNQNTFLR	-10.8	0.33	*Homo sapiens*
Griffithsin	19-36	2GTY	18	LSSIAVRLYSGSDAIIID	-5.3	0.33	*Griffithsia*
Caerin 1.1	1-25	P62568	25	GLLSVLGSVAKHVLPHVVPVIAEHL	-5.1	0.32	*Ranoidea splendida*
Caerin 1.19.3	7-25	P0C2A8	19	GSVAKHLLPHVAPIIAEKL	-5.6	0.32	*Ranoidea gracilenta*
Rabbit neutrophil peptide 1	1-31	P07469	31	ICACRRRFCPNSERFSGYCRVNGARYV RCCS	-4.4	0.32	*Oryctolagus cuniculus*
Corticostatin 1	61-91	P07469	31	ICACRRRFCPNSERFSGYCRVNGARYV RCCS	-4.4	0.32	*Oryctolagus cuniculus*
Uperin 7.1	1-13	P82050	13	GWFDVVKHIASAV	-5.6	0.31	*Litoria ewingii*
Ranatuerin-6	1-13	P82821	13	FISAIASMLGKFL	-6.6	0.31	*Lithobates catesbeianus*
Rabbit neutrophil defensin 2	1-32	P07468	32	RCVCRKQLLCSYRERRIGDCKIRGVRF PFCCP	-4.4	0.31	*Oryctolagus cuniculus*
Corticostatin 2	2-33	P07468	32	RCVCRKQLLCSYRERRIGDCKIRGVRF PFCCP	-4.4	0.31	*Oryctolagus cuniculus*
Ginkbilobin	1-40	P83171	40	ANTAFVSSAHNTQKIPAGAPFNRNLR AMLADLRQNAAFAG	-3.1	0.28	*Ginkgo biloba*
Caerin 1.4	1-25	P62544	25	GLLSSLSSVAKHVLPHVVPVIAEHL	-5.7	0.28	*Ranoidea gilleni*
ALC (3-42)	3-42	2QT4	40	GPTYCWNEANNGPGPNRCCSSSGFCC QKNNSDGARTQGTS	-4.7	0.28	*Scytonema varium*
Polyphemusin 1	1-18	1RKK	18	RRWCFRVCYRGFCYRKCR	-5.5	0.28	*Synthetic construct*
Protegrin 3	1-18	2MZ6	18	RGGGLCYCRRRFCVCVGR	-6.2	0.28	*Sus scrofa*
mCRAMP	1-34	P51473	34	GLLRKGGEKIGEKLKKIGQKIKNFFQK LVPQPEQ	-3.5	0.26	*Xenopus laevis*
RatNP-2	1-31	Q62715	31	TCYCRSTRCGFRERLSGACGYRGRIYR LCCR	-3.9	0.26	*Rattus norvegicus*
RatNP-4	1-31	Q62714	31	ACYCRIGACVSGERLTGACGLNGRIYRL CCR	-4.3	0.26	*Rattus norvegicus*
RNase 3 (1-19)	1-19	1H1H	19	RPPQFTRAQWFAIQHISLN	-10.1	0.26	*Homo sapiens*
Caerin 1.10	1-25	P82104	25	GLLSVLGSVAKHVLPHVVPVIAEKL	-4.2	0.24	*Ranoidea splendida*
Caerin 1.2	1-25	P56227	25	GLLGVLGSVAKHVLPHVVPVIAEHL	-4.8	0.24	*Ranoidea caerulea*
Caerin 1.3	1-25	P56228	25	GLLSVLGSVAQHVLPHVVPVIAEHL	-4.7	0.24	*Ranoidea caerulea*
Cyanovirin-N (40-56)	40-56	2EZM	17	IENVDGSLKWQPSNFIE	-5.4	0.24	*Nostoc ellipsosporum*
GNCP-1	1-30	Q64365	30	RCICTTRTCRFPYRRLGTCIFQNRVYT FCC	-4.7	0.23	*Cavia porcellus*
NCP 1 type B	64-93	Q64365	30	RCICTTRTCRFPYRRLGTCIFQNRVYT FCC	-4.7	0.23	*Cavia porcellus*

Human Beta Defensin 1	33-68	1E4S	36	DHYNCVSSGGQCLYSACPIFTKIQGTCY RGKAKCC	-4.3	0.22	*Homo sapiens*
Human neutrophil peptide-2	1-28	1ZMI	28	CYCRIPACIAGERRYTCIYQGRLWAFCC	-4.8	0.21	*Homo sapiens*
Neutrophil defensin 2	1-28	1ZMI	28	CYCRIPACIAGERRYTCIYQGRLWAFCC	-4.8	0.21	*Homo sapiens*
Plectasin	1-40	3E7R	40	GFGCNGPWDEDDMQCHNHCKSIKGY KGGYCAKGGFVCKCY	-3.8	0.2	*N/A*
EP5-1	1-5	P84182	5	ACSAG	-4.5	0.20	*Eisenia fetida*
Caerin 1.19	1-25	P0C2A8	25	GLFKVLGSVAKHLLPHVAPIIAEKL	-4.3	0.20	*Ranoidea gracilenta*
SLPI	1-50	2Z7F	50	RRKPGKCPVTYGQCCGKSCCQGDMEC CKLDRKCMGMFNPPNLMLVSPVKA	-4.3	0.20	*Homo sapiens*
Human neutrophil peptide-3	1-30	1DFN	30	DCYCRIPACIAGERRYGTCIYQGRLWAF CC	-5.1	0.20	*Homo sapiens*
Defensin HNP-3	1-30	1DFN	30	DCYCRIPACIAGERRYGTCIYQGRLWAF CC	-5.1	0.20	*Homo sapiens*
Circulin B	1-31	2ERI	31	CGESCVFIPCISTLLGCSCKNKVCYRNG VIP	-4.3	0.19	*Chassalia parviflora*
TEWP	1-36	2B5B	36	EKKCPGRCTLKCGKHERPTLPYNCGK YICCVPVKVK	-4.3	0.19	*Caretta caretta*
Human defensin 5	1-32	1ZMP	32	ATCYCRTGRCATRESLSGVCEISGRLYR LCCR	-3.7	0.19	*Homo sapiens*
Human defensin 6	1-32	3QTE	32	AFTCHCRRSCYSTEYSYGTCTVMGIN WRFCCL	-8.6	0.19	*Homo sapiens*
Rabbit neutrophil defensin 3	1-32	1EWS	32	MPCSCKKYCDPWEVIDGSCGLFNSKYI CCREK	-4.5	0.19	*Oryctolagus cuniculus*
hAD 6 (H27W mutant)	1-32	3QTE	32	AFTCHCRRSCYSTEYSYGTCTVMGIN WRFCCL	-4.3	0.19	*Homo sapiens*
Mytilin B	1-34	2EEM	34	SCASRCKGHCRARRCGYYVSVLYRGRC YCKCLRC	-4.3	0.18	*N/A*
Human Beta Defensin 2	28-64	1E4Q	37	PVTCLKSGAICHPVFCPRRYKQIGTCGL PGTKCCKKP	-3.9	0.16	*Homo sapiens*
Elafin	1-50	2R3L	50	AQEPVKGPVSTKPGSCCCCRNPPNLM ACCSGEGMACCPGIKKDTDKLRIL	-2.9	0.16	*Homo sapiens*
Tricyclon A	1-33	1YP8	33	CGESCFLGTCYTKGCSCGEWKLCYGTN GGTIFD	-5.3	0.15	*Viola tricolor*
Kalata B8	1-29	1K48	28	GSVLNCGETCLLGTCYTTGCTCNKYRV CTKD	-5.1	0.14	*Oldenlandia affinis*
Palicourein	1-37	1R1F	37	TFCGETCRVIPVCTYSAALGCTCDDRS DGLCKRNGDP	-4.2	0.14	*Palicourea condensata*
RatNP-1	1-30	Q62716	30	TCYCRRTRCGFRERLSGACGYRGRIYR LCC	-4.3	0.13	*Rattus norvegicus*
Vhl-1	1-31	1ZA8	31	CGESCAMISFCFTEVIGCSCKNKVCYL NSIS	-4.2	0.13	*Viola hederacea*
Cycloviolacin O14	1-31	2GJ0	31	GSIPACGESCFKGKCYTPGCSCSKYPLC AKN	-5.3	0.13	*Viola odorata*
RatNP-3	1-29	Q62713	29	CSCRTSSCRFGERLSGACRLNGRIYRLC C	-4.3	0.10	*Rattus norvegicus*
Kalata B2	1-29	1PT4	29	CGETCFGGTCNTPGCSCTWPICTRDGL PV	-5.2	0.10	*Oldenlandia affinis*
Neutrophil defensin 4	1-31	1ZMM	31	VCSCRLVFCRRTELRVGNCLIGGVSFTY CCT	-4.7	0.10	*Homo sapiens*
Human neutrophil peptide-4	1-31	1ZMM	31	VCSCRLVFCRRTELRVGNCLIGGVSFTY CCT	-4.7	0.097	*Homo sapiens*
mBD-1	1-36	P56386	36	DQYKCLQHGGFCLRSSCPSNTKLQGTC KPDKPNCCK	-3.1	0.08	*Mus musculus*
Kalata B1	1-29	4TTM	29	GLPVCGETCVGGTCNTPGCTCSWPVC TRN	-6.0	0.07	*Oldenlandia affinis*
Circulin A	1-30	1BH4	30	CGESCVWIPCISAALGCSCKNKVCYRN GIP	-3.9	0.07	*Chassalia parviflora*
RNase 3 (alpha)	6-35	1H1H	30	FTRAQWFAIQHISLNPPRCTIAMRAIN NYR	-10.8	0.07	*Homo sapiens*
Human neutrophil peptide-1	1-27	2PM1	27	ACYCRIPACIAGEYGTCIYQGLWAFCC	-4.7	0.07	*Homo sapiens*
HNP1	1-27	2PM1	27	ACYCRIPACIAGEYGTCIYQGLWAFCC	-4.7	0.07	*Homo sapiens*
Subtilosin A	1-37	1PXQ	37	NKGCATCSIGAACLVDGPIPDFEIAGAG LGLWG	-5.1	0.05	*Bacillus subtilis*

RNase 3 (alpha-beta)	21-46	1H1H	26	PPRCTIAMRAINNYRWRCKNQNTFLR	-12.9	0.04	*Homo sapiens*

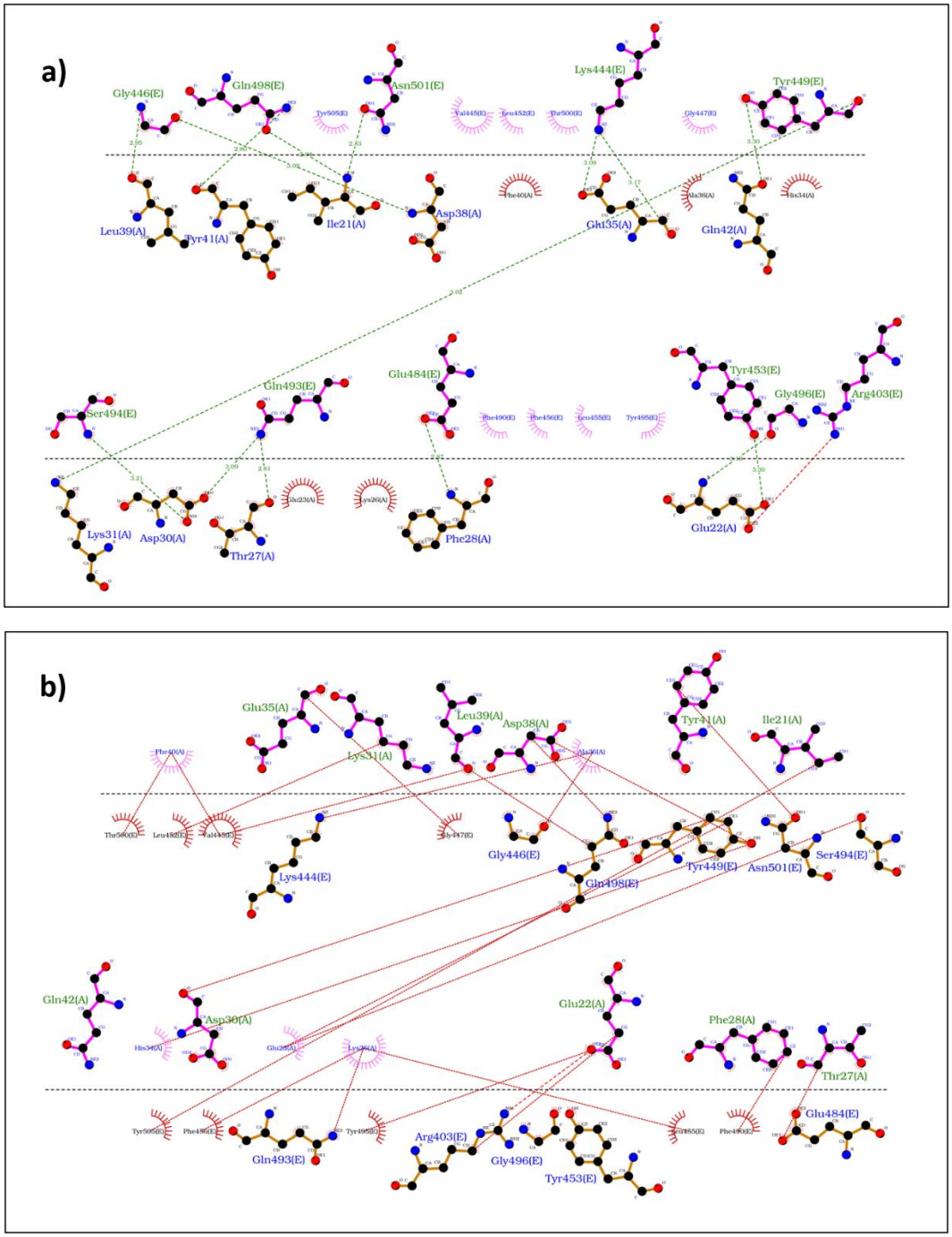


Figure S1: ACE2 docked to the SARS-CoV-2 RBD. (a) Interaction of amino acids by hydrogen bond (green dash line) and (b) representative hydrophobic interactions (red dash line) between ACE2 and RBD.

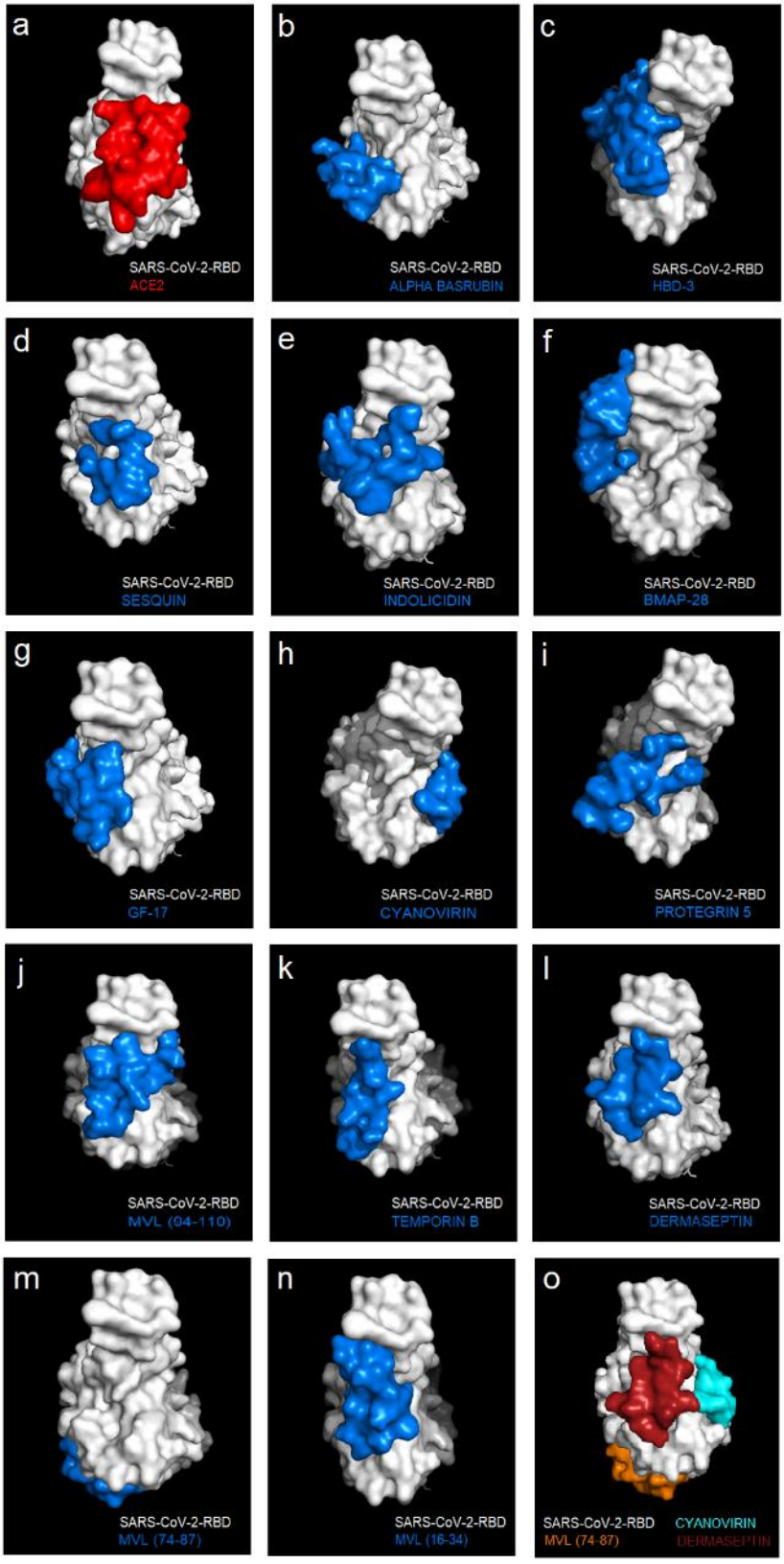
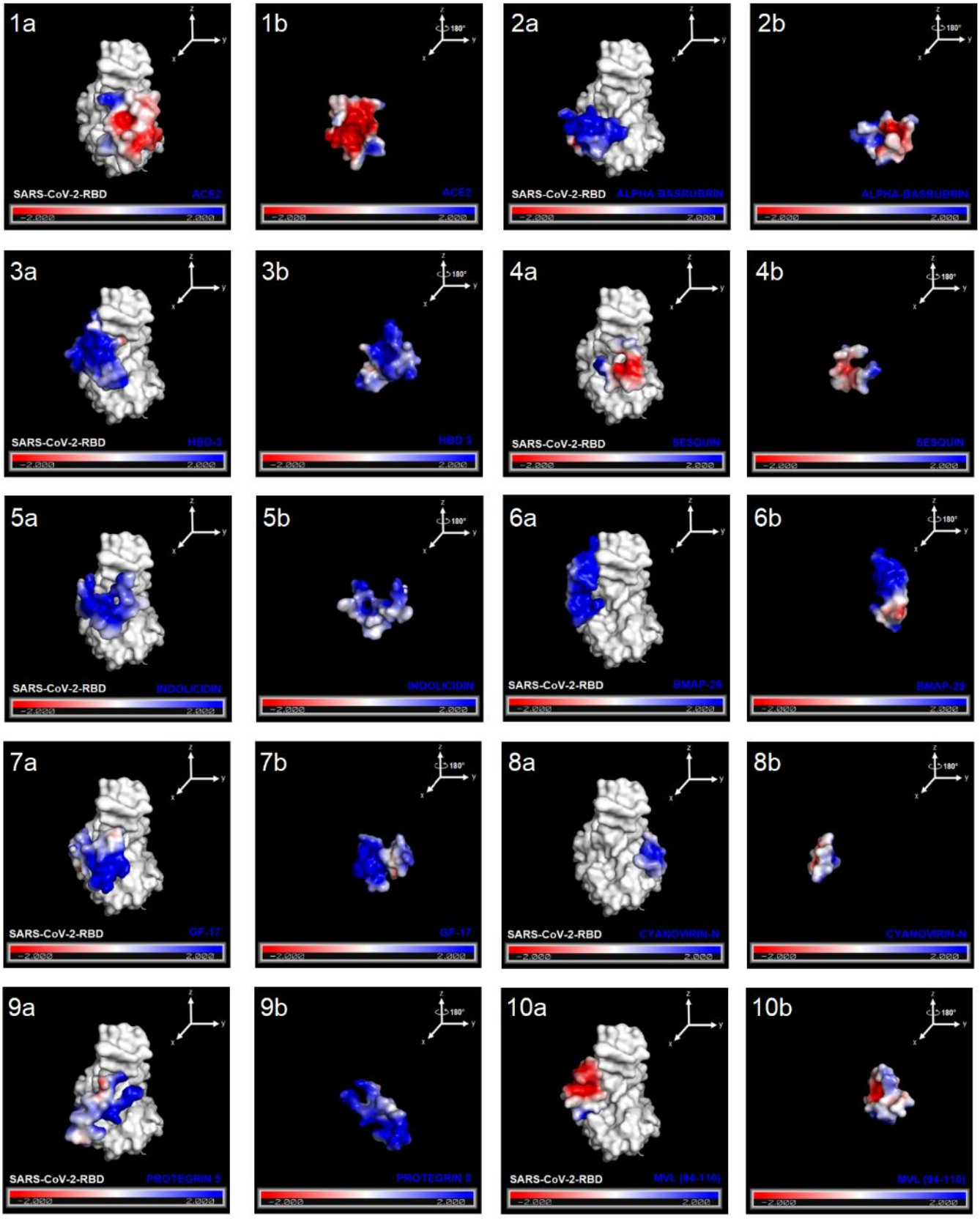


Figure S2: Peptide candidates (blue) docked to the SARS-CoV-2 RBD (white) with the highest binding affinities. (a) ACE2 (red). (b) Alpha basrubrin. (c) HBD-3. (d) Sesquin. (e) Indolicidin. (f) BMAP-28. (g) GF-17. (h) Cyanovirin. (i) Protegrin 5. (j) MVL 94-110. (k) Temporin-B. (l) Dermaseptin S4. (m) MVL (74–87). (n) MVL (16–34). (o) SARS-CoV-2 RBD (white) docked to three non-competing peptides.


1a
SARS-CoV-2-RBD
ACE2
1b
ACE2
2a
SARS-CoV-2-RBD
ALPHA BASRUBRIN
2b
ALPHA BASRUBRIN
3a
SARS-CoV-2-RBD
HBD-3
3b
HBD 3
4a
SARS-CoV-2-RBD
SESQUIN
4b
SESQUIN
5a
SARS-CoV-2-RBD
INDOLICIDIN
5b
INDOLICIDIN
6a
SARS-CoV-2-RBD
BMAP-28
6b
BMAP-28
7a
SARS-CoV-2-RBD
GF-17
7b
GF-17
8a
SARS-CoV-2-RBD
CYANOVIRIN-N
8b
CYANOVIRIN-N
9a
SARS-CoV-2-RBD
PROTEGRIN 5
9b
PROTEGRIN 5
10a
SARS-CoV-2-RBD
MVL (94-110)
10b
MVL (94-110)

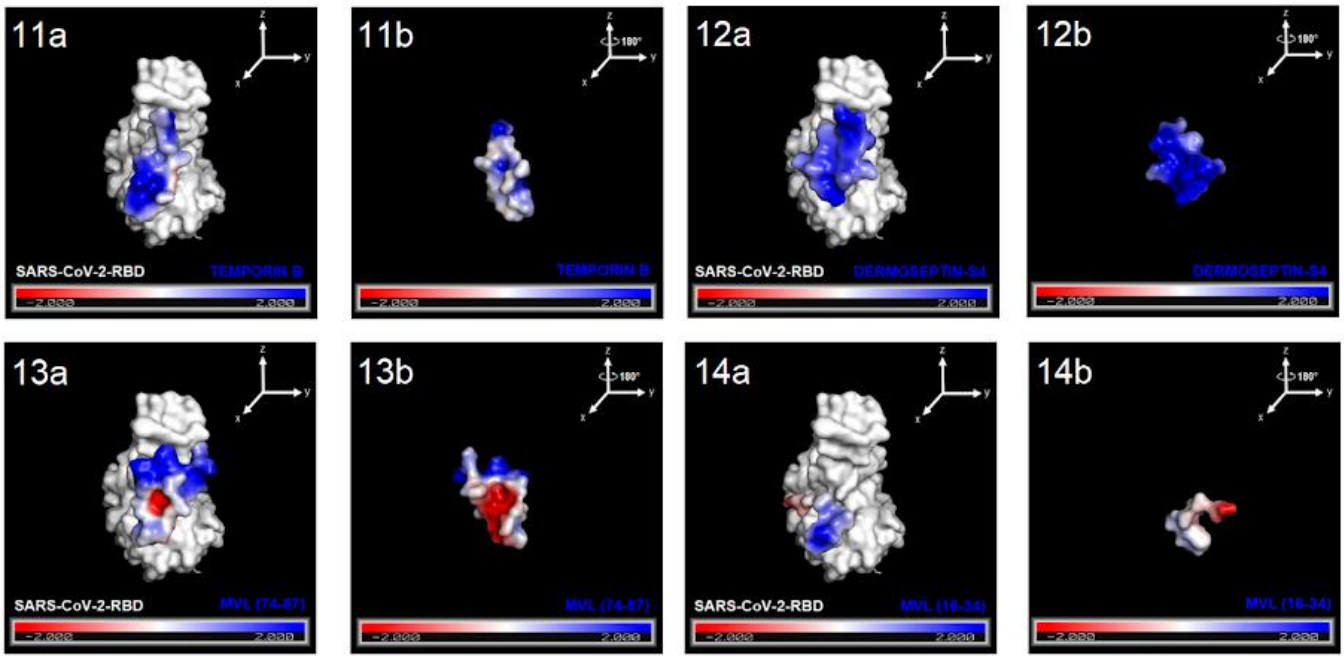


Figure S3: Distribution of electrostatic potential on the surface of APD peptide candidates docked in SARS-CoV-2 RBD. (1a,b) ACE2. (2a,b) Alpha basrubrin. (3a,b) HBD-3. (4a,b) Sesquin. (5a,b) Indolicidin. (6a,b) BMAP-28. (7a,b) GF-17. (8a,b) Cyanovirin-N (70–80). (9a,b) Protegrin 5. (10a,b) MVL (94–110). (11a,b) Temporin B. (12a,b) Dermaseptin-S4. (13a,b) MVL (74-87). (14a,b) MVL (16–34). The potential distribution was calculated by using the APBS module in PyMOL. The values range from −2 (red) over 0 (white) to +2 (blue). The orientation of the peptides in image (b) are rotated by about 180° along the *z*-axis of image (a) to show the peptide surface that binds to the RBD receptor.

Table S3: Hydrogen bonds and hydrophobic interactions of potential peptide candidates against SARS-CoV-2 RBD obtained by LigPlot+.

Peptide	Sequence fragment	PDB/ *UNIPRO*	Residues	Hydrogen bonds	Representative hydrophobic interactions	Isoelectric point (pH)
Alpha Basrubrin	1-20	*P83186*	20	19	30	6.34
Human Beta Defensin 3	27-44	1KJ6	19	18	30	10.41
Sesquin	1-10	*P84868*	10	8	17	3.93
Indolicidin	1-13	1G89	13	10	31	12.13
BMAP-28	1-18	2NDC	18	14	28	11.91
GF-17	1-17	2L5M	17	13	23	11.88
Cyanovirin-N (70-80)	70-80	2EZM	10	8	21	8.89
Protegrin 5	1-18	2NC7	18	13	21	9.67
MVL (94-110)	94-110	1ZHS	17	12	22	10.11
Temporin B	1-13	6GIL	13	9	19	10.12
Dermaseptin-S4	1-13	2DD6	13	9	18	11.17
MVL (74-87)	74-87	1ZHS	14	9	18	3.93
MVL (16-34)	16-34	1ZHS	19	12	31	7.86
ACE2	21-44	6VYB	24	14	24	4.0

Table S4: Immunogenicity analysis of peptides against Human MHC I to determine the number of alleles with IC50 < 50nM and IC50 < 500 nM concentrations.

Peptide	Sequence	No. Alleles IC50 < 50 nM	No. Alleles 50 < IC50 < 500 nM
LI3	WLNHSNNQTWDDWIDQDTQD	0	0
CD3	THDKTQHGQDQDQTTGQDWQQQ	0	0
H3	SGLTSWNDDNTQETWDQTTG	0	0
P1	LWRLGPDQTWGPTKRGPDWQ	0	0
P1a	THDLWDQDDDDTTGDYIQSQ	0	0
P3a	THDLWRQDRTGDRTDYIQSQ	0	0
P9	THRLWDQRRDTTDGSYIQSQ	0	0
P13	THRLWDQRDTTGRQSYDISQ	0	0
P14	THRLWRQRDTTGDSYIDQSQ	0	0
P15	THRLWRQRTDTGDSYIDQSQ	0	0
Cyanovirin-N	AAECKTRAQQ	0	0
Sesquin	KTCENLADTY	0	0
Alpha-Basrubrin	GADFQECMKEHSQKQHQHQG	0	0
LD2	GLTQIQTLNSLRRWDDTRRT	0	1
CD2	THDKTQHGQDQRQTTGQDWQQQ	0	1
H1	SGLTSWNRRNTQETWRQTTG	0	1
H2	SGLTSWNDRNTQETWRQTTG	0	1
P2a	THDLWRQDRDRTTGDYIQSQ	0	1
P3	LDYGGNQDLGGYTSLGGTDL	0	1
P7	THRLWDQRDRDTTGRYIQSQ	0	1
P8	THRLWDQRDRDTTGSYIQSQ	0	1
P10	THRLWDQRDTTRDGSYIQSQ	0	1
P11	THRLWDQRDTTGRDSYIQSQ	0	1
P12	THRLWDQRDTTGRQSYIDSQ	0	1
LD3	GLTQIQTLNSLDDWDDTDDT	1	1
Temporin B	LLPIVGNLLKSLL	0	1
MVL (74-87)	NDEAQKLGPQIAAS	0	1
L3	LSSQQTLDDWIDQDTGQDWY	0	2
P4	NDYGGNQLGSGYTSLGGTDN	0	2
P4a	THDLWRQDTGRDRTDYIQSQ	0	2
P17	THRLWRQRTTGSDYDIWDSQ	0	2
CD1	THRKTQHGQRQRQTTGQRWQQQ	1	2
L2	LSSQQTLDRWIRQDTGQDWY	1	2
P16	THRLWRQRTTGSDYDIQDSQ	1	2
P8a	THDLWDQDTGSRTRYWQRIS	2	2

P9a	THDLWDQDTGSRTYRWQRIS	2	2
ACE2	IEEQAKTFLDKFNHEAEDLFYQSS	3	2
LI2	WLNHSNNQTWDRWIDQRTQD	0	3
P5	NDYGGNQLDGGYTSLGGTDN	0	3
P6a	THDLWDQDTGRDTRYRYQSQ	0	3
P6	THRLWRQRRRRTTGRYIQSQ	1	3
P7a	THDLWDQDTGSRTRYRIQSQ	1	3
P5a	THDLWDQDTGRTRTYIQSRQ	2	3
MVL (16-34)	AEAQQVGPKIAAAHQGNFT	0	3
GF-17	GFKRIVQRIKDFLRNLV	2	3
MVL (94-110)	GQWRTIVEGVMSVIQIK	5	3
Dermaseptin-S4	ALWKTLLKKVLKA	5	3
LI1	WLNHSNNQTWRRWIRQRTQR	5	4
L1	LSSQQTLRRWIRQRTGQRWY	5	5
Protegrin 5	RGGRLCYCRPRFCVCVGR	0	5
Indolicidin	ILPWKWPWWPWRR	1	5
Human Beta Defensin 3	EEQIGKCSTRGRKCCRRKK	0	6
P10a	DTHDLTDQWGSWGYRTQRISR	2	8
LD1	GLTQIQTLNSLRRWIRTRRT	5	10
BMAP-28	GGLRSLGRKILRAWKKYGPIIVPIIRIG	3	12

Table S5: Contact area of peptides docked on SARS-CoV-2 RBDDE and RBDM variants.

RBDδ		RBDm	
OAP	**Ac**	**OAP**	**Ac**
P1	1039.78	**P1**	870.44
ACE2	1245.96	**ACE2**	1222.81
Cyanovirin-N (70-80)	604.08	**Cyanovirin-N (70-80)**	670.43
Liso1_20	919.27	**Liso1_20**	4915.35
Liso111_130	998.72	**Liso111_130**	4984.20
Liso61_80	732.16	**Liso61_80**	4974.99
MVL (16-34)	890.06	**MVL (16-34)**	782.62
P10	924.60	**P10**	856.24
P11	984.05	**P11**	959.13
P12	1171.33	**P12**	791.97
P13	854.73	**P13**	938.85
P15	937.56	**P15**	1039.63
P17	1165.96	**P17**	856.47
P2a	770.42	**P2a**	957.17
P4a	1064.26	**P4a**	1093.94
P6a	944.48	**P6a**	1043.39
P7	1037.59	**P7**	941.23
P8	1118.28	**P8**	897.82
P9	841.20	**P9**	972.60
PH1	871.82	**PH1**	997.86
PH2	833.10	**PH2**	921.22
Sesquin	641.88	**Sesquin**	684.09
TemporinB	681.97	**TemporinB**	704.49