Supplementary Tables for

Generative AI in the Advancement of Viral Therapeutics for Predicting and Targeting Immune-Evasive SARS-CoV-2 Mutations

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Table S5: SARS-CoV-2 Spike Sequence Encoding Scheme for Discriminator Network Training

Amino Acid	Description	Encoding value
A	Alanine	1
R	Arginine	2
N	Asparagine	3
D	Aspartic Acid	4
C	Cysteine	5
Q	Glutamine	6
E	Glutamic Acid	7
G	Glycine	8
H	Histidine	9
I	Isoleucine	10
L	Leucine	11
K	Lysine	12
M	Methionine	13
F	Phenylalanine	14
P	Proline	15
S	Serine	16
T	Threonine	17
W	Tryptophan	18
Y	Tyrosine	19
V	Valine	20
X	Unknown /Unspecified	21
Z	Glutamic Acid or Glutamine	22
J	Leucine or Isoleucine	23
U	Selenocysteine	24
B	Aspartic Acid or Asparagine	25

Table S6: Key Architecture Parameters of Discriminator and Generator Networks

Model Information	Values
All parameters	1611931
Trainable parameters	1607502
Discriminator parameters	528664
Generator parameters	1078838
Batch size	32
Learning rates	0.0001
Beta	0.0
Discriminator step size	1
Generator step size	1

Table S7: Full Parameter Configuration of the Discriminator Network

Layer Name	Weight Shape	Number of Parameters
sn_d_block0/conv1/w:0	(1, 3, 21, 128)	8064
sn_d_block0/conv1/biases:0	(128,)	128
sn_d_block0/conv2/w:0	(1, 3, 128, 128)	49152
sn_d_block0/conv2/biases:0	(128,)	128
sn_d_block0/conv3/w:0	(1, 3, 21, 128)	8064
sn_d_block0/conv3/biases:0	(128,)	128
attention/sn_conv_f/w:0	(1, 1, 128, 11)	1408
attention/sn_conv_f/biases:0	(11,)	11
attention/sn_conv_g/w:0	(1, 1, 128, 11)	1408
attention/sn_conv_g/biases:0	(11,)	11
attention/sn_conv_h/w:0	(1, 1, 128, 128)	16384
attention/sn_conv_h/biases:0	(128,)	128
attention/attention_multiplier:0	(1,)	1
sn_d_block1/conv1/w:0	(1, 3, 128, 128)	49152
sn_d_block1/conv1/biases:0	(128,)	128
sn_d_block1/conv2/w:0	(1, 3, 128, 128)	49152
sn_d_block1/conv2/biases:0	(128,)	128
sn_d_block1/conv3/w:0	(1, 3, 128, 128)	49152
sn_d_block1/conv3/biases:0	(128,)	128
... (additional layers)	...	...
sn_d_block3/conv3/biases:0	(128,)	128
d_sn_linear/Matrix:0	(128, 1)	128
d_sn_linear/bias:0	(1,)	1

Table S8: Full Parameter Configuration of the Generator Network

Layer Name	Weight Shape	Number of Parameters
noise_linear/Matrix:0	(128, 1280)	163840
noise_linear/bias:0	(1280,)	1280
up/sn_up_block1/conv1/w:0	(1, 3, 256, 256)	196608
up/sn_up_block1/conv1/biases:0	(256,)	256
up/sn_up_block1/conv2/w:0	(1, 3, 256, 256)	196608
up/sn_up_block1/conv2/biases:0	(256,)	256
up/sn_up_block1/conv3/w:0	(1, 3, 256, 256)	196608
up/sn_up_block1/conv3/biases:0	(256,)	256
up/attention/sn_conv_f/w:0	(1, 1, 256, 16)	4096
up/attention/sn_conv_f/biases:0	(16,)	16
up/attention/sn_conv_g/w:0	(1, 1, 256, 16)	4096
up/attention/sn_conv_g/biases:0	(16,)	16
up/attention/sn_conv_h/w:0	(1, 1, 256, 256)	65536
up/attention/sn_conv_h/biases:0	(256,)	256
up/attention/attention_multiplier:0	(1,)	1
up/sn_up_block0/conv1/w:0	(1, 3, 256, 128)	98304
up/sn_up_block0/conv1/biases:0	(128,)	128
up/sn_up_block0/conv2/w:0	(1, 3, 128, 128)	49152
up/sn_up_block0/conv2/biases:0	(128,)	128
up/sn_up_block0/conv3/w:0	(1, 3, 256, 128)	98304
up/sn_up_block0/conv3/biases:0	(128,)	128
g_bn/gamma:0	(128,)	128
g_bn/beta:0	(128,)	128
last_conv/w:0	(1, 1, 128, 21)	2688
last_conv/biases:0	(21,)	21

Table S9: Identification of 464 Spike Mutations (>0.95 Escape Strength) from 88,920 In Silico spikes through Sars-Escape Network Analysis

Id	Spike Segment	Mutation	Escape Score
1	VVLSDELLHAPATVCGPKKS	F515D	0.958565
2	VVLSCELLHAPATVCGPKKS	F515C	0.956172
3	VVLSQELLHAPATVCGPKKS	F515Q	0.955096
4	VVLSGELLHAPATVCGPKKS	F515G	0.95137
5	VVLSHELLHAPATVCGPKKS	F515H	0.956211
6	VVLSLELLHAPATVCGPKKS	F515L	0.980287
7	VVLSMELLHAPATVCGPKKS	F515M	0.950655
8	VVLSFELLHAPATVCGTKKS	P527T	0.962898
9	VVLSFELLHAPATVCGPNKS	K528N	0.963247
10	VVLSFELLHAPATVCGPEKS	K528E	0.955724
11	VVLSFELLHAPATVCGPIKS	K528I	0.961375
12	VVLSFELLHAPATVCGPFKS	K528F	0.9806
13	VVLSFELLHAPATVCGPTKS	K528T	0.957067
14	VVLSFELLHAPATVCGPWKS	K528W	0.954727
15	VVLSFELLHAPATVCGPVKS	K528V	0.952985
16	VVLSFELLHAPATVCGPKAS	K529A	0.95919
17	VVLSFELLHAPATVCGPKRS	K529R	0.954041
18	FVFLVQLPLVSSQCVNLTTR	L7Q	0.959789
19	LLHAPATVCGPKKSCNLVKN	T531C	0.966451
20	LLPIVSSQCVNLTTRTQLPP	L10I	0.961575
21	LLPLESSQCVNLTTRTQLPP	V11E	0.966071
22	LPLVSSQCWNLTTRTQLPPA	V16W	0.952694
23	LPLVSSQCVDLTTRTQLPPA	N17D	0.954856
24	LPLVSSQCVELTTRTQLPPA	N17E	0.954797
25	LPLVSSQCVLLTTRTQLPPA	N17L	0.962132
26	LPLVSSQCVKLTTRTQLPPA	N17K	0.952638
27	LPLVSSQCVMLTTRTQLPPA	N17M	0.965687
28	LPLVSSQCVPLTTRTQLPPA	N17P	0.956388
29	LPLVSSQCVNLTTRTQLTPA	P25T	0.950227
30	QLVSSQCVNLTTRTQLPPAY	P9Q	0.969193
31	PLVKSQCVNLTTRTQLPPAY	S12K	0.953729
32	PLVSRQCVNLTTRTQLPPAY	S13R	0.951107
33	PLVSCQCVNLTTRTQLPPAY	S13C	0.953549
34	PLVSPQCVNLTTRTQLPPAY	S13P	0.950947
35	LVMSQCVNLTTRTQLPPAYT	S12M	0.955972
36	LVTSQCVNLTTRTQLPPAYT	S12T	0.953473
37	LVSQQCVNLTTRTQLPPAYT	S13Q	0.965202
38	LVSKQCVNLTTRTQLPPAYT	S13K	0.955253
39	VLSFELLTAPATVCGPKKST	H519T	0.960956
40	VLSFELLHAPYTVCGPKKST	A522Y	0.959761
41	VLSFELLHAPATGCGPKKST	V524G	0.95209
42	VLSFELLHAPATVCGQKKST	P527Q	0.953
43	LSFELFHAPATVCGPKKSTN	L518F	0.950207
44	LSFELTHAPATVCGPKKSTN	L518T	0.950051
45	HAIHVSGTNGAKRFDNPVLP	T76A	0.950844
46	HAIHVSGTNGGKRFDNPVLP	T76G	0.953886
47	SKTQSLLIVWNATNVVIKVC	N121W	0.950789
48	IKVCEFQFCNMPFLGVYYHK	D138M	0.950288
49	KVCEFQFCNDIFLGVYYHKN	P139I	0.950366
50	CEFQFCNDPFLWVYYHKNNK	G142W	0.953299
51	CNDPFLGVHYHKNNKSWMES	Y144H	0.955644
52	CNDPFLGVYFHKNNKSWMES	Y145F	0.952314
53	CNDPFLGVYSHKNNKSWMES	Y145S	0.957089
54	CNDPFLGVYWHKNNKSWMES	Y145W	0.956038
55	CNDPFLGVYYHKNNKSQMES	W152Q	0.950097
56	CNDPFLGVYYHKNNKSWMLS	E154L	0.963086
57	NDQFLGVYYHKNNKSWMESE	P139Q	0.956088
58	NDHFLGVYYHKNNKSWMESE	P139H	0.95635
59	NDMFLGVYYHKNNKSWMESE	P139M	0.952305
60	NDPWLGVYYHKNNKSWMESE	F140W	0.954103
61	NDPFLGVYYPKNNKSWMESE	H146P	0.95971
62	NDPFLGVYYSKNNKSWMESE	H146S	0.95417
63	NDPFLGVYYTKNNKSWMESE	H146T	0.950908
64	NDPFLGVYYHKNNKSVMESE	W152V	0.951489
65	NDPFLGVYYHKNNKSWGESE	M153G	0.95729
66	NPFLGVYYHKNNKSWMESEF	D138N	0.954952

67	GPFLGVYYHKNNKSWMESEF	D138G	0.950254
68	HPFLGVYYHKNNKSWMESEF	D138H	0.957299
69	LPFLGVYYHKNNKSWMESEF	D138L	0.951662
70	PPFLGVYYHKNNKSWMESEF	D138P	0.955251
71	WPFLGVYYHKNNKSWMESEF	D138W	0.950727
72	YPFLGVYYHKNNKSWMESEF	D138Y	0.951792
73	DAFLGVYYHKNNKSWMESEF	P139A	0.95649
74	DPKLGVYYHKNNKSWMESEF	F140K	0.970689
75	PEGKQGNFKNLREFVFKNID	L179P	0.950168
76	VAYSNNSIAIPTNFTISVTD	T724D	0.970184
77	VSKHTPINLVRDLPQGFSAL	Y204V	0.966622
78	YSVHTPINLVRDLPQGFSAL	K206V	0.965675
79	YSKHCPINLVRDLPQGFSAL	T208C	0.955747
80	YSKHKPINLVRDLPQGFSAL	T208K	0.958984
81	YSKHMPINLVRDLPQGFSAL	T208M	0.968233
82	YSKHWPINLVRDLPQGFSAL	T208W	0.956913
83	YSKHTEINLVRDLPQGFSAL	P209E	0.956241
84	YSKHTLINLVRDLPQGFSAL	P209L	0.958604
85	YSKHTFINLVRDLPQGFSAL	P209F	0.960016
86	YSKHTTINLVRDLPQGFSAL	P209T	0.95698
87	YSKHTYINLVRDLPQGFSAL	P209Y	0.958447
88	YSKHTVINLVRDLPQGFSAL	P209V	0.961908
89	YSKHTPANLVRDLPQGFSAL	I210A	0.969631
90	YSKHTPRNLVRDLPQGFSAL	I210R	0.952767
91	YSKHTPNNLVRDLPQGFSAL	I210N	0.973199
92	YSKHTPDNLVRDLPQGFSAL	I210D	0.959655
93	YSKHTPQNLVRDLPQGFSAL	I210Q	0.95762
94	YSKHTPHNLVRDLPQGFSAL	I210H	0.955808
95	YSKHTPKNLVRDLPQGFSAL	I210K	0.956699
96	YSKHTPSNLVRDLPQGFSAL	I210S	0.966575
97	YSKHTPINFVRDLPQGFSAL	L212F	0.960926
98	YSKHTPINPVRDLPQGFSAL	L212P	0.950453
99	YSKHTPINYVRDLPQGFSAL	L212Y	0.950031
100	YSKHTPINLDRDLPQGFSAL	V213D	0.960593
101	YSKHTPINLGRDLPQGFSAL	V213G	0.952176
102	YSKHTPINLKRDLPQGFSAL	V213K	0.958835
103	YSKHTPINLVDDLPQGFSAL	R214D	0.95001
104	YSKHTPINLVRSLPQGFSAL	D215S	0.954761
105	YSKHTPINLVRDAPQGFSAL	L216A	0.95121
106	YSKHTPINLVRDNPQGFSAL	L216N	0.959159
107	YSKHTPINLVRDEPQGFSAL	L216E	0.950062
108	YSKHTPINLVRDIPQGFSAL	L216I	0.960343
109	YSKHTPINLVRDKPQGFSAL	L216K	0.951626
110	YSKHTPINLVRDFPQGFSAL	L216F	0.950628
111	YSKHTPINLVRDWPQGFSAL	L216W	0.951312
112	YSKHTPINLVRDLAQGFSAL	P217A	0.955615
113	YSKHTPINLVRDLRQGFSAL	P217R	0.958235
114	YSKHTPINLVRDLNQGFSAL	P217N	0.950829
115	YSKHTPINLVRDLEQGFSAL	P217E	0.952781
116	YSKHTPINLVRDLGQGFSAL	P217G	0.965235
117	YSKHTPINLVRDLIQGFSAL	P217I	0.952935
118	YSKHTPINLVRDLKQGFSAL	P217K	0.961004
119	YSKHTPINLVRDLFQGFSAL	P217F	0.964903
120	YSKHTPINLVRDLPCGFSAL	Q218C	0.958337
121	YSKHTPINLVRDLPQRFSAL	G219R	0.956292
122	YSKHTPINLVRDLPQWFSAL	G219W	0.954818
123	YSKHTPINLVRDLPQGDSAL	F220D	0.950361
124	YSKHTPINLVRDLPQGISAL	F220I	0.966701
125	YSKHTPINLVRDLPQGSSAL	F220S	0.953582
126	YSKHTPINLVRDLPQGFAAL	S221A	0.964162
127	YSKHTPINLVRDLPQGFHAL	S221H	0.953773
128	YSKHTPINLVRDLPQGFIAL	S221I	0.972205
129	YSKHTPINLVRDLPQGFLAL	S221L	0.957491
130	YSKHTPINLVRDLPQGFMAL	S221M	0.971817
131	YSKHTPINLVRDLPQGFPAL	S221P	0.965952
132	YSKHTPINLVRDLPQGFWAL	S221W	0.957803
133	YSKHTPINLVRDLPQGFSRL	A222R	0.950438
134	YSKHTPINLVRDLPQGFSCL	A222C	0.953064
135	YSKHTPINLVRDLPQGFSGL	A222G	0.957021
136	YSKHTPINLVRDLPQGFSSL	A222S	0.958759
137	YSKHTPINLVRDLPQGFSAA	L223A	0.951394

138	YSKHTPINLVRDLPQGFSAR	L223R	0.963548
139	YSKHTPINLVRDLPQGFSAN	L223N	0.962031
140	YSKHTPINLVRDLPQGFSAD	L223D	0.961614
141	YSKHTPINLVRDLPQGFSAE	L223E	0.961321
142	YSKHTPINLVRDLPQGFSAH	L223H	0.956852
143	YSKHTPINLVRDLPQGFSAI	L223I	0.950678
144	YSKHTPINLVRDLPQGFSAF	L223F	0.957361
145	YSKHTPINLVRDLPQGFSAT	L223T	0.967464
146	YSKHTPINLVRDLPQGFSAV	L223V	0.961903
147	CTPINLVRDLPQGFSALEPL	H207C	0.960367
148	ETPINLVRDLPQGFSALEPL	H207E	0.95016
149	LTPINLVRDLPQGFSALEPL	H207L	0.967067
150	LEPLVDLPIGINITRFQTPL	L241P	0.955426
151	GTRFQTLLALHRSYLTPGDS	I235G	0.954061
152	TLTALHRSYLTPGDSSSGWT	L242T	0.96561
153	TLLAPHRSYLTPGDSSSGWT	L244P	0.953773
154	FHRSYLTPGDSSSGWTAGAA	L244F	0.961181
155	RCYLTPGDSSSGWTAGAAAY	S247C	0.950179
156	RSRLTPGDSSSGWTAGAAAY	Y248R	0.963468
157	RSCLTPGDSSSGWTAGAAAY	Y248C	0.95081
158	SNLKPFERDISTEIYQAGSM	T478M	0.959545
159	SNLKPFERDISTEIYQAGSS	T478S	0.9515
160	DLLFKKVTLADAGFIKQYGD	N824K	0.952909
161	DLLFNYVTLADAGFIKQYGD	K825Y	0.952578
162	TESIVRFQNITNLCPFGEVF	P330Q	0.952292
163	TESIVRFPQITNLCPFGEVF	N331Q	0.951733
164	TESIVRFPSITNLCPFGEVF	N331S	0.966034
165	TESIVRFPTITNLCPFGEVF	N331T	0.966217
166	TESIVRFPWITNLCPFGEVF	N331W	0.963626
167	TESIVRFPVITNLCPFGEVF	N331V	0.963756
168	TESIVRFPNATNLCPFGEVF	I332A	0.968765
169	TESIVRFPNNTNLCPFGEVF	I332N	0.986923
170	TESIVRFPNDTNLCPFGEVF	I332D	0.950039
171	TESIVRFPNCTNLCPFGEVF	I332C	0.967007
172	TESIVRFPNWTNLCPFGEVF	I332W	0.951303
173	TESIVRFPNIKNLCPFGEVF	T333K	0.952881
174	DSIVRFPNITNLCPFGEVFN	E324D	0.958959
175	QSIVRFPNITNLCPFGEVFN	E324Q	0.950048
176	HSIVRFPNITNLCPFGEVFN	E324H	0.979795
177	KSIVRFPNITNLCPFGEVFN	E324K	0.96671
178	MSIVRFPNITNLCPFGEVFN	E324M	0.950368
179	FSIVRFPNITNLCPFGEVFN	E324F	0.957579
180	PSIVRFPNITNLCPFGEVFN	E324P	0.978492
181	SSIVRFPNITNLCPFGEVFN	E324S	0.95883
182	YSIVRFPNITNLCPFGEVFN	E324Y	0.973969
183	VSIVRFPNITNLCPFGEVFN	E324V	0.958879
184	ERIVRFPNITNLCPFGEVFN	S325R	0.972281
185	ECIVRFPNITNLCPFGEVFN	S325C	0.986977
186	EQIVRFPNITNLCPFGEVFN	S325Q	0.952552
187	EGIVRFPNITNLCPFGEVFN	S325G	0.968992
188	EHIVRFPNITNLCPFGEVFN	S325H	0.966548
189	ELIVRFPNITNLCPFGEVFN	S325L	0.966718
190	EKIVRFPNITNLCPFGEVFN	S325K	0.974014
191	EMIVRFPNITNLCPFGEVFN	S325M	0.963912
192	ESPVRFPNITNLCPFGEVFN	I326P	0.954328
193	SIVRFHNITNLCPFGEVFNA	P330H	0.950576
194	TNLCPFGEVDNATRFASVYA	F342D	0.95547
195	LCPFGEVFNDTRFASVYAWN	A344D	0.95048
196	LCPFGEVFNATAFASVYAWN	R346A	0.963104
197	LCPFGEVFNATRNASVYAWN	F347N	0.957731
198	SVYAWNRKRQSNCVADYSVL	I358Q	0.967656
199	SVYAWNRKRESNCVADYSVL	I358E	0.963088
200	SVYAWNRKRMSNCVADYSVL	I358M	0.956607
201	SVYAWNRKRYSNCVADYSVL	I358Y	0.951919
202	SVYAWNRKRIHNCVADYSVL	S359H	0.951373
203	SVYAWNRKRISNCVAGYSVL	D364G	0.950501
204	SVYAWNRKRISNCVAHYSVL	D364H	0.955803
205	SVYAWNRKRISNCVAKYSVL	D364K	0.952858
206	SVYAWNRKRISNCVADLSVL	Y365L	0.9515
207	SVYAWNRKRISNCVADFSVL	Y365F	0.953976
208	SVYAWNRKRISNCVADYRVL	S366R	0.957115

209	SVYAWNRKRISNCVADYCVL	S366C	0.954096
210	SVYAWNRKRISNCVADYQVL	S366Q	0.956659
211	LYAWNRKRISNCVADYSVLY	V350L	0.953246
212	MYAWNRKRISNCVADYSVLY	V350M	0.960428
213	FYAWNRKRISNCVADYSVLY	V350F	0.9592
214	YYAWNRKRISNCVADYSVLY	V350Y	0.951336
215	VNAWNRKRISNCVADYSVLY	Y351N	0.953244
216	VDAWNRKRISNCVADYSVLY	Y351D	0.953288
217	VQAWNRKRISNCVADYSVLY	Y351Q	0.950778
218	VGAWNRKRISNCVADYSVLY	Y351G	0.950066
219	VYAWARKRISNCVADYSVLY	N354A	0.953074
220	VYAWNPKRISNCVADYSVLY	R355P	0.962521
221	AWNRYRISNCVADYSVLYNS	K356Y	0.957119
222	SNCVADYSVLYNSASFSMFK	T376M	0.953537
223	CVADYSVLYNSASFQTFKCY	S375Q	0.964985
224	YNSASFSTFKCYGSSPTKLN	V382S	0.954157
225	YNSASFSTFKCYGVIPTKLN	S383I	0.961146
226	YNSASFSTFKCYGVWPTKLN	S383W	0.960362
227	YNSASFSTFKCYGVSRTKLN	P384R	0.956748
228	YNSASFSTFKCYGVSNTKLN	P384N	0.95186
229	YNSASFSTFKCYGVSDTKLN	P384D	0.959324
230	YNSASFSTFKCYGVSQTKLN	P384Q	0.957134
231	YNSASFSTFKCYGVSETKLN	P384E	0.952266
232	YNSASFSTFKCYGVSHTKLN	P384H	0.951818
233	NSAEFSTFKCYGVSPTKLND	S373E	0.954529
234	NSASWSTFKCYGVSPTKLND	F374W	0.963975
235	NSASFSTFFCYGVSPTKLND	K378F	0.955508
236	NSASFSTFTCYGVSPTKLND	K378T	0.962766
237	NSASFSTFWCYGVSPTKLND	K378W	0.952635
238	NSASFSTFKAYGVSPTKLND	C379A	0.954375
239	NSASFSTFKQYGVSPTKLND	C379Q	0.951414
240	NSASFSTFKGYGVSPTKLND	C379G	0.951337
241	NSASFSTFKCCGVSPTKLND	Y380C	0.96698
242	ASFSTFKRYGVSPTKLNDLC	C379R	0.953964
243	ASFSTFKCGGVSPTKLNDLC	Y380G	0.962275
244	ASFSTFKCYGFSPTKLNDLC	V382F	0.967407
245	ASFSTFKCYGVSSTKLNDLC	P384S	0.96564
246	ASFSTFKCYGVSPVKLNDLC	T385V	0.954491
247	STFKCYGVSPTALNDLCFTN	K386A	0.969037
248	STFKCYGVSPTYLNDLCFTN	K386Y	0.962712
249	CYGVSPTFLNDLCFTNVYAD	K386F	0.950831
250	CYGVSPTPLNDLCFTNVYAD	K386P	0.957011
251	CYGVSPTYLNDLCFTNVYAD	K386Y	0.959657
252	CYGVSPTKLNDLCFTNVHAD	Y396H	0.958465
253	CYGVSPTKLNDLCFTNVKAD	Y396K	0.959381
254	CYGVSPTKLNDLCFTNVYAA	D398A	0.95578
255	CYGVSPTKLNDLCFTNVYAR	D398R	0.956649
256	YGVSATKLNDLCFTNVYADS	P384A	0.951599
257	YGVSTTKLNDLCFTNVYADS	P384T	0.957175
258	YGVSPDKLNDLCFTNVYADS	T385D	0.961371
259	YGVSPGKLNDLCFTNVYADS	T385G	0.968946
260	YGVSPLKLNDLCFTNVYADS	T385L	0.960594
261	YGVSPSKLNDLCFTNVYADS	T385S	0.961531
262	YGVSPTSLNDLCFTNVYADS	K386S	0.962461
263	YGVSPTTLNDLCFTNVYADS	K386T	0.967791
264	VSPTKLNDLHFTNVYADSFV	C391H	0.95583
265	VSPTKLNDLMFTNVYADSFV	C391M	0.966488
266	VSPTKLNDLFFTNVYADSFV	C391F	0.970908
267	VSPTKLNDLTFTNVYADSFV	C391T	0.974137
268	VSPTKLNDLYFTNVYADSFV	C391Y	0.975355
269	VSPTKLNDLCATNVYADSFV	F392A	0.961883
270	VSPTKLNDLCMTNVYADSFV	F392M	0.954621
271	VSPTKLNDLCFGNVYADSFV	T393G	0.952211
272	VSPTKLNDLCFTNVYADSVV	F400V	0.952296
273	SPLKLNDLCFTNVYADSFVI	T385L	0.95151
274	SPFKLNDLCFTNVYADSFVI	T385F	0.959323
275	SPTSLNDLCFTNVYADSFVI	K386S	0.954963
276	SPTVLNDLCFTNVYADSFVI	K386V	0.960217
277	SPTKDNDLCFTNVYADSFVI	L387D	0.963674
278	SPTKENDLCFTNVYADSFVI	L387E	0.972162
279	SPTKINDLCFTNVYADSFVI	L387I	0.977186

280	SPTKPNDLCFTNVYADSFVI	L387P	0.962667
281	SPTKWNDLCFTNVYADSFVI	L387W	0.965758
282	SPTKLADLCFTNVYADSFVI	N388A	0.976797
283	SPTKLRDLCFTNVYADSFVI	N388R	0.957291
284	SPTKLDDLCFTNVYADSFVI	N388D	0.958323
285	SPTKLCDLCFTNVYADSFVI	N388C	0.973381
286	SPTKLGDLCFTNVYADSFVI	N388G	0.956382
287	SPTKLHDLCFTNVYADSFVI	N388H	0.958247
288	SPTKLIDLCFTNVYADSFVI	N388I	0.979525
289	KLNDLCFWNVYADSFVIRGD	T393W	0.960293
290	CFQNVYADSFVIRGDEVRQI	T393Q	0.956289
291	MTNVYADSFVIRGDEVRQIA	F392M	0.963916
292	FRNVYADSFVIRGDEVRQIA	T393R	0.959244
293	VYADSFVIRGDEVRQIEPGQ	A411E	0.973738
294	VYADSFVIRGDEVRQIPPGQ	A411P	0.951693
295	VYADSFVIRGDEVRQIAPTQ	G413T	0.950615
296	ADSDVIRGDEVRQIAPGQTG	F400D	0.958117
297	DSFNIRGDEVRQIAPGQTGK	V401N	0.956013
298	DEVRSIAPGQTGKIADYNYK	Q409S	0.962844
299	DEVRTIAPGQTGKIADYNYK	Q409T	0.95799
300	EVRQIAPGYTGKIADYNYKL	Q414Y	0.956116
301	EVRQIAPGQTGMIADYNYKL	K417M	0.959268
302	KIADYNYMLPDDFTGCVIAW	K424M	0.95727
303	KIADYNYKQPDDFTGCVIAW	L425Q	0.958159
304	PDMFTGCVIAWNSNNLDSKV	D428M	0.950829
305	CVIAWNSNKLDSKVGGNYNY	N440K	0.957466
306	SNNLMSKVGGNYNYLYRLFR	D442M	0.95671
307	SNNLDSKVGGNYNYLYRLKR	F456K	0.950194
308	RNLDSKVGGNYNYLYRLFRK	N439R	0.954907
309	QNLDSKVGGNYNYLYRLFRK	N439Q	0.961811
310	HNLDSKVGGNYNYLYRLFRK	N439H	0.972474
311	MNLDSKVGGNYNYLYRLFRK	N439M	0.952963
312	SNLDSKVGGNYNYLYRLFRK	N439S	0.964439
313	YNLDSKVGGNYNYLYRLFRK	N439Y	0.961832
314	NRLDSKVGGNYNYLYRLFRK	N440R	0.951689
315	NHLDSKVGGNYNYLYRLFRK	N440H	0.960581
316	RLFRKSNLKPFERDMSTEIY	I468M	0.958208
317	RLFRKSNLKPFERDIATEIY	S469A	0.95075
318	KPFERDISTEIYQAGSTPCV	N481V	0.953154
319	ERDIQTEIYQAGSTPCNGVE	S469Q	0.972752
320	ERDISTEIYQAGSTLCNGVE	P479L	0.968822
321	ERDISTEIYQAGSTWCNGVE	P479W	0.957833
322	ERDISTEIYQAGSTPRNGVE	C480R	0.956414
323	ERDISTEIYQAGSTPHNGVE	C480H	0.974241
324	NGVEGFNCYFPLQSYGHQPT	F497H	0.964528
325	VVEGFNCYFPLQSYGFQPTN	G482V	0.956821
326	GNEGFNCYFPLQSYGFQPTN	V483N	0.951865
327	GSEGFNCYFPLQSYGFQPTN	V483S	0.951854
328	GVRGFNCYFPLQSYGFQPTN	E484R	0.953875
329	GVHGFNCYFPLQSYGFQPTN	E484H	0.965081
330	GVEGFNCYFPLQSYGFQPTC	N501C	0.953912
331	IEGFNCYFPLQSYGFQPTNG	V483I	0.95368
332	TEGFNCYFPLQSYGFQPTNG	V483T	0.957068
333	VAGFNCYFPLQSYGFQPTNG	E484A	0.968791
334	VRGFNCYFPLQSYGFQPTNG	E484R	0.973605
335	VNGFNCYFPLQSYGFQPTNG	E484N	0.973225
336	VDGFNCYFPLQSYGFQPTNG	E484D	0.951624
337	VCGFNCYFPLQSYGFQPTNG	E484C	0.963856
338	VQGFNCYFPLQSYGFQPTNG	E484Q	0.97161
339	VHGFNCYFPLQSYGFQPTNG	E484H	0.98661
340	VIGFNCYFPLQSYGFQPTNG	E484I	0.952673
341	VLGFNCYFPLQSYGFQPTNG	E484L	0.974494
342	VMGFNCYFPLQSYGFQPTNG	E484M	0.950308
343	VVGFNCYFPLQSYGFQPTNG	E484V	0.958902
344	VENFNCYFPLQSYGFQPTNG	G485N	0.965195
345	VEGDNCYFPLQSYGFQPTNG	F486D	0.958943
346	VEGENCYFPLQSYGFQPTNG	F486E	0.950681
347	VEGFNCYFPLQSYWFQPTNG	G496W	0.950919
348	VEGFNCYFPLQSYGHQPTNG	F497H	0.965744
349	VEGFNCYFPLQSYGLQPTNG	F497L	0.953321
350	VEGFNCYFPLQSYGMQPTNG	F497M	0.97273

351	VEGFNCYFPLQSYGPQPTNG	F497P	0.952365
352	VEGFNCYFPLQSYGTQPTNG	F497T	0.974173
353	VEGFNCYFPLQSYGWQPTNG	F497W	0.961304
354	VEGFNCYFPLQSYGYQPTNG	F497Y	0.955969
355	VEGFNCYFPLQSYGVQPTNG	F497V	0.978963
356	VEGFNCYFPLQSYGFAPTNG	Q498A	0.961308
357	VEGFNCYFPLQSYGFNPTNG	Q498N	0.952665
358	VEGFNCYFPLQSYGFDPTNG	Q498D	0.970265
359	VEGFNCYFPLQSYGFCPTNG	Q498C	0.955887
360	VEGFNCYFPLQSYGFGPTNG	Q498G	0.972746
361	VEGFNCYFPLQSYGFHPTNG	Q498H	0.959948
362	VEGFNCYFPLQSYGFLPTNG	Q498L	0.987716
363	VEGFNCYFPLQSYGFKPTNG	Q498K	0.960083
364	VEGFNCYFPLQSYGFMPTNG	Q498M	0.955563
365	VEGFNCYFPLQSYGFFPTNG	Q498F	0.97251
366	VEGFNCYFPLQSYGFPPTNG	Q498P	0.966208
367	VEGFNCYFPLQSYGFTPTNG	Q498T	0.967643
368	VEGFNCYFPLQSYGFWPTNG	Q498W	0.971462
369	VEGFNCYFPLQSYGFYPTNG	Q498Y	0.969409
370	VEGFNCYFPLQSYGFQPQNG	T500Q	0.958688
371	GFHCYFPLQSYGFQPTNGVG	N487H	0.956468
372	FNTYFPLQSYGFQPTNGVGY	C488T	0.962757
373	FNCYNPLQSYGFQPTNGVGY	F490N	0.969582
374	FNCYFDLQSYGFQPTNGVGY	P491D	0.956904
375	FNCYFFLQSYGFQPTNGVGY	P491F	0.953628
376	FNCYFPRQSYGFQPTNGVGY	L492R	0.956114
377	FNCYFPNQSYGFQPTNGVGY	L492N	0.955429
378	FNCYFPDQSYGFQPTNGVGY	L492D	0.959063
379	FNCYFPQQSYGFQPTNGVGY	L492Q	0.95318
380	FNCYFPEQSYGFQPTNGVGY	L492E	0.959998
381	FNCYFPGQSYGFQPTNGVGY	L492G	0.961383
382	FNCYFPHQSYGFQPTNGVGY	L492H	0.957615
383	FNCYFPKQSYGFQPTNGVGY	L492K	0.963299
384	FNCYFPMQSYGFQPTNGVGY	L492M	0.950151
385	FNCYFPFQSYGFQPTNGVGY	L492F	0.950547
386	FNCYFPPQSYGFQPTNGVGY	L492P	0.954193
387	FNCYFPSQSYGFQPTNGVGY	L492S	0.975223
388	FNCYFPTQSYGFQPTNGVGY	L492T	0.974808
389	FNCYFPWQSYGFQPTNGVGY	L492W	0.976125
390	FNCYFPVQSYGFQPTNGVGY	L492V	0.970035
391	FNCYFPLASYGFQPTNGVGY	Q493A	0.951583
392	FNCYFPLNSYGFQPTNGVGY	Q493N	0.959997
393	FNCYFPLESYGFQPTNGVGY	Q493E	0.9567
394	FNCYFPLHSYGFQPTNGVGY	Q493H	0.965163
395	FNCYFPLMSYGFQPTNGVGY	Q493M	0.960248
396	FNCYFPLFSYGFQPTNGVGY	Q493F	0.953482
397	FNCYFPLPSYGFQPTNGVGY	Q493P	0.952305
398	FNCYFPLQRYGFQPTNGVGY	S494R	0.9562
399	FNCYFPLQSDGFQPTNGVGY	Y495D	0.952951
400	FNCYFPLQSIGFQPTNGVGY	Y495I	0.951726
401	FNCYFPLQSYYFQPTNGVGY	G496Y	0.955296
402	FNCYFPLQSYGHQPTNGVGY	F497H	0.95522
403	FNCYFPLQSYGFWPTNGVGY	Q498W	0.961084
404	FNCYFPLQSYGFYPTNGVGY	Q498Y	0.968095
405	FNCYFPLQSYGFQDTNGVGY	P499D	0.951002
406	FNCYFPLQSYGFQQTNGVGY	P499Q	0.953825
407	FNCYFPLQSYGFQETNGVGY	P499E	0.970695
408	FNCYFPLQSYGFQPTRGVGY	N501R	0.955294
409	FNCYFPLQSYGFQPTHGVGY	N501H	0.951723
410	FNCYFPLQSYGFQPTKGVGY	N501K	0.954452
411	FNCYFPLQSYGFQPTMGVGY	N501M	0.953013
412	FNCYFPLQSYGFQPTFGVGY	N501F	0.954351
413	FNCYFPLQSYGFQPTNAVGY	G502A	0.958597
414	FNCYFPLQSYGFQPTNRVGY	G502R	0.96186
415	FNCYFPLQSYGFQPTNDVGY	G502D	0.954552
416	FNCYFPLQSYGFQPTNCVGY	G502C	0.967626
417	FNCYFPLQSYGFQPTNQVGY	G502Q	0.96005
418	FNCYFPLQSYGFQPTNEVGY	G502E	0.958522
419	FNCYFPLQSYGFQPTNHVGY	G502H	0.954412
420	FNCYFPLQSYGFQPTNIVGY	G502I	0.965168
421	FNCYFPLQSYGFQPTNLVGY	G502L	0.95296

422	FNCYFPLQSYGFQPTNKVGY	G502K	0.955374
423	FNCYFPLQSYGFQPTNFVGY	G502F	0.960769
424	FNCYFPLQSYGFQPTNPVGY	G502P	0.961536
425	FNCYFPLQSYGFQPTNSVGY	G502S	0.954559
426	FNCYFPLQSYGFQPTNTVGY	G502T	0.956596
427	FNCYFPLQSYGFQPTNWVGY	G502W	0.962783
428	FNCYFPLQSYGFQPTNVVGY	G502V	0.96168
429	FNCYFPLQSYGFQPTNGRGY	V503R	0.952147
430	FNCYFPLQSYGFQPTNGFGY	V503F	0.96113
431	FNCYFPLQSYGFQPTNGVKY	G504K	0.980158
432	FNCYFPLQSYGFQPTNGVGF	Y505F	0.953439
433	NWYFPLQSYGFQPTNGVGYQ	C488W	0.964537
434	NCDFPLQSYGFQPTNGVGYQ	Y489D	0.954774
435	NCCFPLQSYGFQPTNGVGYQ	Y489C	0.954114
436	NCQFPLQSYGFQPTNGVGYQ	Y489Q	0.955998
437	NCEFPLQSYGFQPTNGVGYQ	Y489E	0.966016
438	NCIFPLQSYGFQPTNGVGYQ	Y489I	0.96082
439	NCLFPLQSYGFQPTNGVGYQ	Y489L	0.952025
440	NCKFPLQSYGFQPTNGVGYQ	Y489K	0.962407
441	NCMFPLQSYGFQPTNGVGYQ	Y489M	0.952878
442	NCPFPLQSYGFQPTNGVGYQ	Y489P	0.953228
443	NCSFPLQSYGFQPTNGVGYQ	Y489S	0.951573
444	NCWFPLQSYGFQPTNGVGYQ	Y489W	0.955387
445	NCVFPLQSYGFQPTNGVGYQ	Y489V	0.955361
446	NCYAPLQSYGFQPTNGVGYQ	F490A	0.951626
447	NCYRPLQSYGFQPTNGVGYQ	F490R	0.957671
448	NCYFPFQSYGFQPTNGVGYQ	L492F	0.954181
449	CYFDLQSYGFQPTNGVGYQP	P491D	0.962303
450	YFALQSYGFQPTNGVGYQPY	P491A	0.971334
451	YFPRQSYGFQPTNGVGYQPY	L492R	0.962103
452	FWLQSYGFQPTNGVGYQPYR	P491W	0.960361
453	FPLQMYGFQPTNGVGYQPYR	S494M	0.951184
454	LQSRGFQPTNGVGYQPYRVV	Y495R	0.953192
455	LQSWGFQPTNGVGYQPYRVV	Y495W	0.95477
456	LQSYGTQPTNGVGYQPYRVV	F497T	0.973769
457	SSGFQPTNGVGYQPYRVVVL	Y495S	0.957395
458	YKFQPTNGVGYQPYRVVVLS	G496K	0.972307
459	GFQPTNGVGYQPYRVVVLGF	S514G	0.967521
460	PTNGVGYQPYRVVVLMFELL	S514M	0.965877
461	NGVGYQPYRVVVLSFEKLHA	L517K	0.957434
462	NGVGYQPYRVVVLSFELVHA	L518V	0.958416
463	NGVGYQPYRVVVLSFELLFA	H519F	0.952232
464	NGVGYQPYRVVVLSFELLHQ	A520Q	0.956128

Table S10: Known vs. Predicted Escape Potential: High-Confidence Mutants (Score > 0.95)

Insilco Mutated spike	Mutant	Score	Remarks (Known escape mutants)
EVRQIAPGQTGMIADYNYKL	K417M	0.959268	K417T/N/E
FNCYFPLASYGFQPTNGVGY	Q493A	0.951583	
FNCYFPLNSYGFQPTNGVGY	Q493N	0.959997	Q493R/L:
FNCYFPLESYGFQPTNGVGY	Q493E	0.9567	
FNCYFPLHSYGFQPTNGVGY	Q493H	0.965163	
FNCYFPLMSYGFQPTNGVGY	Q493M	0.960248	
FNCYFPLFSYGFQPTNGVGY	Q493F	0.953482	
GVEGFNCYFPLQSYGFQPTC	N501C	0.953912	N501Y
FNCYNPLQSYGFQPTNGVGY	F490N	0.969582	F490S
NCYAPLQSYGFQPTNGVGYQ	F490A	0.951626	
NCYRPLQSYGFQPTNGVGYQ	F490R	0.957671	
PLVSRQCVNLTTRTQLPPAY	S13R	0.951107	(Epsilon) [S13Q, S13T, S13G, S13N, S13R, S13C]
PLVSCQCVNLTTRTQLPPAY	S13C	0.953549	
LVSQQCVNLTTRTQLPPAYT	S13Q	0.965202	
LVSKQCVNLTTRTQLPPAYT	S13K	0.955253	
IKVCEFQFCNMPFLGVYYHK	D138M	0.950288	(Gamma) [D138H, D138C, D138B, D138G, D138F, D138P, D138N, D138A, D138V]
NPFLGVYYHKNNKSWMESEF	D138N	0.954952	
GPFLGVYYHKNNKSWMESEF	D138G	0.950254	
HPFLGVYYHKNNKSWMESEF	D138H	0.957299	
LPFLGVYYHKNNKSWMESEF	D138L	0.951662	
PPFLGVYYHKNNKSWMESEF	D138P	0.955251	
WPFLGVYYHKNNKSWMESEF	D138W	0.950727	

YPFLGVYYHKNNKSWMESEF	D138Y	0.951792	
CEFQFCNDPFLWVYYHKNNK	G142W	0.953299	(Kappa, Delta) [G142Y, G142F, G142S, G142V, G142A, G142C, G142L]
CNDPFLGVYYHKNNKSQMES	W152Q	0.950097	(Epsilon) [W152L, W152S, W152R, W152K, W152F]
NDPFLGVYYHKNNKSVMESE	W152V	0.951489	
CNDPFLGVYYHKNNKSWMLS	E154L	0.963086	(Kappa) [E154A, E154W, E154F, E154Q, E154D, E154G, E154V, E154S]
YSKHTPINLVRSLPQGFSAL	D215S	0.954761	(Beta) [D215Y, D215A, D215H, D215P, D215N, D215R, D215E, D215V]
EVRQIAPGQTGMIADYNYKL	K417M	0.959268	(Beta, Delta) [K417T, K417R, K417A, K417E, K417M]
SNLKPFERDISTEIYQAGSM	T478M	0.959545	(Delta) [T478R, T478C, T478I, T478A]
SNLKPFERDISTEIYQAGSS	T478S	0.9515	
GVRGFNCYFPLQSYGFQPTN	E484R	0.953875	(Alpha, Beta, Gamma, Eta, Iota, Zeta, Mu) [E484Q, E484Z, E484G, E484A, E484D, E484F, E484R, E484V, E484S]
GVHGFNCYFPLQSYGFQPTN	E484H	0.965081	
VAGFNCYFPLQSYGFQPTNG	E484A	0.968791	
VRGFNCYFPLQSYGFQPTNG	E484R	0.973605	
VNGFNCYFPLQSYGFQPTNG	E484N	0.973225	
VDGFNCYFPLQSYGFQPTNG	E484D	0.951624	
VCGFNCYFPLQSYGFQPTNG	E484C	0.963856	
VQGFNCYFPLQSYGFQPTNG	E484Q	0.97161	(Kappa) [E484K, E484Z, E484G, E484A, E484D, E484F, E484R, E484V, E484S]
VHGFNCYFPLQSYGFQPTNG	E484H	0.98661	
VIGFNCYFPLQSYGFQPTNG	E484I	0.952673	
VLGFNCYFPLQSYGFQPTNG	E484L	0.974494	
VMGFNCYFPLQSYGFQPTNG	E484M	0.950308	
VVGFNCYFPLQSYGFQPTNG	E484V	0.958902	
FNCYFPLQRYGFQPTNGVGY	S494R	0.9562	(Alpha) [S494G, S494L, S494R, S494T, S494A, S494Q]
FPLQMYGFQPTNGVGYQPYR	S494M	0.951184	

Table S11: The escape strength predicted for previously documented escape mutants from Source(7) was analyzed.

Known Escape Mutants	Score
E484Q	0.9716099
Q493H	0.9651634
V483A	0.9405139
N501Y	0.9400368
N501T	0.93983227
N501T	0.93983227
Q493R	0.9379125
F490L	0.93625504
G496S	0.9359501
F486L	0.93161404
P384S	0.9281772
K378N	0.9281772
Q493L	0.9256511
N439K	0.9247697
P384L	0.9221824
L452R	0.9213229
L452R	0.9213229
E484K	0.91984993
E484K	0.91984993
R403K	0.9103772
R408I	0.896423
I410V	0.89030313
K417N	0.8850127
K417N	0.8850127
F490S	0.88340324
A475S	0.8792438
S494P	0.85049033
K444N	0.83746934
R346S	0.8371327
K417T	0.81694216
S477N	0.7965423
S477R	0.7180186
E484Q	0.6639752