

Cell, Volume 184

Supplemental information

Structure-guided T cell vaccine design for SARS-CoV-2 variants and sarbecoviruses

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Gene	AA	Network Score	Source
spike	L18F	-	P.1 Brazil variant
spike	T19R	-	B.1.617 India variant
spike	T20N	-	P.1 Brazil variant
spike	P26S	-	P.1 Brazil variant
spike	H69 deletion	-1.43669928	B.1.1.7 UK variant
spike	V70 deletion	-	B.1.1.7 UK variant
spike	K77T	-	B.1.617 India variant
spike	D80A	-0.55792993	B.1.351 South Africa variant
spike	T95I	0.139518417	B.1.617 India variant
spike	D138Y	-1.19761315	P.1 Brazil variant
spike	Y144 deletion	-	B.1.1.7 UK variant
spike	G142D	-1.106929906	B.1.617 India variant
spike	E154K	-	B.1.617 India variant
spike	R190S	-0.69165936	P.1 Brazil variant
spike	D215G	-0.67499802	B.1.351 South Africa variant
spike	K417N	-0.86401417	B.1.351 South Africa variant
spike	K417T	-0.86401417	P.1 Brazil variant
spike	L452R	-0.49721763	B.1.617 India variant
spike	T478K	-	B.1.617 India variant
spike	E484K	-	B.1.351 South Africa variant, P.1 Brazil variant
spike	E484Q	-	B.1.617 India variant
spike	N501Y	-0.71155894	B.1.1.7 UK variant, B.1.351 South Africa variant, P.1 Brazil variant
spike	A570D	2.591760471	B.1.1.7 UK variant
spike	D614G	-0.35946146	D614G variant
spike	H655Y	-0.83131904	P.1 Brazil variant
spike	P681H	-	B.1.1.7 UK variant
spike	P681R	-	B.1.617 India variant
spike	A701V	-1.15312712	B.1.351 South Africa variant
spike	T716I	-0.73685512	B.1.1.7 UK variant
spike	D950N	-1.3712576755	B.1.617 India variant
spike	S982A	-0.40343483	B.1.1.7 UK variant
spike	T1027I	-0.1777623	P.1 Brazil variant
spike	Q1071H	-1.2224565185	B.1.617 India variant
spike	H1101D	-1.1893484655	B.1.617 India variant
spike	D1118H	-0.637657	B.1.1.7 UK variant
nucleocapsid	D3L	-	B.1.1.7 UK variant
nucleocapsid	P80R	0.00090473	P.1 Brazil variant
nucleocapsid	T205I	-	B.1.351 South Africa variant
nucleocapsid	S235F	-	B.1.1.7 UK variant
envelope	P71L	-	B.1.351 South Africa variant
orf3a	G174C	-0.21344791	P.1 Brazil variant
orf1ab	T1001I	-	B.1.1.7 UK variant
orf1ab	S1188L	-2.0172435	P.1 Brazil variant
orf1ab	K1655N	-0.63445263	B.1.351 South Africa variant
orf1ab	I2230T	-	B.1.1.7 UK variant
orf1ab	A1708D	0.653393624	B.1.1.7 UK variant
orf1ab	K1795Q	0.425004214	P.1 Brazil variant
orf1ab	nuc 11288:9 deletion	-	P.1 Brazil variant
orf1ab	3675-3677 deletion	-	B.1.1.7 UK variant
orf8	Q27stop	-	B.1.1.7 UK variant
orf8	R52I	-	B.1.1.7 UK variant
orf8	Y73C	-	B.1.1.7 UK variant
orf8	E92K	-	P.1 Brazil variant
spike	N148	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	K150	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	S151	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	R346	-1.152342	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	C361	0.161711413	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	V362	2.620429496	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	N370	-1.28466009	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	A372	-1.23763738	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	T376	-0.57234679	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	V382	2.715374696	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	P384	1.511814942	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	R408	-1.21333506	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	A411	0.408285701	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	K417	-0.86401417	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	K444	-1.304022	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	V445	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	G446	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	N450	-1.25547496	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	L452	-0.49721763	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	P463	-0.89226659	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	A475	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	E484	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	G485	-	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	F490	-1.061427	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	Q493	-1.033094	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	S494	-1.22954023	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	N501	-0.71155894	Greaney et al., Cell Host and Microbe, Jan 13, 2021
spike	V503	-0.79318694	Greaney et al., Cell Host and Microbe, Jan 13, 2021

Table S1. Network scores of SARS-CoV-2 residues with mutations in naturally occurring SARS-CoV-2 variants of concern and *in vitro* studies, Related to Figure 1.

AA Mutation	Network Score	Entropy (CoV-2)	Entropy (CoV-1/Bat)	AA Nuc #	Codon	Mutant	Forward Primer (Mutant)	Reverse Primer
R1039K	10.09356945	0	0	3117...3119	AGG	AAG	GCAGTCAAAGagGTAGATTCTG	CCAAGCACACATTGAGAC
R1039A	10.09356945	0	0	3117...3119	AGG	GCG	GCAGTCAAAGgagGTAGATTCTG	CCAAGCACACATTGAGAC
R815A	-0.709030275	0	0	2445...2447	AGG	GCG	ACCTAGTAAAGgagTCATTTCATTGAGGATCTTCTGTTTAAACA AAG	TTGGAAGGGTCCGGCAGG
G311A	3.661155681	0	0	933...935	GGC	GCC	GGTGAGAAAgccATTATCAGAC	GTGAAGCTCTTAAGGGTG
G311V	3.661155681	0	0	933...935	GGC	GTC	GGTGAGAAAgctATTATCAGAC	GTGAAGCTCTTAAGGGTG
G1085V	-0.75244586	0	0	3255...3257	GGT	GTC	ATGCCATGATgtcAAGGCCACTTTCCAAGG	ATAGCGGGCCCGCTGTA
I870L	3.756766712	0	0.186051098	2610...2612	ATA	CTA	CGATGAGATGctcGCGCAGTACACG	GTGAGCAGAGGGCAGCAGA
I870A	3.756766712	0	0.186051098	2610...2612	ATA	GCT	CGATGAGATGgctGCGCAGTACACGAGCG	GTGAGCAGAGGGCAGCAGA
I794A	-1.26346564	0.003504911	0.5085052	2382...2384	ATA	GCT	GACACCACCgctAAGGACTTCG	TTGTAGATTTGTTGACCTG
L865M	4.48979055	0	0	2595...2597	CTC	ATG	GCCGCCTCTGatgACCGATGAGA	AGAACGGTGAAGCCGTTAAATTTTC
L865A	4.48979055	0	0	2595...2597	CTC	GCT	GCCGCCTCTGgctACCGATGAGA	AGAACGGTGAAGCCGTTAAATTTTC
L754A	-1.197532573	0	0	2262...2264	CTT	GCT	TAACCTTGCTCgctCAGTACGGTTCTCTCTGTAC	CTGCACTCCGCTGTCTG
F1042Y	4.858035945	0	0	3126...3128	TTC	TAC	GAGGGTAGATtacTCCGGAAGG	TTTGACTGCCCAAGCACA
F1042A	4.858035945	0	0	3126...3128	TTC	GCC	GAGGGTAGATgctTCCGGAAGG	TTTGACTGCCCAAGCACA
F140A	-1.2406754	0	0.080572811	420...422	TTC	GCC	TAATGATCCGccCTGGGCGTCT	CAGAATTTGAAACTCCGAC
M731I	2.062407959	0.00645564	0.065211682	2193...2195	ATG	ATC	GCCGCTCTCcatcACCAAGACAT	AGAATCTCAGTGGTGACCG
M731A	2.062407959	0.00645564	0.065211682	2193...2195	ATG	GCG	GCCGCTCTCCgctACCAAGACATC	AGAATCTCAGTGGTGACCG
M900A	0.405929624	0	0	2700...2702	ATG	GCG	ACCCCTTTGCTgagCAGATGGCTTATC	ATCTCGCAACGCTGCTCT
V911I	3.558971164	0	0	2733...2735	GTC	ATC	CGGGATTGGcatcACGCAAGACG	TTAAATCGATAAGCCATCTGCATAGC
V911A	3.558971164	0	0	2733...2735	GTC	GCT	CGGGATTGGCgctACGCAAGACG	TTAAATCGATAAGCCATCTGCATAG
V991A	-1.436699275	0	0	2973...2975	GTT	GCT	AGAAGCCGAAgctCAGATTGACC	ACCTTGTCCAACCGTGAC
Q1036E	4.825122097	0	0	3108...3110	CAG	GAG	TGTGCTTGGGgagTCAAAGAGGG	CATTGACATCTTAGTGGCAGC
Q1036A	4.825122097	0	0	3108...3110	CAG	GCT	TGTGCTTGGGgctTCAAAGAGGGTAG	CATTGACATCTTAGTGG
Q134A	-1.315359112	0.003513972	0.629091648	402...404	CAA	GCA	GTGCGAGTTTgcaTTCTGTAATG	ACCTTGATGACCACGTTCT
C391A	6.583868745	0	0	1173...1175	TGT	GCT	GAACGATCTCgctTTCACAAACGTTTATGCCG	AGCTTCGTTGGAGACACG
C391R	6.583868745	0	0	1173...1175	TGT	AGG	GAACGATCTCaggTTCACAAACGTTTATG	AGCTTCGTTGGAGACACG
C136R	-1.391725931	0	0	408...410	TGT	AGG	GTTTCAATTCaggAATGATCCCTTCC	TCGCACACTTTGATGACC
W436F	2.307786446	0	0	1308...1310	TGG	TTT	TGTCATAGCTtttAATAGCAATAATTTG	CATCCTGTGAAATCGTCC
W436A	2.307786446	0	0	1308...1310	TGG	GCT	TGTCATAGCTgctAATAGCAATAATTTG	CATCCTGTGAAATCGTCC
W64A	-0.369087936	0.003491004	0.688997042	192...194	TGG	GCG	CAATGTGACGgagTTTCATGCCATTC	CTAAAGAAAGGGAGGAAC
V362I	2.620429497	0	0.042400539	1086...1088	GTG	ATC	TTCCAATTGTatcGCGGACTACTC	ATTCTCTTTGGTTCATG
V362A	2.620429497	0	0.042400539	1086...1088	GTG	GCG	TTCCAATTGTgagGCGGACTACT	ATTCTCTTTGGTTCATG
V524I	4.420173389	0	0	1572...1574	GTA	ATC	TCCAGCAACGatcTGCAGTCCCTA	CGGTGGAGCAATTCGAAAC
V524A	4.420173389	0	0	1572...1574	GTA	GCA	TCCAGCAACGgcaTGCAGTCCCTA	CGGTGGAGCAATTCGAAACTC
C525A	4.44682697	0	0.081462027	1575...1577	TGC	GCT	AGCAACGGTAgctGGTCTAAGAAATCCACAAATC	GGAGCGTGGAGCAATTCG
C525R	4.44682697	0	0.081462027	1575...1577	TGC	AGG	AGCAACGGTAgggGGTCTAAGAAATC	GGAGCGTGGAGCAATTCG
A363V	4.014172971	0	0.023508256	1089...1091	GCG	GTG	CAATTGTGTgctGACTACTCAG	GAAATTCCTTTGGTTCATG
A363F	4.014172971	0	0.023508256	1089...1091	GCG	TTT	CAATTGTGTGtttGACTACTCAGTATTGTATAATAG	GAAATTCCTTTGGTTCATG

Table S2. Engineered Mutations in HDM-SARS2-Spike-delta21, Related to Figure 2. The table depicts the engineered mutations in the HDM-SARS2-Spike-delta21 plasmid with mutations, network scores, conservation scores and forward and reverse primers utilized for mutagenesis.

	Pfizer-BioNTech (n = 13)	Moderna (n = 10)
Age (years)	28-39 (median = 32, IQR = 6.3)	25-70 (median = 46, IQR = 32)
Gender		
Male (%)	46.2% (6/13)	70% (7/10)
Female (%)	53.8% (7/13)	30% (3/10)
Sample Collection Date (Range)	Jan 2021-Mar 2021	Jan 2021-Feb 2021
Days Post-2nd Dose at Collection	14-58 (Median = 48, IQR = 42)	15-104 (Median = 20.5, IQR = 3)
Prior COVID-19 Infection		
Mild (%)	15.3% (2/13)	10% (1/10)
Moderate (%)	0% (0/13)	0% (0/10)
Severe (%)	0% (0/13)	0% (0/10)

Table S5. Characteristics of mRNA-based vaccine recipients, Related to Figure 5.