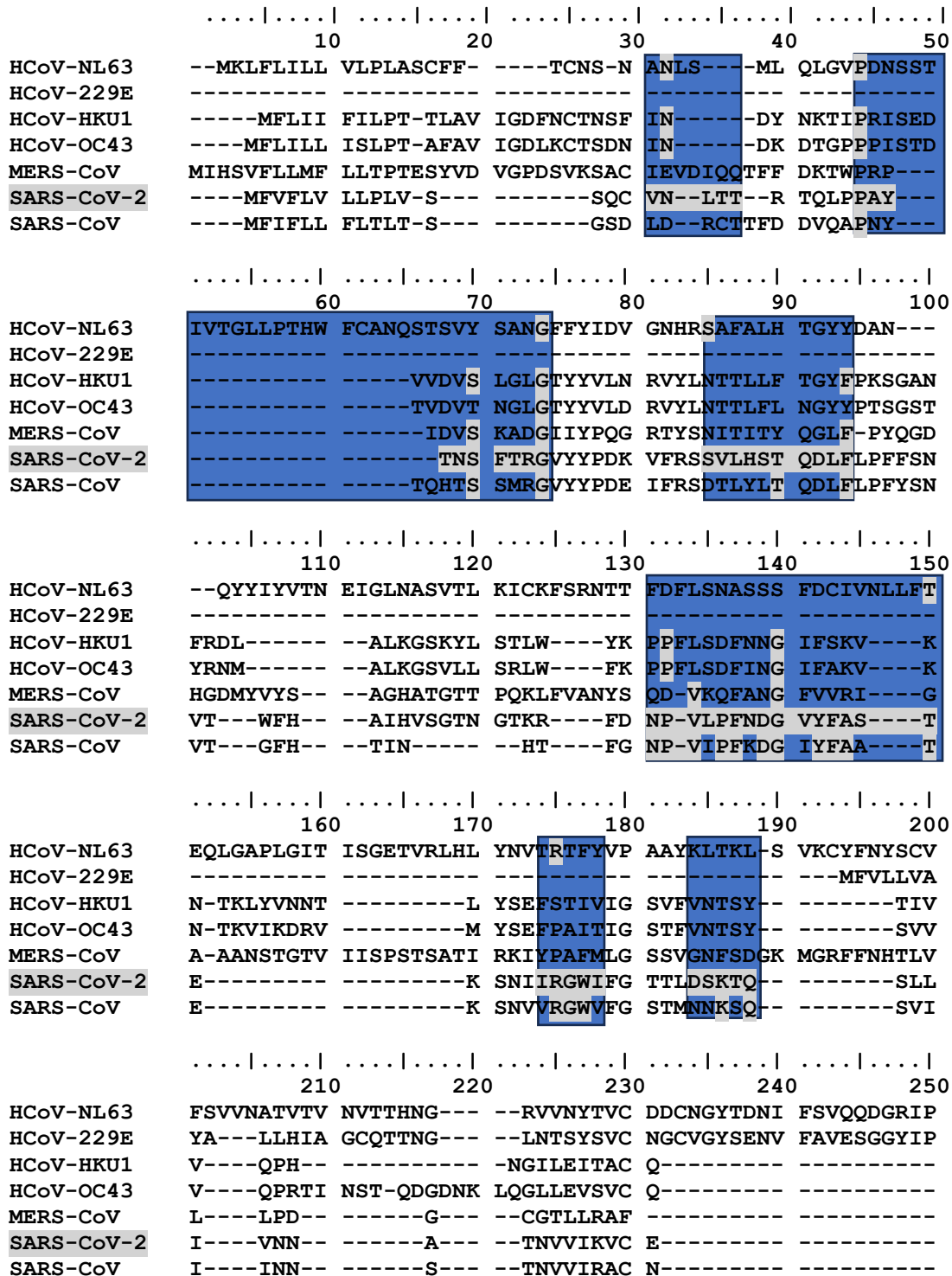


Figure S1: Multiple sequence alignment of the six-coronaviruses spike proteins deposited in the database with a higher degree of identity ( $\geq 97\%$ ) with SARS-CoV-2. BLAST was carried out in the UniProt (Universal Protein) database of the EBI (European Bioinformatics Institute), using the P0DTC2 protein from the SARS-CoV-2 as input. HCoV-NL63 (YP\_003767.1), HCoV-229E (NP\_073551.1), HCoV-HKU1 (Q14EB0.1), HCoV-OC43 (P36334.1), MERS-CoV (YP\_007188579.1), SARS-CoV-2 (P0DTC2), and SARS-CoV (P59594.1).



	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	260 270 280 290 300
HCoV-NL63	NGFPFNNWFL LTNGSTLVDG VSRLYQPLRL TCLWPVPGLK SSTGFVYF--
HCoV-229E	SDFAFNNWFL LTNTSSVVDG VVRSFQPLLL NCLWSVSGLR FTTGFVYF--
HCoV-HKU1	-----YT MCEYPHTVCK S-KGSIRN--
HCoV-OC43	-----YN MCEYPQTICH PNLGNHRK--
MERS-CoV	-----Y CILEPRSGNH CPAGNSYTSF
SARS-CoV-2	-----FQ FCNDPFLGVY YHKNN----
SARS-CoV	-----FE LCDNPFFAVS KPMGT-----

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	310 320 330 340 350
HCoV-NL63	---NATGSDV NCGYQHNSV VD-----VMR YNLNFSANSL ---DNLKSG-
HCoV-229E	---NGTGR-G DCKGFSSDVL SD-----VIR YNLNFEE--- ---NLRRG-
HCoV-HKU1	-----ESWH IDSSE-PLCL FKKNFYTNVS A-----DWL
HCoV-OC43	-----ELWH LDTGV-VSCL YKRNFTYDVN A-----DYL
MERS-CoV	ATYHTPATDC SDGNYNRNAS LNSFKEYFNL RNCTFMYTYN ITEDEILEWF
SARS-CoV-2	-----KSWM ESEFRVYSSA NNCTFEYVSQ PFLMDLEGKQ
SARS-CoV	-----QTHMIFDNA FNCTFEYISD AFSLDVSEKS

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	360 370 380 390 400
HCoV-NL63	-----VIV FKTLYQDVLF YCSNSSSGV- ---LDTTIPFGP
HCoV-229E	-----TIL FKTSYGVVVF YCTNNTLVS- ---GDAHIPFGT
HCoV-HKU1	-----YFH FYQERG VFYA YYADV--G-- ---MP-T TFLFSLYLGT
HCoV-OC43	-----YFH FYQEGGTFYA YFTDT--G-- ---VV-T KFLFNVYLGM
MERS-CoV	GITQTAQG-V HLFSSRYVDL YGGN-----M FQFATLPVYD
SARS-CoV-2	GNFKNLREFV FKNIDGYFKI YSKHTPINLV RDLPGQFSAL EPLVDLPIGI
SARS-CoV	GNFKHLREFV FKNKDGFLYV YKGYQPIDVV RDLPSGFNTL KPFIKFLPLGI

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	410 420 430 440 450
HCoV-NL63	SSQPYCYFIN STINTTHVST FVGILPPTVR EIVVARTGQF YINGFKYFDL
HCoV-229E	VLGNFYCFVN TTIGNETTSF FVGALPKTVR EFVISRTGHF YINGRYFTL
HCoV-HKU1	ILSHYYVM-- ---PLTCK ---
HCoV-OC43	ALSHYYVM-- ---PLTCN ---
MERS-CoV	TIKYYSII-- ---PHSIR ---SI
SARS-CoV-2	NITRFQTL-- ---LALHR SYL-----TP
SARS-CoV	NITNFRAL-- ---LTAFS ---

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	460 470 480 490 500
HCoV-NL63	GFIEAVNFNV TTASATDFWT VAFATFVDVL VNVSATNIQN LLYCD-SPFE
HCoV-229E	GNVEAVNFNV TTAETTDECT VALASYADVL VNVSQTSIAN IIYCN-SVIN
HCoV-HKU1	-A----ISSN TDNETLEYWV TPLSRQYLL NFDEHGVITN AVDCSSSFLS
HCoV-OC43	-S----- --KLITLEYWV TPLTSRQYLL AFNQDGIIFN AEDCMSDFMS
MERS-CoV	QS-----DRKA W---AAFYV YKLQPLTFLL DFSVDGYIRR AIDCGFNDLS
SARS-CoV-2	GD-----SSSG WTAGAAAYYV GYLQPRTFLL KYNENGTITD AVDCALDPLS
SARS-CoV	-P-----AQDI WGTSAAYYFV GYLKPTTFML KYDENGITITD AVDCSQNPLA

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	510 520 530 540 550
HCoV-NL63	KLQCEHLQFG LQDGFYSANF LDDNVLPEY VALPIY----
HCoV-229E	RLRCDQLSFD VPDGFYSTSP IQSVELPVS VSLPVY----
HCoV-HKU1	EIQCKTQSFA PNTGVYDL SGFTVKPVATVY RRIPNLPDCD IDNWLNNVSV
HCoV-OC43	EIKCKTQSIA PPTGVYELNG YTVQPIADV RRKPNLPNCN IEAWLNDKSV
MERS-CoV	QLHCSYESFD VESGVYSVSS FEAKPSGSV EQAEG-VECD FSPLLSTP

SARS-CoV-2	ETKCTLKSFT	VEKGIYQTSN	FRVQPTESIV	RFPNITNLCP	FGEVFNATRF
SARS-CoV	ELKCSVKSE	IDKGIYQTSN	FRVVPBGDVV	RFPNITNLCP	FGEVFNATKF
	..... .....	..... .....	..... .....	..... .....	..... .....
	560	570	580	590	600
HCoV-NL63	-----YQHT	DINFT-----	-----ATASF	GGSCYVCKPH	
HCoV-229E	-----HKHT	FIVLYV-----	-----DFKPQSG	GGKCFNCYPA	
HCoV-HKU1	PSPLNWERRI	FSNCNFNLSL	LLRLVHVDSF	SCNNLDKSKI	FGSCFNSI--
HCoV-OC43	PSPLNWERKT	FSNCNFMSS	LMSFIQADSF	TCNNIDAANK	YGMCFSSI--
MERS-CoV	PQVYNFKRLV	FTNCNYNLTK	LLSLFSVNDF	TCSQISPAAI	ASNCYSSL--
SARS-CoV-2	ASVYAWNRRK	ISNCVADYSV	LYNSASFSTF	KCYGVSPTKL	NDLCFTNV--
SARS-CoV	PSVYAWERKK	ISNCVADYSV	LYNSTFFSTF	KCYGVSATKL	NDLCFSNV--
	..... .....	..... .....	..... .....	..... .....	..... .....
	610	620	630	640	650
HCoV-NL63	QVNISLNG--	-----NTSVC	VRTSHFSIRY	IYNRVKSGSP	GDSSWHIYLK
HCoV-229E	GVNITLANFN	ET--KGPLC	VDTSHTTKY	VAVYA----	NVGRWSASIN
HCoV-HKU1	----TVDKFA	IPNRRRDDLQ	LGSSGFLQSS	NYKIDISSSS	CQLYYSPLPV
HCoV-OC43	----TIDKFA	IPNGRKVDLQ	LGNLGYLQSF	NYRIDTTATS	CQLYYNLPAA
MERS-CoV	----ILDYFS	YPLSMKSDLS	VSSAGPISQF	NYKQSFSNPT	CLILATVPHN
SARS-CoV-2	----YADSFV	IRGDEVQRQA	PGQTGKIADY	NYKLPDDFTG	CVIAWNSNNL
SARS-CoV	----YADSFV	VKGDDVRQIA	PGQTGVIADY	NYKLPDDFMG	CVLAWNTRNI
	..... .....	..... .....	..... .....	..... .....	..... .....
	660	670	680	690	700
HCoV-NL63	--SGTCPF--	-----SFS	KLNNFQ----	-----KF	KTICFSTVEV
HCoV-229E	--TGNCPF--	-----SFG	KVNNFV----	-----KF	GSVCFSLKDI
HCoV-HKU1	NVTINN-FNP	SSWNRRYGFQ	SFN-----	--VSSYDVVY	SDHCFSVNSD
HCoV-OC43	NVSISR-FNP	STWNKRFGFI	EDSVFKPRPA	GVLTHNDVVY	AQHCFKAPKN
MERS-CoV	LTTITKPLKY	SYINKCSRFL	SD-----DRT	E-----V	PQLVNA--NQ
SARS-CoV-2	DSKVGGNVNY	LYRLFRKSNL	KP-----FER	D-----I	STEIYQ--AG
SARS-CoV	DATSTGNVNY	KYRYLRHGKL	RP-----FER	D-----I	SNVPFS--PD
	..... .....	..... .....	..... .....	..... .....	..... .....
	710	720	730	740	750
HCoV-NL63	P-----	GSCNF-----	-----	-----	-----
HCoV-229E	P-----	GGCAM-----	-----	-----	-----
HCoV-HKU1	FCPCADPSVV	NSCVKSKP--	--LSAICPAG	TKYRHCDLDT	TLYVNNWCRC
HCoV-OC43	FCPCKLN---	GSCVGSPPGK	NNGIGTCPAG	TNYLTCD---	-----N
MERS-CoV	YSPCVSIVP-	ST-VW-----	-----EDG	DYYRK-----	-----
SARS-CoV-2	STPCNGVEG-	FNCYF-----	-----	-----	-----
SARS-CoV	GKPCTP-PA-	LNCYW-----	-----	-----	-----
	..... .....	..... .....	..... .....	..... .....	..... .....
	760	770	780	790	800
HCoV-NL63	----PLEAT	WHYT-----	-----	-----	----SYTIV
HCoV-229E	----PIVAN	WAYS-----	-----	-----	----KYYTI
HCoV-HKU1	SCLPDPISTY	SPNTCPQKKV	VVGIGEHCPCG	LGINEEKCCTG	QLNHSSSCSCS
HCoV-OC43	LCTPDPIFTT	GTYPKCPQTKS	LVGIGEHCSCG	LAVKSDYCGG	----NSCTCR
MERS-CoV	--QLSPLEGG	GWL-----	-----	-----	----ASGSTVA
SARS-CoV-2	----PLQSY	GFQP-----	-----	-----	----TNGVGYQ
SARS-CoV	----PLNDY	GFYT-----	-----	-----	----TTGIGYQ
	..... .....	..... .....	..... .....	..... .....	..... .....
	810	820	830	840	850
HCoV-NL63	GALYVTWSEG	NSITGV----	-----	PYPV-----S	GIREFSNLVL
HCoV-229E	GSLYVSWSDG	DGITGV----	-----	PQPV-----E	GVSSFMNVTL

HCoV-HKU1	PDAFLGWSFD	SCISNNRCNI	FSNFIFNGIN	SGTTCSN--D	LLYSNTEVST
HCoV-OC43	PQAFLGWSAD	SCLQGDKCNI	FANFILHDVN	SGLTCST--D	LQKANTDIIL
MERS-CoV	MTEQLQMGFG	IT-----	----VQYGT	TNSVCPKLEF	ANDTKIASQL
SARS-CoV-2	PYRVVVLSE	LL-----	-----HA	PATVCGP---	--KKSTNLVK
SARS-CoV	PYRVVVLSE	LL-----	-----NA	PATVCGP---	--KLSTDLIK

	860	870	880	890	900
HCoV-NL63	NNCTKYNIYD	YVGTGIIRSS	NQSLAGGIT-	-YVSNSGNLL	G-FKNVSTGN
HCoV-229E	DKCTKYNIYD	VSGVGIVRVS	NDTFLNGIT-	-YTSTSGNLL	G-FKDVTKGT
HCoV-HKU1	GVCVNYDLYG	ITGQGIFKEV	SAAYYNNWQN	LLYDSNGNII	G-FKDFLTNK
HCoV-OC43	GVCVNYDLYG	ILGQGIFVEV	NATYYNSWQN	LLYDSNGNLY	G-FRDYIINR
MERS-CoV	GNCVEYSLYG	VSGRGVFQNC	TAVG-VRQQR	FVYDAYQNLV	GYYS--DGN
SARS-CoV-2	NKCVNFNFNG	LTGTGVLTES	NKKF-LPFQQ	FGRDIADTT-	DAVRDPQTLE
SARS-CoV	NQCVNFNFNG	LTGTGVLTPS	SKRF-QPFQQ	FGRDVSDFT-	DSVRDPKTSE

	910	920	930	940	950
HCoV-NL63	IFIVTPCNQP	DQVAVYQQ--	-----	SIIGAMTAVN	ESRYGLQ---
HCoV-229E	IYSITPCNPP	DQLVVYQQ--	-----	AVVGAMLSN	FTSYGFS---
HCoV-HKU1	TYTILPCYSG	RVSAAFY--Q	NSSSPALLYR	NLKCSYVLNN	IS--FIS---
HCoV-OC43	TFMIRSCYSG	RVSAAFH--A	NSSEPALLFR	NIKCNVVFNN	SLTRQLQ---
MERS-CoV	YYCLRACVSV	PVSVIYD--K	ETKTHATLFG	SVACEHISST	MSQYSRSTRS
SARS-CoV-2	ILDITPCSFG	GVSVITPGTN	TSNQVAVLYQ	DVNCTEVPVA	IHADQLT--P
SARS-CoV	ILDISPCSFG	GVSVITPGTN	ASSEVAVLYQ	DVNCTDVSTA	IHADQLT--P

	960	970	980	990	1000
HCoV-NL63	--NLLQLPNF	YYVSNGG---	--NNCT----	TAVMTYSNFG	ICADGSLIP-
HCoV-229E	--NVVELPKF	FYASNGT---	--YNCT----	DAVLTYSSFG	VCADGSIIA-
HCoV-HKU1	-----QPF	YFDSYLGCVL	NAVNLTSYSV	SSCDLRMGSG	FCIDYALPSS
HCoV-OC43	-----PIN	YFDSYLGCVV	NAYNSTAISV	QTCDLTVGSG	YCVDYSK--N
MERS-CoV	MLKRRDSTYG	PLQTPVGCVL	GLVNSS-LFV	EDCKLPLGQS	LCALPDTPST
SARS-CoV-2	TWRVYSTGSN	VFQTRAGCLI	GAEHVN--NS	YECDIPIGAG	ICASYQTQT-
SARS-CoV	AWRIYSTGNN	VFQTAGCLI	GAEHVD--TS	YECDIPIGAG	ICASYHTVS-

	1010	1020	1030	1040	1050
HCoV-NL63	VRPR--NSS	DNGIS-----	-----	-AIITANLSI	PSNWTTTSVQV
HCoV-229E	VQPR--NVS	YDSVS-----	-----	-AIVTANLSI	PSNWTTTSVQV
HCoV-HKU1	RRKRRGISSP	YRFVT-FEPF	NVSFVNSDVE	TVGGLFEIQI	PTNFTIAGHE
HCoV-OC43	RRSRGAITTG	YRFTN-FEPF	TVNSVNSDLE	PVGGLYEIQI	PSEFTIGNMV
MERS-CoV	LTPRSVRSVP	GEMRLASIAF	NHPIQ-V-DQ	LNSSYFKLSI	PTNFSEFVGTQ
SARS-CoV-2	NSPRRARSVA	SQSI---IAY	TMSLG-AENS	VAYSNNNSIAI	PTNFTISVTT
SARS-CoV	L----LRSTS	QKSI---VAY	TMSLG-ADSS	IAYSNNNTIAI	PTNFSISITT

	1060	1070	1080	1090	1100
HCoV-NL63	EYLQITSTPI	VVDCATYVCN	GNPRCKNLLK	QYTSACKTIE	DALRLSAHLE
HCoV-229E	EYLQITSTPI	VVDCSTYVCN	GNVRCVELLK	QYTSACKTIE	DALRNSARLE
HCoV-HKU1	EFIQTSSPKV	TIDCSAFVCS	NYAACHDLLS	EYGTFCDNIN	SILNEVNDLL
HCoV-OC43	EFIQTSSPKV	TIDCAAFVCG	DYAACKSQLV	EYGSFCDNIN	AILTEVNELL
MERS-CoV	EYIQTTIQKV	TVDCQYVCN	GFQKCEQLLR	EYGFCSKIN	QALHGANLRQ
SARS-CoV-2	EILPVSMTKT	SVDCTMYICG	DSTECNLLL	QYGSFCTQLN	RALTGIAVEQ
SARS-CoV	EVMPVMAKT	SVDCNMYICG	DSTECANLLL	QYGSFCTQLN	RALSIGIAAEQ

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1110      1120      1130      1140      1150
HCoV-NL63 TNDVSSMLTF DSNAFSLAN- ----VTSFGD -YNLSSVLPQ RNIRSSRIAG
HCoV-229E SADVSEMLTF DKKAFTLAN- ----VSSFGD -YNLSSVIPs LPTSGSRVAG
HCoV-HKU1 DITQLQVANA LMQGVTLSSN LNTNLHSDVD NIDFKSLLGC LGSQCGS-SS
HCoV-OC43 DTTQLQVANS LMNGVTLSTK LKDGVNFNVD DINFSPVLGC LGSECSKASS
MERS-CoV DDSVRNLFAS VKSSQSSPI- ----IPGFGG DFNLTLLEP- VSISTGSRSA
SARS-CoV-2 DKNTQEVFAQ VKQIYKTPP- ----IKDFGG F-NFSQILP- DP---SKPSK
SARS-CoV DENTREVFQA VKQMYKTPT- ----LKVFEGG F-NFSQILP- DP---IKPTK

```

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1160      1170      1180      1190      1200
HCoV-NL63 RSAIEDLLFS KVVTSGLGTV DVDYKSC-- KGLSIADLAC AQYYNGIMVL
HCoV-229E RSAIEDILFS KLVTSGLGTV DADYKKT-- KGLSIADLAC AQYYNGIMVL
HCoV-HKU1 RSLLEDLLFN KVKLSDVGfV E-AYNNCT-- GGSEIRDLLC VQSFNGIKVL
HCoV-OC43 RSAIEDLLFD KVKLSDVGfV E-AYNNCT-- GGAEIRDLIC VQSYKGIKVL
MERS-CoV RSAIEDLLFD KVTIADPGYM Q-GYDDCMQO GPASARDLIC AQYVAGYKVL
SARS-CoV-2 RSFIEDLLFN KVTIADAGFI K-QYGDCL-- GDIAARDLIC AQKFNGLTVL
SARS-CoV RSFIEDLLFN KVTIADAGFM K-QYGECL-- GDINARDLIC AQKFNGLTVL

```

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1210      1220      1230      1240      1250
HCoV-NL63 PGVADAERMA MYTGLSIGGM VLGGLTSA-- --AAIPFSLA LQARLNYVAL
HCoV-229E PGVADAERMA MYTGLSIGGI ALGGLTSA-- --VSIPFSLA IQARLNYVAL
HCoV-HKU1 PPILSETQIS GYTAAATVAA MFPPWSAA-- --AGVPFSLN VQYRINGLGV
HCoV-OC43 PPLISENQIS GYTAAATSAS LFPPWTAA-- --AGVPFYLN VQYRINGLGV
MERS-CoV PPLMDVNMEA AYTSSLLGSI AGVGWTAGLS SFAAIPFAQS IFYRLNGVGI
SARS-CoV-2 PPLLTDEMIA QYTSALLAGT ITSGWTFGAG AALQIPFAMQ MAYRFNGIGV
SARS-CoV PPLLTDDMIA AYTAALVSGT ATAGWTFGAG AALQIPFAMQ MAYRFNGIGV

```

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1260      1270      1280      1290      1300
HCoV-NL63 QTDVLQENQK ILAASFNKAI NNIVASFSSV NDAITQTAEA IHTVTIALNK
HCoV-229E QTDVLQENQK ILAASFNKAM TNIVDAFTGV NDAITQTSQA LQTVATALNK
HCoV-HKU1 TMDVLNKNQK LIANAFNKAL LSIQNGFTAT N----- ----SALAK
HCoV-OC43 TMDVLSQNQK LIANAFNNAL YAIQEGFDAT N----- ----SALVK
MERS-CoV TQQVLSQENQK LIANKFNQAL GAMQTGFTTT N----- ----EAFHK
SARS-CoV-2 TQNVLYENQK LIANQFNSAI GKIQDSLST A----- ----SALGK
SARS-CoV TQNVLYENQK QIANQFNKAI SQIQESLTTT S----- ----TALGK

```

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1310      1320      1330      1340      1350
HCoV-NL63 IQDVVNQOGS ALNHLTSQLR HNFQAISNSI QAIYDRLD SI QADQQVDR LI
HCoV-229E IQDVVNQOGN SLNHLTSQLR QNFQAISSSI QAIYDRLD TI QADQQVDR LI
HCoV-HKU1 IQSVVNANAA ALNSLLQQLF NKFGAISSSL QEILSR LDNL EAQVQIDR LI
HCoV-OC43 IQAVVNANAE ALNNLLQQLS NRFGAISASL QEILSR LDAL EAEAQIDR LI
MERS-CoV VQDAVNNNAQ ALSKLASELS NTFGAISASI GDIIQR LDVL EQDAQIDR LI
SARS-CoV-2 LQDVVNQNAQ ALNTLVKQLS SNFGAISSVL NDILSR LDKV EAEVQIDR LI
SARS-CoV LQDVVNQNAQ ALNTLVKQLS SNFGAISSVL NDILSR LDKV EAEVQIDR LI

```

```

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|
1360      1370      1380      1390      1400
HCoV-NL63 TGRILAALNAF VSQVLNKYTE VRGSRRLAQQ KINECVKSQS NRYGFCGNGT
HCoV-229E TGRILAALNVF VSHTLT KYTE VRASRQLAQQ KVNECVKSQS KRYGFCGNGT
HCoV-HKU1 NGRLTALNAY VSQQLSDITL IKAGASRAIE KVNECVKSQS PRINFCGNGN
HCoV-OC43 NGRLTALNAY VSQQLSDSTL VKFSAAQAME KVNECVKSQS SRINFCGNGN
MERS-CoV NGRLTTLNAF VAQQLVRSES AALSAQLAKD KVNECVKAQS KRS GF CGQT

```

SARS-CoV-2	TGRLQSLQTY VTQQLIRAAE	IRASANLAAT	KMSECVLGQS	KRVDFCGKGY
SARS-CoV	TGRLQSLQTY VTQQLIRAAE	IRASANLAAT	KMSECVLGQS	KRVDFCGKGY

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	1410 1420 1430 1440 1450
HCoV-NL63	HIFSIVNSAP DGLLFLHTVL LPTDYKNVKA WSGICVDGIY --GYVLRQPN
HCoV-229E	HIFSIVNAAP EGLVFLHTVL LPTQYKDVEA WSGLCVDGTN --GYVLRQPN
HCoV-HKU1	HILSLVQNAF YGLLFIHFSY KPTSFKTVLV SPGLCLSGDR --GIAPKQGY
HCoV-OC43	HIISLVQNAF YGLYFIHFSY VPTKYVTARV SPGLCIAGDR --GIAPKSGY
MERS-CoV	HIVSFVFNAP NGLYFMHVG YPSNHIEVVS AYGLCDAANP TNCIAPVNGY
SARS-CoV-2	HLMSFPQSAP HGVVFLHVTY VPAQEKNTTT APAICHGKA ---HFPREGV
SARS-CoV	HLMSFPQAAP HGVVFLHVTY VPSQERNFTT APAICHEGKA ---YFPREGV

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	1460 1470 1480 1490 1500
HCoV-NL63	LVLY---SDN GVFRVTSRVM FQPRLPVLSF FVQIYNCNVT FVNISRVEL-
HCoV-229E	LALY---KEG NYRITSRIM FEPRIPTMAD FVQIENCNVT FVNISRSEL-
HCoV-HKU1	FIKQ-----N DSWMFTGSS YYPEPISDKN VVFMNSCSVN FTKAPFIYL-
HCoV-OC43	FVNV-----N NTWMTGSGY YYPEPITENN VVMSTCAVN YTKAPYVML-
MERS-CoV	FIKTNNTRIV DEWSTGSSF YAPEPITSLN TKYVAPQVTY QN-ISTNLPP
SARS-CoV-2	FVSN-----G THWFTQRNF YEPQIITTDN TFSVGNCDVV IGIIVNTVYD
SARS-CoV	FVFN-----G TSWFITQRNF FSPQIITTDN TFSVGNCDVV IGIINNTVYD

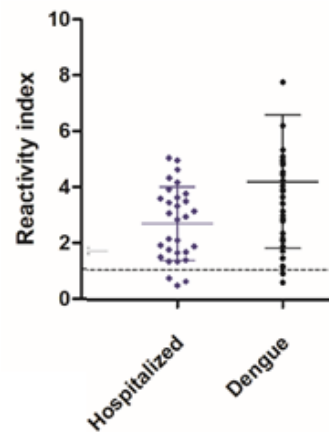
	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	1510 1520 1530 1540 1550
HCoV-NL63	-HTVIPDYVD VNKTLQEFQ NLPKYVKPNF -DLTPFNLT YLNLSELKQL
HCoV-229E	-QTIVPEYID VNKTLQELSY KLPNYTVPDL -VVEQYNQTI LNLTSISTL
HCoV-HKU1	-NNSIPNLSD FEAELSFWFK NHTSI-APNL TFNSHINATF LDLYY----
HCoV-OC43	-NTSIPNLPD FKEELDQWFK NQTSV-APDL SLD-YINVTF LDLYQV----
MERS-CoV	PLLGSTGID FQDELDEFK NVSTS-IPNF GSLTQINTTL LDLYY----
SARS-CoV-2	PLQ--PELDS FKEELDKYFK NHTSP-DVDL GDISGINASV VNIQK----
SARS-CoV	PLQ--PELDS FKEELDKYFK NHTSP-DVDL GDISGINASV VNIQK----

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	1560 1570 1580 1590 1600
HCoV-NL63	EAKTASLFQT TVELQGLIDQ INSTYVDLKL LNRFFENYIKW PWWVWLIISV
HCoV-229E	ENKSAELNYT VQKLQTLIDN INSTLVDLKW LNRVETYIKW PWWVWLCISV
HCoV-HKU1	-----E MNVIQESIKS LNSSFINKLKE IGTYEMYVKW PWYIWLIV
HCoV-OC43	-----E MNRLQEAIVK LNQSYINKLKE IGTYEYVVKW PWYVWLLICL
MERS-CoV	-----E MSLQQVVKV LNESYIDLKE LGNYTYYNKW PWYIWLGFIA
SARS-CoV-2	-----E IDRLNEVAKN LNESLIDLQE LGKYEQYIKW PWYIWLGFIA
SARS-CoV	-----E IDRLNEVAKN LNESLIDLQE LGKYEQYIKW PWYVWLGFA

	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
	1610 1620 1630 1640 1650
HCoV-NL63	VFVLLSLLV FCCLSTGCCG CCNCLTSSMR GCCDCGSTKL PYYEFKVVH
HCoV-229E	VLIFVVSMLL LCCCSTGCCG FFSCFASSIR GCCE--STKL PYYDVEKIHI
HCoV-HKU1	LFIIFLMILF FICCTGCGS ACF----- S--KCHNCCD EYGGHNDFVI
HCoV-OC43	AGVAMLVLLF FICCTGCGT SCF----- K--KCGGCCD DYTGYQELVI
MERS-CoV	GLVALALCVF FILCCTGCGT NCM----- GKLKCNRCCD RYEEYDLEPH
SARS-CoV-2	GLIAIVMTI MLCCMTSCCS CLK----- GCCSCGSCK F-DEDDSEPV
SARS-CoV	GLIAIVMTI LLCCMTSCCS CLK----- GACSCGSCK F-DEDDSEPV

HCoV-NL63	Q-----
HCoV-229E	Q-----
HCoV-HKU1	K-ASHDD--
HCoV-OC43	K-TSHDD--
MERS-CoV	KVHVH----
SARS-CoV-2	LKGVKLHYT
SARS-CoV	LKGVKLHYT

Figure S2: Analysis of pre-pandemic sera from patients with DENV ( $n = 24$ ) and sera from hospitalized patients with SARS-CoV-2 (first wave) using a commercial enzyme-linked immunosorbent assay for IgA-SARS-CoV-2. The methodology described by the manufacturer (Serion Immunomat, Würzburg, Germany).





**Table S1.** Clinical characteristics of COVID-19 patients sera used in the study. <sup>1</sup>Mild Illness: Individuals presenting with various signs and symptoms of COVID-19, such as cough, fever, sore throat, malaise, headache, myalgias, nausea, vomiting, gastrointestinal symptoms, and loss of taste and smell. However, they do not exhibit shortness of breath, dyspnea, or abnormal chest imaging. <sup>2</sup>Moderate Illness: Individuals who display evidence of lower respiratory disease during clinical assessment or imaging and maintain an oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>) of  $\geq 94\%$  while breathing room air at sea level. <sup>3</sup>Severe Illness: Individuals with a SpO<sub>2</sub> measurement of  $< 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) below 300 mm Hg, a respiratory rate exceeding 30 breaths per minute, or lung infiltrates covering more than 50% of their lung field.

	<b>COVID (n= 33)</b>	<b>Mild<sup>1</sup> (n= 5)</b>	<b>Mod<sup>2</sup> (n=12)</b>	<b>Severe<sup>3</sup> (n=16)</b>	<b>p- value</b>
Median Age (IQR)	(27–48)	(26–39)	(27–47)	(41–58)	<0.001
Age group, n (%)	100	15.16	36.36	48.48	<0.001
• < 20	4 (50)	2 (25)	1 (12.5)	1 (12.5)	
• 20–39	17 (50)	1 (2.94)	10 (29.41)	6 (17.64)	
• 40–59	12 (50)	2 (8.33)	1 (4.16)	9 (37.50)	
Male, n (%)	19 (50)	3 (7.89)	7 (18.42)	9 (23.68)	<0.001

<sup>1</sup>Mild Illness: Individuals presenting with various signs and symptoms of COVID-19, such as cough, fever, sore throat, malaise, headache, myalgias, nausea, vomiting, gastrointestinal symptoms, and loss of taste and smell. However, they do not exhibit shortness of breath, dyspnea, or abnormal chest imaging. <sup>2</sup>Moderate Illness: Individuals who display evidence of lower respiratory disease during clinical assessment or imaging and maintain an oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>) of  $\geq 94\%$  while breathing room air at sea level. <sup>3</sup>Severe Illness: Individuals with a SpO<sub>2</sub> measurement of  $< 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) below 300 mm Hg, a respiratory rate exceeding 30 breaths per minute, or lung infiltrates covering more than 50% of their lung field.

Table S2: List of synthesized peptides covering the entire sequence of spike protein (P0DTC2, Uniprot database) from SARS-CoV-2. Positive controls (F3, F4, F5, F11, F12, F13) and negative controls (F9, F17). The overlapping of positive peptides defined by the epitopes is labeled in red.

Spot	Peptide Sequence	Spot	Peptide Sequence	Spot	Peptide Sequence	Spot	Peptide Sequence
A1	IHLVNNESEVIVHK	C17	LSETKCTLSFTVEK	F9	NCTEVPVAIHADQLT	I1	DSLSTASALGKLQD
A2	GYPKDGNAFNLDRI	C18	CTLKSFTVEKGIYQT	F10	PVAIHADQLTPTWRV	I2	TASALGKLQDVVNQN
A3	KEVPALTAVETGATN	C19	FTVEKGIYQTSNFRV	F11	ADQLTPTWRVYSTGS	I3	GKLQDVVNQNAQALN
A4	YPYDVPDYAGYPYDV	C20	GIYQTSNFRVQPTES	F12	PTWRVYSTGSNVFQT	I4	VVNQNAQALNTLVKQ
A5		C21	SNFRVQPTESIVRFP	F13	YSTGSNVFQTRAGCL	I5	AQALNTLVKQLSSNF
A6	MFVFLVLLPLVSSQC	C22	QPTESIVRFPNITNL	F14	NVFQTRAGCLIGAEH	I6	TLVKQLSSNFGAISS
A7	VLLPLVSSQCVNLTT	C23	IVRFPNITNLCPFGE	F15	RAGCLIGAEHVNNYSY	I7	LSSNFGAISSVLNDI
A8	VSSQCVNLTTTRTQLP	C24	NITNLCPFGEVFNAT	F16	IGAEHVNNSYECDIP	I8	GAISSVLNDILSRLD
A9	VNLTTTRTQLPPAYTN	D1	CPFGEVFNATRFASV	F17	VNNSYECDIPIGAGI	I9	VLNDILSRLDKVEAE
A10	RTQLPPAYTNSFTRG	D2	VFNATRFASVYAWNR	F18	ECDIPIGAGICASYQ	I10	LSRLDKVEAEVQIDR
A11	PAYTNSFTRGVVYPD	D3	RFASVYAWNRKRISN	F19	IGAGICASYQTQTNS	I11	KVEAEVQIDRLITGR
A12	SFTRGVVYPDKVFRS	D4	YAWNRKRISNCVADY	F20	CASYQTQTNSPRRAR	I12	VQIDRLITGRLQSLQ
A13	VVYPDKVFRSSVLHS	D5	KRISNCVADYSVLYN	F21	TQTNSPRRARSVASQ	I13	LITGRLQSLQTYVTQ
A14	KVFRSSVLHSTQDLF	D6	CVADYSVLVNSASF	F22	PRRARSVASQSIIAY	I14	LQSLQTYVTQQLIRA
A15	SVLHSTQDLFLPFFS	D7	SVLVNSASFSTFKCY	F23	SVASQSIIAYTMSLG	I15	TYVTQQLIRAAEIRA
A16	TQDLFLPFFSNVTWF	D8	SASFSTFKCYGVSPT	F24	SIIAYTMSLGAENSV	I16	QLIRAAEIRASANLA
A17	LPFFSNVTWFHAIHV	D9	TFKCYGVSPTKLNLD	G1	TMSLGAENSVAYSNN	I17	AEIRASANLAATKMS
A18	NVTWFHAIHVSGTNG	D10	GVSPTKLNLCFTNV	G2	AENSVAYSNNIAIP	I18	SANLAATKMSECVLG
A19	HAIHVSGTNGTKRFD	D11	KLNDLCFTNVYADSF	G3	AYSNNIAIPTNFTI	I19	ATKMSECVLGQSKRV
A20	SGTNGTKRFDNPVLP	D12	CFTNVYADSFVIRGD	G4	SIAIPTNFTISVTTE	I20	ECVLGQSKRVDFCGK
A21	TKRFDNPVLPFNDGV	D13	YADSFVIRGDEVIRQI	G5	TNFTISVTTEILPVS	I21	QSKRVDFCGKGYHLM
A22	NPVLPFNDGVYFAST	D14	VIRGDEVIRQIAPGQT	G6	SVTTEILPVSMTKTS	I22	DFCGKGYHLMSPQS
A23	FNDGVYFASTSKSNI	D15	EVIRQIAPGQTGKIAD	G7	ILPVSMTKTSVDCTM	I23	GYHLMSPQSAPHGV
A24	YFASTSKSNIIRGWI	D16	APGQTGKIADYNYKL	G8	MTKTSVDCTMYICGD	I24	SFPQSAPHGVVFLHV
B1	EKSNIIRGWIFGTTL	D17	GKIADYNYKLPPDFT	G9	VDCTMYICGDSTEC	J1	APHGVVFLHVTYVPA

B2	IRGWIFGTTLDSKTQ	D18	YNYKLPPDFTGCVIA	G10	YICGDSTECSNLLLQ	J2	VFLHVTYVPAQEKNF
B3	FGTTLDSKTQSLLIV	D19	PDDFTGCVIAWNSNN	G11	STECSNLLLQYGSFC	J3	TYVPAQEKNFTTAPA
B4	DSKTQSLLIVNNATN	D20	GCVIAWNSNNLDSKV	G12	NLLLQYGSFCTQLNR	J4	QEKNFTTAPAICHDG
B5	SLLIIVNNATNVVIKV	D21	WNSNNLDSKVGNYN	G13	YGSFCTQLNRALTGI	J5	TTAPAICHDGKAHFP
B6	NNATNVVIKVCEFAQF	D22	LDSKVGGNYNYLYRL	G14	TQLNRALTGIAVEQD	J6	ICHDGKAHFPREGVF
B7	VVIKVCEFAQCNDPF	D23	GGNYNYLYRLFRKSN	G15	ALTGIAVEQDKNTQE	J7	KAHFPREGVFVSNGT
B8	CEFAQCNDPFLGVYY	D24	YLYRLFRKSNLKPFE	G16	AVEQDKNTQEVFAQV	J8	REGVFVSNGTHWFVT
B9	CNDPFLGVYYHKNNK	E1	FRKSNLKPFERDIST	G17	KNTQEVFAQVKQIYK	J9	VSNGTHWFVTQRNFY
B10	LGVYYHKNNKSWMES	E2	LKPFERDISTEIQYA	G18	VFAQVKQIYKTPPIK	J10	HWFVTQRNFYEPQII
B11	HKNNKSWMESEFRVY	E3	RDISTEIQAGSTPC	G19	KQIYKTPPIKDFGGF	J11	QRNFYEPQIITTDNT
B12	SWMESEFRVYSSANN	E4	EIQAGSTPCNGVEG	G20	TPPIKDFGGFNFSQI	J12	EPQIITTDNTFVSGN
B13	EFRVYSSANNCTFEY	E5	GSTPCNGVEGFNCYF	G21	DFGGFNFSQILPDPS	J13	TTDNTFVSGNCDVVI
B14	SSANNCTFEYVSQPF	E6	NGVEGFNCYFPLQSY	G22	NFSQILPDPSKPSKR	J14	FVSGNCDVVIGIVNN
B15	CTFEYVSQPFLMDLE	E7	FNCYFPLQSYGFQPT	G23	LPDPSKPSKRSFIED	J15	CDVVIGIVNNTVYDP
B16	VSQPFLMDLEGKQGN	E8	PLQSYGFQPTNGVGY	G24	KPSKRSFIEDLLFNK	J16	GIVNNTVYDPLQPEL
B17	LMDLEGKQGNFKNLR	E9	GFQPTNGVGYQPYRV	H1	SFIEDLLFNKVTLAD	J17	TVYDPLQPELDSFKE
B18	GKQGNFKNLREFVFK	E10	NGVGYQPYRVVLSF	H2	LLFNKVTLADAGFIK	J18	LQPELDSFKEELDKY
B19	FKNLREFVFKNIDGY	E11	QPYRVVLSFELLHA	H3	VTLADAGFIKQYGDC	J19	DSFKEELDKYFKNHT
B20	EFVFKNIDGYFKIYS	E12	VVLSFELLHAPATVC	H4	AGFIKQYGDCLGDIA	J20	ELDKYFKNHTSPDVD
B21	NIDGYFKIYSKHTPI	E13	ELLHAPATVCGPKKS	H5	QYGDCLGDIAARDLI	J21	FKNHTSPDVDLGDIS
B22	FKIYSKHTPINLVRD	E14	PATVCGPKKSTNLVK	H6	LGDIAARDLICAQKF	J22	SPDVDLGDISGINAS
B23	KHTPINLVRDLPQGF	E15	GPKKSTNLVKNKCVN	H7	ARDLICAQKFNGLTV	J23	LGDISGINASVVNIQ
B24	NLVRDLPQGFSALEP	E16	TNLVKNKCVNFNFNG	H8	CAQKFNGLTVLPPLL	J24	GINASVVNIQKEIDR
C1	LPQGFSALEPLVDLP	E17	NKCVNFNFNGLTGTG	H9	NGLTVLPPLLTDAMI	K1	VVNIQKEIDRLNEVA
C2	SALEPLVDLPIGINI	E18	FNFNGLTGTGVLTES	H10	LPPLLTDEMIAQYTS	K2	KEIDRLNEVAKNLNE
C3	LVLDLPIGINITRFQT	E19	LTGTGVLTESNKKFL	H11	TDEMIAQYTSALLAG	K3	LNEVAKNLNESLIDL
C4	IGINITRFQTLALH	E20	VLTESNKKFLPFQQF	H12	AQYTSALLAGTITSG	K4	KNLNESLIDLQELGK
C5	TRFQTLALHRSYLT	E21	NKKFLPFQQFGRDIA	H13	ALLAGTITSGWTFGA	K5	SLIDLQELGKYEQYI
C6	LLALHRSYLTTPGDSS	E22	PFQQFGRDIADTTDA	H14	TITSGWTFGAGAALQ	K6	QELGKYEQYIKWPWY
C7	RSYLTTPGDSSSGWTA	E23	GRDIADTTDAVRDPQ	H15	WTFGAGAALQIPFAM	K7	YEQYIKWPWYIWLGF

C8	PGDSSSGWTAGAAAY	E24	DTTDAVRDPQTLEIL	H16	GAALQIPFAMQMAYR	K8	KWPWYIWLGFIAGLI
C9	SGWTAGAAAYYVGYL	F1	VRDPQTLEILDITPC	H17	IPFAMQMAYRFNGIG	K9	IWLGFIAGLIAIVMV
C10	GAAAYYVGYLQPRTF	F2	TLEILDITPCSFGGV	H18	QMAYRFNGIGVTQNV	K10	IAGLIAIVMVTIMLC
C11	YVGYLQPRTFLLKYN	F3	DITPCSFGGVSVITP	H19	FNGIGVTQNVLYENQ	K11	AIVMVTIMLCCMTSC
C12	QPRTFLLKYNENGTI	F4	SFGGVSVITPGTNTS	H20	VTQNVLYENQKLIAN	K12	TIMLCCMTSCCSCLK
C13	LLKYNENGTITDAVD	F5	SVITPGTNTSNQVAV	H21	LYENQKLIANQFNSA	K13	CMTSCCSCLKGCCSC
C14	ENGTITDAVDCALDP	F6	GTNTSNQVAVLYQDV	H22	KLIANQFNSAIGKIQ	K14	CSCLKGCCSCGSCCK
C15	TDAVDCALDPLSETK	F7	NQVAVLYQDVNCTEV	H23	QFNSAIGKIQDSLSS	K15	GCCSCGSCCKFDEDD
C16	CALDPLSETKCTLKS	F8	LYQDVNCTEVPVAIH	H24	IGKIQDSLSTASAL	K16	GSCCKFDEDDSEPVL
						K17	FDEDDSEPVLKGVKL
						K18	DDSEPVLKGVKLHYT

Table S3: List of the synthesized peptides covering the sequence of RBD mutated spike proteins from SARS-CoV-2 variants. Positive controls: YPGEFADYEELREQL (*Influenza virus*), spots 09 (A, B, C, D, E and F); negative controls: QEVRY (Cowpox virus); spot 11 (A, B, C, D, E and F); KEVPALTAVETGATN (Poliovirus) spot 10 (A, B, C, D, E and F).

Spot	Peptides	Spot	Peptides	Spot	Peptides
A1	GGGCVADYSVLYNGG	B1	GGGCVADYSVLYNGG	C1	GGGCVADYSVLYNGG
A2	GGGYADSFVIRGDGG	B2	GGGYADSFVIRGDGG	C2	GGGYADSFVIRGDGG
A3	GGGYNYKLPDDFTGG	B3	GGGYNYKLPDDFTGG	C3	GGGYNYKLPDDFTGG
A4	WNSNNLDSKVGGNYN	B4	WNSNNLDSKVGGNYN	C4	WNSNNLDSKVGGNYN
A5	GGGLKPFERDISTGG	B5	GGGLKPFERDISTGG	C5	GGGLKPFERDISTGG
A6	PLQSYGFQPTNGVGY	B6	PLQSYGFQPTNGVGY	C6	PLQSYGFQPTNGVGY
A7	PLRSYSFRPPYGVGH	B7	PLRSYSFRPPYGVGH	C7	PLRSYSFRPPYGVGH
A8	PLQSYGFRPTYGVGH	B8	PLQSYGFRPTYGVGH	C8	PLQSYGFRPTYGVGH
A9	YPGEFADYEELREQL	B9	YPGEFADYEELREQL	C9	YPGEFADYEELREQL
A10	KEVPALTAVETGATN	B10	KEVPALTAVETGATN	C10	KEVPALTAVETGATN
A11	GGGQEVRYGGG	B11	GGGQEVRYGGG	C11	GGGQEVRYGGG