



## CORRESPONDENCE

## Epitopes for a 2019-nCoV vaccine

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After causing an initial cluster of Pneumonia in Wuhan City, Hubei Province, the 2019-nCoV has quickly spread through South East Asia and within a few weeks to Europe, Africa, and America. Initial estimates suggested a mortality rate of 2% and that ~18% of the cases show severe symptoms, although such estimates are still subject to rapid changes ([https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-\(2019-ncov\)](https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov))).<sup>1-3</sup>

To facilitate the swift development of a candidate vaccine for 2019-nCoV we compared here the viral and the human proteomes, searching for pentapeptides that are unique to the pathogen. We followed the rationale that non-self sequences are highly immunogenic and uniquely viral epitopes should improve safety and efficacy by minimizing the risk for cross-reactions and increasing anti-viral specificity.<sup>4-6</sup> The analysis was conducted on the entire viral proteome but primarily focused on the surface spike glycoprotein (id = "QHD43416.1) because immune response against it is highly likely to exert a neutralizing effect.<sup>2</sup>

The entire amino acid (aa) sequence of the 2019-nCoV was retrieved from <https://www.ncbi.nlm.nih.gov/nuccore/MN908947> and dissected into pentapeptides overlapped by four residues for a total of  $n = 9661$ . Then, each pentamer was analyzed for occurrences in the human proteome using the Peptide Match program (<https://research.bioinformatics.udel.edu/peptidematch/index.jsp>).<sup>7</sup>

It resulted that  $n = 933$  viral pentapeptides are absent in the human proteome, and therefore foreign to the human immune system (Table S1). Among these non-self pentapeptides,  $n = 107$  are embedded in the viral surface glycoprotein (spike protein) that mediates binding to the human ACE2 and cellular entry.<sup>2</sup>

The recommended oligopeptides for a multi-epitope 2109-nCoV-vaccine are presented in Table 1, Panel a. They can be rapidly tested in animal models for immunogenicity and safety in order to timely develop a vaccine for preventing uncontrolled spreading of the novel coronavirus.

Three points need to be stressed.

First, short peptides that are foreign to the host immune system have been experimentally validated not only as positive immunomodulators (i.e., adjuvants) in conjunction to vaccines, but are also evidenced as providing direct protection against lethal viral infections, at least in animal models.<sup>6</sup>

Second, searching for the 107 human-foreign spike protein pentapeptides in the Immune Epitope Database (IEDB; [www.iedb.org](http://www.iedb.org))<sup>8</sup> yielded a list of  $n = 66$  epitopes (Table 1, Panel b). The IEDB is a publicly available, curated epitope repository. The presence of a peptide sequence in the IEDB indicates that it has a recognized and experimentally proven immunologic relevance. These results

provide experimental proof for the immunogenic potential of the non-self peptides identified in the present study through comparative *Homo sapiens*-coronavirus proteome analysis.

**Table 1.** (a) Oligopeptides ( $n = 73$ ) of the spike protein absent in the human proteome to be tested for a potential vaccine. Contiguous pentapeptides with a four residue overlap were considered as a single, longer oligopeptidic sequence; the length of each of these oligopeptides was dictated by the extension of the overlap. Oligopeptides from epitopes in panel b are in bold. (b) Experimentally validated epitopes ( $n = 66$ ) containing at least one of the 107 pentapeptides (capitalized) of the spike protein that are absent in the human proteome

(a) <b>RGVYYPDK</b> , NVTWFHA, FHAIH, PFNDG, IRGWIF, IFGTT, VCEFQFC, CNDPF, VYYHK, NPKSW, NKSWM, WMESEF, YSSAN, <b>CTFEY</b> , GNFKN, <b>GYFKI</b> , IYSKHT, PIGIN, GWTAG, AYYVG, NENGT, SETKC, <b>GIYQT</b> , VYAWNR, <b>CVADY</b> , <b>STFKC</b> , <b>FKCYGVS</b> , TNVYA, <b>IADYN</b> , <b>DYNYKL</b> , VIAWN, AWNSNN, STPCN, PCNGV, GFNCYF, QSYGF, VKNKC, NKCVN, <b>CVNFN</b> , CTEVP, <b>IGAEH</b> , YQTQTN, <b>IAYTMS</b> , <b>TSVDC</b> , DCTMY, <b>TMVICG</b> , <b>DSTEC</b> , <b>FACTQL</b> , PIKDF, QYGDCL, GDCLG, DLICAAQKF, MIAQY, SGWTF, <b>WTFGA</b> , <b>FAMQM</b> , <b>MQMAYRF</b> , <b>RFNGI</b> , <b>MSECV</b> , <b>GYHLS</b> , KNFTT, <b>PAICH</b> , NGTHWFVTQ, <b>TQRNF</b> , NFEYP, IGVN, <b>NTVYD</b> , IKWPWYI, YIWLGF, <b>IAIVM</b> , <b>LCCMTS</b> , <b>MTSCC</b> , <b>CCKFD</b>	
(b) <b>IEDB-ID-Number</b> <b>Epitope</b>	
307	aalvsगतatagWTFGAg
462	aatkMSECVlgskrvd
1460	agcllGAEHvdtseyecd
3176	aMQMAYRF
6011	canlllygysFCTQLnralsgia
6333	cgpkldstliiknqCVNFNfngltgtgvltpsskrfqpfqf
6334	cgpkldstliiknqCVNFNfngltgtgvltpsskrfqpfqfgrvdsdftd
7066	csqnplaelkcsvksfeidkGIYQTSnfrvpsgd
7217	cttfdvqapnyhtqhtssmRGVYYPDeifr
7383	CYGVSatklndlcsnv
8239	dfcggkGYHLSfppqaap
12417	eidkGIYQTSnfrvps
15903	ffSTFKCYGVSatklnd
18161	fvfngtswfiTQRNFs
18515	gaalqipFAMQMAYRFn
21464	gnliaprGYFKlrgkssim
22321	gsFCTQLn
24978	htssmRGVYYPDeifrs
25250	IADYNYKLpddfmngcvl
25293	iagllIAIVMvtillccm
25378	iappqtgviADYNYKLp
25382	iaprGYFKlrgkssimrsdapigtcssecit
29728	iywtkvpgdillinstgnliaprGYFKln
30987	kGIYQTSn
30988	kGIYQTSnfrvpsgdvrvf
31581	kkisnCVADYsvlynst
31582	kkisnCVADYsvlynstf
33305	ksfeidkGIYQTSnfrv

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**Table 1** continued

33358	ksivAYTMSIlgadssia
33874	kTSVDCnMYICGDSTEC
36579	liknqCVNFnfnlgtgt
36815	lkcsvksfeidkGIYQT
36856	lkgacscgsCCKFDeddd
37758	llrstsqksivAYTMSI
39023	lqygsFCTQLnralsgl
41177	MAYRFNGIlgvtqnvlye
42999	mvtilLCCMTSCCscik
43145	nafnCTFEYisdafslld
46379	nvftqtqagclIGAEHvd
46822	PAICHEgkayfpregvfvngtswftqrmffs
47479	pFAMQMAYRFNGIlgvtq
49968	pvsmaKTSVDCnMYICGds
50058	pwyywlgfiagllAIVM
53202	rasanlaatkMSECVlg
54989	rnfttaPAICHEgkayf
58143	sgncdvvigiinNTVYD
58730	sivAYTMSI
61554	stdliknqCVNFnfn
61598	stffSTFKCYGVSatkl
62872	tagWTFGAgaaqqipfa
63309	tecanllqygsFCTQL
68971	vigiinNTVYDplqpel
72205	VYYPDeifrsdtlyltqd
74173	yicgDSTECanllqyg
75920	ysvlynstffSTFKCYG
99918	CTFEYisdafslld
100048	gaalqipFAMQMAYRF
100230	ksivAYTMSIlgadssia
100300	MAYRFNGIlgvtqnvly
100316	nafnCTFEYisdafslld
100537	swftTQRNFfspqii
100711	agclIGAEHvdtsyecdi
129239	liaprGYFKlrgkssi
532052	gtswftTQRNFfspq
873061	mmcehiyytcrTSDVDCc
874104	ytcrTSDVDCcmkgaep

IEDB Immune Epitope Database, aa amino acid

Third, an immune response induced by the spike protein oligopeptides that are absent in the human proteins would exert a neutralizing effect on the coronavirus, in light of the mounting evidence for the surface glycoprotein as a ligand for the human ACE2 in viral entry processes.<sup>2</sup>

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#### ADDITIONAL INFORMATION

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