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Epitopes for a 2019-nCoV vaccine

Guglielmo Lucchese[1]

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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)).[1–3]

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.[4–6] 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.[2]

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).[7]

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.[2]

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 immunomodulants (i.e., adjuvants) in conjunction to vaccines, but are also evidenced as providing direct protection against lethal viral infections, at least in animal models.[6]

Second, searching for the 107 human-foreign spike protein pentapeptides in the Immune Epitope Database (IEDB; www.iedb.org)[8] 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) **RGVYYPD**K, NVTWFHA, FHAIH, PFNDG, IRGWIF, IFGTT, VCEFQFC, CNDPF, VYYHK, NNKSW, NKSWM, WMESEF, YSSAN, **CTFEY**, GNFKN, **GYFKI**, IYSKHT, PIGIN, GWTAG, AYYVG, NENGT, SETKC, **GIYQT**, VYAWNR, **CVADY**, **STFKC**, **FKCYGVS**, TNVYA, **IADYN**, **DYNYKL**, VIAWN, AWNSNN, STPCN, PCNGV, GFNCYF, QSYGF, VKNKC, NKCVN, **CVNFN**, CTEVP, **IGAEH**, YQTQTN, I**AYTMS**, **TSVDC**, DCTMY, T**MYICG**, **DSTEC**, **FCTQL**, PIKDF, QYGDCL, GDCLG, DLICAQKF, MIAQY, SGWTF, **WTFGA**, **FAMQM**, **MQMAYRF**, **RFNGI**, **MSECV**, **GYHLMS**, KNFTT, **PAICH**, NGTHWFVTQ, **TQRNF**, NFYEP, IGIVN, **NTVYD**, IKWPWYI, YIWLGF, **IAIVM**, **LCCMTS**, **MTSCC**, **CCKFD**

(b)

IEDB-ID-Number	Epitope
307	aalvsgtatagWTFGAg
462	aatkMSECVlgqskrvd
1460	agclIGAEHvdtsyecd
3176	aMQMAYRF
6011	canlllqygsFCTQLnralsgia
6333	cgpklstdliknqCVNFNfngltgtgvltpsskrfqpfqqfg
6334	cgpklstdliknqCVNFNfngltgtgvltpsskrfqpfqqfgrdvsdftd
7066	csqnplaelkcsvksfeidkGIYQTsnfrvvpsgd
7217	cttfddvqapnytqhtssmRGVYYPDeifr
7383	CYGVSatklndlcfsnv
8239	dfcgkGYHLMSfpqaap
12417	eidkGIYQTsnfrvvps
15903	ffSTFKCYGVSatklnd
18161	fvfngtswfiTQRNFfs
18515	gaalqipFAMQMAYRFn
21464	gnliaprGYFKIrsgkssim
22321	gsFCTQLn
24978	htssmRGVYYPDeifrs
25250	IADYNYKLpddfmgcvl
25293	iagllAIVMvtillccm
25378	iapgqtgvIADYNYKLp
25382	iaprGYFKIrngkssimrsdapigtcssecit
29728	iywtivkpgdillinstgnliaprGYFKIrn
30987	kGIYQTsn
30988	kGIYQTsnfrvvpsgdvvrf
31581	kkisnCVADYsvlynst
31582	kkisnCVADYsvlynstf
33305	ksfeidkGIYQTsnfrvv

[1]Universitätsmedizin Greifswald, Department of Neurology, 17475 Greifswald, Germany
Correspondence: Guglielmo Lucchese (guglielmo.lucchese@uni-greifswald.de)

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Table 1 continued

33358	ksivAYTMSlgadssia
33874	kTSVDCnMYICGDSTEC
36579	liknqCVNFNfngltgt
36815	lkcsvksfeidkGIYQT
36856	lkgacscgsCCKFDedd
37758	llrstsqksivAYTMSl
39023	lqygsFCTQLnralsgi
41177	MAYRFNGlgvtqnvlye
42999	mvtilLCCMTSCCsclk
43145	nafnCTFEYisdafsld
46379	nvfqtqagcllGAEHvd
46822	PAICHegkayfpregvfvfngtswfitqrnffs
47479	pFAMQMAYRFNGlgvtq
49968	pvsmakTSVDCnMYICGds
50058	pwyvwlgfiaglIAIVM
53202	rasanlaatkMSECVlg
54989	rnfttaPAICHegkayf
58143	sgncdvvigiinNTVYD
58730	sivAYTMSl
61554	stdliknqCVNFNfn
61598	stffSTFKCYGVSatkl
62872	tagWTFGAgaalqipfa
63309	tecanlllqygsFCTQL
68971	vigiinNTVYDplqpel
72205	VYYPDeifrsdtlyltqd
74173	yicgDSTECanlllqyg
75920	ysvlynstffSTFKCYG
99918	CTFEYisdafsld
100048	gaalqipFAMQMAYRF
100230	ksivAYTMSlgadssiay
100300	MAYRFNGlgvtqnvly
100316	nafnCTFEYisdafsldv
100537	swfiTQRNFfspqii
100711	agcllGAEHvdtsyecdi
129239	liaprGYFKlrsgkssi
532052	gtswfiTQRNFfspq
873061	mmcehiyytcvrTSVDCc
874104	ytcvrTSVDCcmkgaep

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.[2]

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ADDITIONAL INFORMATION

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