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Homology between SARS CoV-2 and human proteins

Vladimir Khavinson^{1,3}, Alexander Terekhov¹, Dmitry Kormilets² & Alexander Maryanovich¹✉

An extremely high contagiousness of SARS CoV-2 indicates that the virus developed the ability to deceive the innate immune system. The virus could have included in its outer protein domains some motifs that are structurally similar to those that the potential victim's immune system has learned to ignore. The similarity of the primary structures of the viral and human proteins can provoke an autoimmune process. Using an open-access protein database Uniprot, we have compared the SARS CoV-2 proteome with those of other organisms. In the SARS CoV-2 spike (S) protein molecule, we have localized more than two dozen hepta- and octamers homologous to human proteins. They are scattered along the entire length of the S protein molecule, while some of them fuse into sequences of considerable length. Except for one, all these n-mers project from the virus particle and therefore can be involved in providing mimicry and misleading the immune system. All hepta- and octamers of the envelope (E) protein, homologous to human proteins, are located in the viral transmembrane domain and form a 28-mer protein E₁₄₋₄₁ VNSVLLFLAFVVFLLVTLAILTALRLCA. The involvement of the protein E in provoking an autoimmune response (after the destruction of the virus particle) seems to be highly likely. Some SARS CoV-2 nonstructural proteins may also be involved in this process, namely ORF3a, ORF7a, ORF7b, ORF8, and ORF9b. It is possible that ORF7b is involved in the dysfunction of olfactory receptors, and the S protein in the dysfunction of taste perception.

The interaction of SARS CoV-2 with the host immune system is largely determined by the structural similarities between viral and host proteins. The studies of SARS CoV-2 are still focused on the S protein¹.

An extremely high contagiousness of the coronavirus SARS CoV-2 indicates that during its evolution the virus developed the ability to deceive the innate immune system. The simplest way to achieve this ability would be to incorporate into its membrane the proteins that share structural similarity with those which the immune system of the potential victim has learnt to ignore. Probably, the virus borrowed some n-mers from bats or other mammals. Any motif of any mammalian protein was suitable for borrowing, if only the immune system considered it to be of its own.

The knowledge of the homology between the SARS CoV-2 and human proteins would help understand the mechanisms of mimicry at the moment of infection. The SARS CoV-2 proteins may simulate human proteins, mislead the immune system, and slow down its response.

However, mimicry is not the only process that is determined by the protein homology between the virus and host organism. After the inevitable destruction of the virus particle, the proteins or their domains, which were inside the virus until then, come into contact with the immune system. With some structural similarity, a part of the immune response will be directed against the proteins of the host organism, i.e., an autoimmune response will arise.

This study aimed to identify the human proteins which share a significant structural homology with the SARS CoV-2 proteins. We hope this information will be useful to the developers of vaccines against coronavirus.

Joshua Lederberg² believed that "microbes and their human hosts constitute a *superorganism*." According to this, we considered the concept of "human proteins" as a combination of human own proteome and the proteomes of gut microbiota. We have paid particular attention to the proteins that are involved in the three functions that are almost necessarily affected in this disease, namely digestion, olfaction and taste.

¹Mechinkov North-Western State Medical University, 47 Piskaryovsky Prosp., 195067 St. Petersburg, Russia. ²Kirov Military Medical Academy, St. Petersburg, Russia. ³Saint Petersburg Institute of Bioregulation and Gerontology, St. Petersburg, Russia. ✉email: atm52atm52@gmail.com

Methods

Using an open-access protein database Uniprot and our original computer program Ouroboros³, we compared the SARS CoV-2 proteome⁴ with those of other organisms. We also searched for a separate database of 75,777 human proteins⁵. The algorithm we used compares primary sequences of SARS CoV-2 and human proteins, presented in the form of a one-letter code. We performed a comparison of proteins by a consecutive search for regions of one protein in the others, which is essentially a standard task of finding a substring in a string. This algorithm is implemented in standard methods of many programming languages, including Python, in which the main program was coded. The URL to the source code is provided above³.

When assessing the homology between the viral and human proteins, we took into account the presence of the common 7-/8-mers and especially their fusion into longer sequences. For example, 7-dimensional viruses, one of which is homologous to the human protein A, and the other to the protein B, can "overlap" at the ends, forming regions of 8 to 14 amino acid residues in length.

Results and discussion

Structural proteins. Spike glycoprotein. S protein, 1273 aa.

S protein, 1273 aa

MFVFLVLLPLVSSQCVNLTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGTKRFDNPVLPFNDGVYFASTEKSNIIRG
WIFGTTLDSTQSLIVNNATNVVVKVCEFCNDPFLGVYHKNKSWMESEFRVYSSANNCTFEYVSQPFLLMDLEGKQGNFKNLREFVFNKIDGYFKIYSK
HTPINLVRLDPQGFSALEPLVDLPIGINITRFQTLALHRSYLTGPDSSSGWTAGAAAYVGYLQPRFTLLKYNGTITDAVDCALDPLSETKCTLKSTFVE
KGIYQTSNFRVQPTESIVRFPNITNLCPPGEVFNATRFASVYAWNKRISNCVADYSVLNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVQRQIAP
GQTGKIADYNYKLPDDFTGCVIAWNSNNLDSKVGNGYNYLRLFRKSNLKPFFERDISTEYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVLSF
ELLHAPATVCGPKKSTNLVKNKCVNFNGLTGTGVLTSNKKFLPFQFGRDIADTTDAVRDPQTLILDITPCSFGGVSVITPGTNTSNQVAVLYQDVNCT
EVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNSSEYCDIPIGAGICASYQTQTSNPRRARSVASQSI IAYTMSLGAENSVAYSNNIAIPTNFTIS
VTTEILPVSMTKTSVDCMTYICGDSTECNLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKIYKTPPIKDFGGFNFSQILPDPSPKPSKRSFIEDLLFN
KVTLADAGFIKQYGDCLGDIARDLCAQKFNGLTVLPPLLTDEMAIQYTSALLAGTITSGWTFGAGALQIPFAMQMAYRFNGIGVTQNVLYENQKLIANQF
NSAIGKIQDSLSSSTASALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRDLKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMS
ECVLGQSKRVDFCGKGYHLSFPQSAPHGVVFLHVTVYVPAQEKNFETAPAI CHDGKAHFPREGVFSNGTHWFVTQRNFYEPQIITDNTFVSGNCDVVGIV
NNTVYDPLQPELDSFKEELDKYFKNHTSPDVLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEYQIKWPWYIWLGFIAGLIAIVMVTIMLCC
MTSCCSCCLKGCCSCGCKCFDEDDSEPV LKGVKLHYT

Hereinafter, regions homologous to human proteins are highlighted in red. Transmembrane tail TM₁₂₁₄₋₁₂₃₇ is underlined.

In the S protein molecule, we localized more than two dozen of 7-/8-mers homologous to human proteins (Table 1).

Fragments homologous to human proteins are scattered along the entire length of the S protein molecule, and some of them fuse in sequences of considerable length, namely 10-mers SPRRARSVAS₆₈₀₋₆₈₉, 11-mers GLTVLP-PLLT₈₅₇₋₈₆₇ and two closely spaced 7-mers NASVVNI₁₁₇₃₋₁₁₇₉ and EIDRLNE₁₁₈₂₋₁₁₈₈. Octamer RRARSVAS₆₈₂₋₆₈₉ is located at the junction of the S1 and S2 subunits. All these n-mers stand out from the virus particles and may be involved in the effect of mimicry.

SARS CoV-2 can cause smell and taste dysfunction, as well as muscle injury⁶.

The 8-mer DEDDSEPV₁₂₅₇₋₁₂₆₄, located in the cytoplasmic tail, can be released during the destruction of the virus particle and get involved in orchestrating the immune system's response, directing a part of it to the homologous 8-mer in human unconventional myosin-XVI₁₄₀₄₋₁₄₂₁. The role of this mechanism in muscle dysfunction in coronavirus infection deserves a special investigation.

The 8-mer RRARSVAS₆₈₂₋₆₈₉ is homologous to the amiloride-sensitive sodium channel subunit alpha₂₀₁₋₂₀₈, which is involved in salt taste perception⁷.

With a high degree of probability, it can be argued that the S protein is involved in the process of mimicry. It may also take some part in provoking an autoimmune response.

We have checked the S protein homology across 10 species, specifically primates, bats and some other mammals. The results are presented in Table entitled *Similarity of SARS CoV-2 spike glycoprotein structure with some mammalian proteins* in the electronic attachment. Probably, attention should be paid to the homologous regions common to SARS CoV-2, humans, and bats. The data presented so far do not allow us to derive a more general rule.

MYSFVSEETGTTLIVNSVLLFLAFVVFLLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYSRVKNLNSSRVPDLLV

Envelope small membrane protein. E protein, 75 aa (transmembrane domain₈₋₃₈ is underlined).

In the E protein molecule, we localized seven 7-mers and one 8-mer homologous to human proteins (Table 2).

A fragment of the E₈₋₃₈ protein transmembrane domain can be represented as follows:

ETGTTLIVNSVLLFLAFVVFLLVTLAILTALRLCA

The size of the letters (point size) corresponds to the frequency of the viral 7-/8-mers in the human proteome.

The protein E transmembrane domain contains 7-/8-mers, homologous to the proteins of some gut bacteria and even cereals, for example, corn, sorghum, wheat, and barley (Table 3).

Subunit	SARS CoV-2 S protein domain	In S protein	In human proteins
S1	Signal peptide (N-terminus) ₁₋₁₃	None	—
	N-terminus domain NTD ₁₄₋₃₀₅	DKVFRSS ₄₀₋₄₆	Zinc finger protein 528 ₂₇₅₋₂₈₁
		FLPFFSN ₅₅₋₆₁	OTU domain-containing protein 6A ₁₈₅₋₁₉₁
		VSGTNGT ₇₀₋₇₆	Lysosome-associated membrane glycoprotein 1 ₁₇₁₋₁₇₇
		SLLIIVNN ₁₁₆₋₁₂₂	ATP-binding cassette sub-family A member 10 ₈₂₅₋₈₃₁
		FKNLREF ₁₈₆₋₁₉₂	Isovaleryl-CoA dehydrogenase, mitochondrial ₇₇₋₈₃
		TRFQTL ₂₃₆₋₂₄₂	Disheveled-associated activator of morphogenesis 2 ₂₅₁₋₂₅₇
		KIYSKHT ₂₀₂₋₂₀₈	Uncharacterized protein C1orf105 ₇₋₁₃
		SSSGWTA ₂₅₄₋₂₆₀	Uncharacterized protein KIAA1109 (Fragment) ₆₁₀₋₆₁₆
	Uncharacterized fragment ₃₀₆₋₃₁₈	None	—
	Receptor-binding domain RBD ₃₁₉₋₅₄₁	KLNDLCF ₃₈₆₋₃₉₂	Interleukin-7 ₁₄₉₋₁₅₅
		DEVQRQA ₄₀₅₋₄₁₁	Histone-lysine N-methyltransferase 2C ₄₅₃₀₋₄₅₃₆
	Uncharacterized fragment ₅₄₂₋₇₈₇	VYSTGSN ₆₃₅₋₆₄₁	Neural cell adhesion molecule L1-like protein ₃₄₁₋₃₄₇
		IGAGICA ₆₆₆₋₆₇₂	Hepatitis A virus cellular receptor 2 ₂₀₅₋₂₁₁
		SPRRARS ₆₈₀₋₆₈₆	Hermansky-Pudlak syndrome 1 protein ₂₅₈₋₂₆₄
		RRARSVAS ₆₈₂₋₆₈₉	Amiloride-sensitive sodium channel subunit alpha ₂₀₁₋₂₀₈
S2	Fusion peptide FP ₇₈₈₋₈₀₆	None	—
	Uncharacterized fragment ₈₀₇₋₉₁₁	VTLDAG ₈₂₆₋₈₃₂	Non-receptor tyrosine-protein kinase TNK1 ₄₄₀₋₄₄₆
		GLTVLPP ₈₅₇₋₈₆₃	FH1/FH2 domain-containing protein 3 ₉₇₂₋₉₇₈
		LPPLLT ₈₆₁₋₈₆₇	Maestro heat-like repeat-containing protein family member 9 ₂₅₀₋₂₅₆
	Heptapeptide repeat sequence 1 HR1 ₉₁₂₋₉₈₄	SSTASAL ₉₃₉₋₉₄₅	40S ribosomal protein S13 ₁₄₃₋₁₄₉
		LVKQLSS ₉₆₂₋₉₆₈	E3 SUMO-protein ligase PIAS1 ₂₈₄₋₂₉₀
		KVEAEVQ ₉₈₆₋₉₇₄	Emilin-3 ₆₂₅₋₆₃₁
		TGRLQSL ₉₉₈₋₁₀₀₄	Neuron navigator 3 ₁₆₁₀₋₁₆₁₆
	Uncharacterized fragment ₉₈₅₋₁₁₆₂	LIRAAEI ₁₀₁₂₋₁₀₁₈	Unconventional myosin-XVIIIa ₁₃₅₂₋₁₃₅₈
		LDKYFKN ₁₁₅₂₋₁₁₅₈	Follistatin-related protein 1 ₁₄₉₋₁₅₅
		NASVVNI ₁₁₇₃₋₁₁₇₉	Thyroid adenoma-associated protein ₁₀₂₂₋₁₀₂₈
	Heptapeptide repeat sequence 2 HR2 ₁₁₆₃₋₁₂₁₃	EIDRLNE ₁₁₈₂₋₁₁₈₈	Protein SETSIP ₆₄₋₇₀ ; Protein SET ₅₄₋₆₀
	Transmembrane tail TM ₁₂₁₄₋₁₂₃₇	None	—
	Cytoplasm tail CT ₁₂₃₈₋₁₂₇₃	DEDDSEPV ₁₂₅₇₋₁₂₆₄	Unconventional myosin-XVI ₁₄₀₄₋₁₄₂₁

Table 1. Localization of homologous 7-/8-mers in the S protein and human proteins.

E protein domains ^a	In E protein	In human proteins
Signal peptide (N-terminus domain) ₁₋₇	None	—
Transmembrane domain ₈₋₃₈	VNSVLLF ₁₄₋₂₀	Heterogeneous nuclear ribonucleoprotein L ₁₉₁₋₁₉₇
	VNSVLLFL ₁₄₋₂₁	Ran-binding protein 6 ₄₀₉₋₄₁₆
	NSVLLFL ₁₅₋₂₁	Lysosomal amino acid transporter 1 homolog ₁₃₃₋₁₃₉
	SVLLFLA ₁₆₋₂₂	Cytochrome P450 2B6 ₄₋₁₀ ; Cytochrome P450 2B7 ₄₋₁₀ ; GPI ethanolamine phosphate transferase 3 ₅₋₁₁
	LAFVVFL ₂₁₋₂₇	Solute carrier family 15 member 4 ₂₃₅₋₂₄₁
	VFLVTL ₂₅₋₃₁	Alpha-(1,3)-fucosyltransferase 10 ₂₀₋₂₆
	LAILTAL ₃₁₋₃₇	Transient receptor potential cation channel subfamily M member 6 ₃₉₄₋₄₀₀ ; Transient receptor potential cation channel subfamily M member 3 ₄₆₅₋₄₇₁
	TALRLCA ₃₅₋₄₁ ^b	Protein disulfide-isomerase TMX3 ₈₋₁₄
Internal domain ₃₉₋₇₅	None	—

Table 2. Localization of homologous 7-/8-mers in the E protein and human proteins. ^aDomain boundaries see in⁸. ^bHeptamer TALRLCA₃₅₋₄₁ is located at the junction of the transmembrane domain₈₋₃₈ and internal domain₃₉₋₇₅.

The simulation targets may have been the proteins synthesized by a macroorganism itself or by its normal gut microbiota.

All protein E 7-/8-mers, homologous to proteins of humans, gut bacteria and cereals, are located in the transmembrane domain of the virus and form the 28-mer protein E₁₄₋₄₁. A random selection of 28 amino acid residues in a row would require an astronomical number of iterations: $20^{28} = 2.7 \cdot 10^{36}$.

In E protein	In bacterial and plant proteins
AFVVFLLV ₂₂₋₂₉	Lpp126 large-conductance mechanosensitive channel: Lactobacillus casei ₈₀₋₈₇ ; L. paracasei ₈₀₋₈₇ ; L. florum ₈₀₋₈₇
TLAILTA ₃₀₋₃₆	Uncharacterized proteins: Zea mays ₉₀₋₁₆₄ ; Sorghum bicolor ₉₇₋₁₂₇ ; Triticum aestivum ₁₁₆₋₁₉₀ ; Hordeum vulgare ₈₇₋₁₆₁

Table 3. Localization of some of homologous 7-/8-mers in the E protein and human gut proteome.

In M protein	In human proteins
VEELKKL ₁₀₋₁₆	Glutaredoxin-related protein 5, mitochondrial ₁₃₅₋₁₄₁
EELKKL ₁₁₋₁₇	GDP-fucose protein O-fucosyltransferase 2 ₃₄₀₋₃₄₆
ELKKLE ₁₂₋₁₈	Cullin-1 ₃₃₅₋₃₄₁
LKKLLEQ ₁₃₋₁₉	Filamin-A-interacting protein 1 ₂₁₁₋₂₁₇
LLESELV ₁₃₃₋₁₃₉	Leucine-rich repeat-containing protein 71 ₄₃₉₋₄₄₅
AGDSGFA ₁₈₈₋₁₉₄	Myosin-14 ₃₅₉₋₃₆₅

Table 4. Localization of homologous 7-mers in the M protein and human proteins.

The involvement of the E protein in mimicry is hardly possible, but its implication in provoking an autoimmune response (after the destruction of the virus particle) seems very likely.

As a major target, the viral E protein has usually been used for the development of vaccines, specifically against HIV-1⁹, Dengue virus¹⁰, hepatitis B virus¹¹, SARS CoV-2¹² and many other viruses. A deletion of the SARS-CoV E protein reduces pathogenicity and mortality in laboratory animals¹³. In the transmembrane domain of the SARS-CoV E protein, specific critical virulence-determining features have been identified¹⁴.

MADSNGTITVEELKKLLEQWNLVIGFLFTWICLLQFAYANRNRFYIIKLIFLWLLWPVTLACFVLAAYRINWITGGIAIAMACL
VGLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRP LLESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSR
TLSYYKLGASQQRVAGDSGFAAAYSRYRIGNYKLNTHSSSSDNIALLVQ

Membrane protein. Membrane protein, 222 aa.

In the M protein molecule, we localized six 7-mers homologous to human proteins (Table 4).

A N-terminus fragment₁₋₁₉ of the M protein can be represented as follows:

MADSNGTITVEELKKLLEQWNLVIGFLF

In the protein M, four 7-dimensional homologues of human proteins are fused into 10-mer VEELKKLLEQ₁₀₋₁₉, the hydrophilic composition of which indicates a possible contact with the external environment, i.e., with the host's immune system, and the involvement in mimicry.

Outside of the 10-mer, we found only two homologous 7-mers. It is unlikely that the M protein is involved in provoking an autoimmune response (after the destruction of the virus particle).

MSDNGPQNQRNAPRITFGGSDSTGSNQNNGERSGARSQQRPPQGLPNNTASWFTALTQHGKEDLKFFRGQGVPIINTNSSPDDQ
IGYYRRATRRIRGGDGKMKDLSPRWYFYLLGTGPEAGLPYGANKDGIWVATEGALNTPKDHIGTRNPANNAIIVLQLPQGT
LPKGFYAEGRGGSQAASSRSSRSRNSRNPSTPGSSRGTSAPARMAGNGGDAALALLLDRLNQLSKMSGKGQQQQGQTVTKK
SAAEASKKPRQKRTATKAYNVTQAFGRGPEQTQGNFGDQELIRQGTQDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLT
YTGAIKLDDKDPNFKDQVILNKHIDAYKTFPTEPKKDKKKKADETQALPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSAD
STQA

Nucleoprotein. Nucleoprotein, 419 aa.

In the N protein molecule, we localized eleven 7-mers homologous to human proteins (Table 5).

The N protein is located completely inside the virus particle and cannot be involved in mimicry. All heptamers homologous to human proteins form several rather long fragments, including the 13-mer SKQLQQSMSSADS₄₀₄₋₄₁₆ and 10-mer AEGSRGGSQA₁₇₃₋₁₈₂, which increases the likelihood of the protein involvement in provoking an autoimmune response.

Nonstructural proteins. All non-structural proteins of SARS CoV-2 are located completely inside the virus particle and, by definition, cannot be involved in the process of mimicry. It remains to consider the possibility of their implication in provoking an autoimmune process.

In N protein	In human proteins
RPQGLPN ₄₁₋₄₇	GATOR complex protein WDR59 ₇₅₇₋₇₆₃
RGQGVPI ₆₈₋₇₄	Putative uncharacterized protein encoded by LINC00346 ₁₅₄₋₁₆₀
NSSPDDQ ₇₇₋₈₃	NEDD4-binding protein 2 ₁₅₄₋₁₆₀
GKMKDLS ₉₉₋₁₀₅	Chromodomain-helicase-DNA-binding protein 1-like ₇₇₀₋₇₇₆
VLQLPQG ₁₅₇₋₁₆₃	Prestin ₉₂₋₉₈
AEGSRGG ₁₇₃₋₁₇₉	snRNA-activating protein complex subunit ₃₂₋₈
SRGGSQA ₁₇₆₋₁₈₂	Ras-associating and dilute domain-containing protein ₈₈₆₋₈₉₂
KADETQA ₃₇₅₋₃₈₁	Myopalladin ₉₀₋₉₆
LLPAADL ₃₉₄₋₄₀₀	Probable E3 ubiquitin-protein ligase HERC1 ₁₀₉₈₋₁₁₀₄
SKQLQSS ₄₀₄₋₄₁₀	Codanin-1 ₂₅₉₋₂₆₅
SMSSADS ₄₁₀₋₄₁₆	Protein PRRC2B ₄₁₆₋₄₂₂

Table 5. Localization of homologous 7-mers in the N protein and human proteins.

In ORF3a protein	In human proteins
VGVALLA ₄₈₋₅₄	Manganese-transporting ATPase 13A1 ₈₇₆₋₈₈₂
LLVAAGL ₉₅₋₁₀₁	Glycerophosphoinositol inositolphosphodiesterase GPD2 ₁₂₉₋₁₃₅
KCRSKNP ₁₃₂₋₁₃₈	Vacuolar protein sorting-associated protein 13A ₂₀₆₆₋₂₀₇₂
SVTSSIV ₁₆₂₋₁₆₈	Protein piccolo ₂₇₇₉₋₂₇₈₅
TQLSTDT ₂₁₇₋₂₂₃	Septin-14 ₄₁₈₋₄₂₄

Table 6. Localization of homologous 7-mers in the ORF3a protein and human proteins.

In ORF7a protein	In human proteins
VAAIVFI ₁₀₄₋₁₁₀	Transmembrane protein 255B ₈₆₋₉₂
FTLKRKT ₁₁₄₋₁₂₀	Cytosolic 5'-nucleotidase 3A ₃₆₋₄₂

Table 7. Localization of homologous 7-mers in the ORF7a protein and human proteins.

MDLFMRIFTIGTVTLKQGEIKDATPSDFVRATATIPQASLPFGWLI**VGVALLA**VFQSASKIITLKKRWQLALSKGVHFCNLLLLF
 VTVYSHL**LLVAAGL**EAPFLYLYALVYFLQSINFVRIIMRLWLCW**KCRSKNP**LLYDANYFLCWHNTCYDYCIPYNS**SVTSSIV**ITSGDG
 TTSPISEHDYQIGGYTEKWESGVKDCVVLHSYFTSDYYQLYST**TQLSTDT**GVEHVTFFIYNKIVDEPEEHVQIHTIDGSSGVVNPVME
 PIYDEPTTTTSVPL

ORF3a protein. ORF3a protein, 275 aa.

In the ORF3a protein molecule, we localized five 7-mers homologous to human proteins (Table 6).

The 7-mers scattered along the entire length of its molecule do not form long n-mers anywhere else. ORF3a does not appear to be involved in provoking an autoimmune response.

MKIILFLALITLATCELYHYQECVRGTTVLLKEPCSSGTYEGNSPFHPLADNKFALTCFSTQFAFACPDGVKHVYQLRARSVSPKLF
 IRQEEVQELYSPIFLI**VAAIVFI**TLC**FTLKRKT**E

ORF7a protein. ORF7a 121 aa.

In the ORF7a protein molecule, we found two 7-mers homologous to human proteins and located in close proximity to each other (Table 7).

It is possible that ORF7a is involved in provoking an autoimmune response.

MIELSLIDFYLCFLAFLFLVLIML**IIWF**SLELQDHNETCHA

ORF7b protein. ORF7b protein, 43 aa.

In this polypeptide, we found only one 7-mer homologous to the human protein (Table 8).

ORF7b may be involved in provoking an autoimmune response, contributing to olfactory dysfunction.

In ORF7b protein	In human protein
IIFWFS _{L26-32}	Olfactory receptor 7D ₄₁₅₁₋₁₅₇

Table 8. Localization of the homologous 7-mer in ORF7b and a human protein.

In ORF8 protein	In human proteins
LVFLGI _{L4-10}	Zinc finger protein 486 ₄₉₋₅₅
LGIITTV ₇₋₁₃	D-2-hydroxyglutarate dehydrogenase, mitochondrial ₂₆₂₋₂₆₈
KLGS _{L94-100}	Sodium leak channel non-selective protein ₅₀₅₋₅₁₁

Table 9. Localization of homologous 7-mers in the ORF8 protein and human proteins.

In ORF9b protein	In human proteins
LVDPQIQL ₁₄₋₂₁	Valine—tRNA ligase, mitochondrial ₉₉₆₋₁₀₀₂
MENAVGR ₂₆₋₃₂	Neprilysin ₄₁₉₋₄₂₅
LGSP _{L48-54}	Stress-responsive DNAJB4-interacting membrane protein 1 ₃₇₋₄₃
GSPLSLN ₄₉₋₅₅	E3 ubiquitin-protein ligase HERC2 ₄₅₃₃₋₄₅₃₉
TEELPDE ₈₄₋₉₀	KH homology domain-containing protein 4 ₄₆₅₋₄₇₁
ELPDEFV ₈₆₋₉₃	Maestro heat-like repeat-containing protein family member 2B ₁₀₃₋₁₁₀

Table 10. Localization some of homologous 7-/8-mers in ORF9b protein and human proteins.

MKFLVFLGIITTVAAFHQECSLQSQCTQHQPYYVDDPCPIHFYSKWYIRVGARKSAPLIELCVDEAGSKSPIQYIDIGNYTVSCLPFT
INCQEPKLGS_{L94-100}RVCSFYEDFLEYHDVRVVLDFI

ORF8 protein. ORF8 protein, 121 aa.

The primary structure of SARS-CoV-2 ORF8 is close to that of bat RaTG13-CoV¹⁵. In this polypeptide, there are three 7-mers homologous to human proteins (Table 9).

Due to the fusion of two 7-mers into 10-mer LVFLGIITTV₄₋₁₃, the ORF8 protein can be involved in provoking an autoimmune response.

MDPKISEMHPALRLVDPQIQLAVTRMENAVGRDQNNVGPKVYPIILRLGSP_{L48-54}LSLNMARKTLNSLEDKAFQLTPIAVQMTKLAT
TEELPDEFV₈₆₋₉₃VTVK

ORF9b protein. ORF9b protein, 97 aa.

In the ORF9b protein molecule, we localized six 7-/8-mers, homologous to human proteins (Table 10).

Some of these 7-/8-mers merge into larger n-mers TEELPDEFV₈₄₋₉₃ and LGSP_{L48-54}LSLN.

Octamer ELPDEFV₈₆₋₉₃ is homologous to the Maestro heat-like repeat-containing protein family member 2B (Fig. 1), which may play a role in the sperm capacitation¹⁶. Male reproductive dysfunction was proposed as a likely consequence of COVID-19¹⁷.

After the destruction of the virus particle, ORF9b can take part in provoking an autoimmune response.

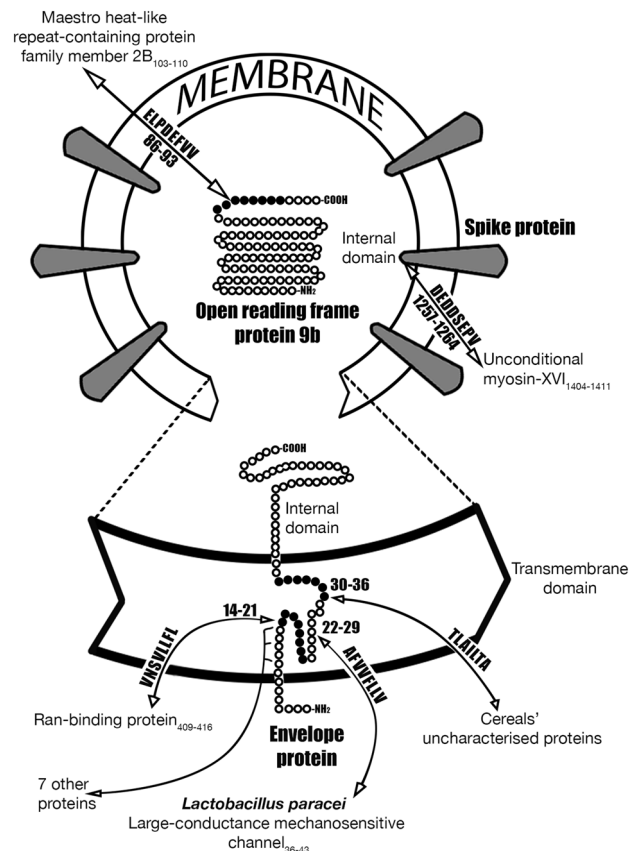


Figure 1. The SARS CoV-2 S, E and ORF9b protein molecules contain hepta/octamers that are homologous to proteins in the human body, including some nutrients and intestinal commensal bacteria.

In Replicate polyprotein 1a	In human proteins
EVEKGLVP ₅₅₋₆₂	Bifunctional heparan sulfate N-deacetylase/N-sulfotransferase 1 ₂₁₄₋₂₂₁
ESGLKTI _{L390-397}	Annexin A7 ₄₀₄₋₄₁₁
REETGLLM ₇₂₄₋₇₃₁	Estrogen-related receptor gamma ₃₀₋₃₇
GGSCVLSG ₁₁₀₀₋₁₁₀₇	Sorting nexin-27 ₁₁₂₋₁₁₉
DIQLLKSA ₁₁₂₇₋₁₁₃₄	Echinoderm microtubule-associated protein-like 1 ₃₈₋₄₅
RRSFYVYA ₂₄₃₁₋₂₄₃₈	Transmembrane protein adipocyte-associated 1 ₂₂₅₋₂₃₂
AKKNNLPF ₂₇₃₃₋₂₇₄₀	Acyl-CoA:lysophosphatidylglycerol acyltransferase 1 ₁₉₉₋₂₀₆
YNYEPLTQ ₃₅₀₀₋₃₅₀₇	DNA helicase ₁₉₉₋₂₀₆
SLKELLQN ₃₅₃₀₋₃₅₃₇	Centromere protein I ₄₉₆₋₅₀₃
DTSLSGFK ₃₆₇₁₋₃₆₇₈	Solute carrier family 12 member 7 ₉₉₅₋₁₀₀₂
PEANMDQE ₄₃₁₂₋₄₃₁₉	Arachidonate 5-lipoxygenase-activating protein ₅₄₋₆₁

Table 11. Localization of homologous 8-mers in RPP 1a and human proteins.

MESLVPGFNEKTHVQLSLPVLQVRDVLVRGFGDSVEEVLSEARQHLKDGTCGLVEVEKGVLPQLEQPYVFIKRS DARTAPHGHVMVLEVALEGIQYGRSGETGLVLVPH
 VGEIPVAYRKVLLRKNNGKAGGHSYGADLKSFDLDELGTDPYEDFQENWNTKHS SGTRELMRELNGGAYTRYVDNNFCGPDGYPLECIKDLLARAGKASCTLSEQLD
 FIDTKRGVYCCREHEHEIAWYTERSEKSYELQTPFEIKLAKKFTDFNGECNPFVFPPLNSI IKTIQRPVEKKKLDGFMGRIRSVYPVSPNECQMCLSTLMKCDHCGETS
 WQTGFVKATCEFCGTENLTKEGATTCGYLPQNAVVKIYCPACHNSVEGPEHSLAEYHNESGLKTLIRKGGRTIAFGGCVFSYVGCNKCAYWVPRASANICGNHTGVVG
 EGSEGLNDNLLEILQKEVKNINIVGDFKLNEEITAIILASFASSTSAFVETVKGDLKYAFKQI VESCGNFKVTGKAKKGAWNI GEQKSI LSPLYAFASEAARVRSIFSR
 TLETAQNSVRVLQAAITILDGISQSLRLIDAMMFTS DLTANNLVVMAYITGGVQVQLTSQWL TNIFGTVYEKLPVLDWLEEFKEGVEFLRDGWEIVKFI STCACEIV
 GGQIVTCAKEIKESVQTFKLVNKFALCADSI IIGAKL KALNLGETFVTHSKGLYRKCVRKREETGLLMPLKAPKEIIFLEGETLPTVLTTEEVLVLTGDLQPLEQPT
 SEAVEAPLVGTPVCINGMLLEIKDKTEKYCALAPNMVNTNFTFLKGGAPRTVTFGDDTVIEVQGYKSVNITFELDERIDKVLNEKCSAYTVELGTVEVNEFACVADAVI
 KTLQPVSELLTPLGIDLDSEWMATYYLFDSEGEFKLASHMYCSFYPPDEDEEEDGCEEEEFEPSTQYEGTDEDDYQGGKPLEFGATSAALQPEEEQEEEDWLDDSDQTVGQ
 QDGEDNQTTTIQTIVEVQPLEMELTPVVTIEVNSFSGLYKLTNDVYIKNADIVEEAKKVKPTVVVNAANVYLKHGGGVAGALNKATNNAMQVESDDYIATNGPLKVG
 GSCVLSGHNLAHKLHVGPVNVNKGEDIQLLKSAYENFNQHEVLLAPLLSAGIFGADPIHSLRVCDTVRTNVYLA VFDKNLYDKLVSSFLEMKEKQVEQKIAEIPKEE
 VKPFIITESKPSVEQRKQDDKKIKACVEEVTTTLEETKFLTENLLLYIDINGNLHPDSATLVSDIDITFLKKDAPYIVGDVVGEGVLTAVIPTKAGGTTEMLAKALRKV
 PTDNYITTPYGGQGLNGYTVEEAKTVLKKCSAFYILPSII SNEKQEI LGTVSWNLREMLAHAEETRLKMPVCVETKAIVSTIQRKYKGIKIQEGVVDYGARFYFYTSKTT
 VASLINTLNDLNETLVTMPLGVTHGLNLEEAARYMRS LKVPATVSVSSPDVAVTAYNGYLTSSSKTPEEHFIETISLAGSYKDWSSGQSTQLGIEFLKRGDKSVYYTSN
 PTFHLDGEVITFDNLKTLSSLREVRTIKVFTTVDNINLHTQVVDMSMTYGGQFGPTYLDGADVTKIKPHNSHEGKTFYVLPNDTDLRVEAFYYHTDPDFLGRYMSAL
 NHTKWKYPQVNGLTISKWADNCKSLATALLTQOIELKFNPNRAGGAANFCALILAYCNKTVGELGDVRETMYSFTLLQLTCLVNLNVTGFI SAARQG
 TLKGVEAVMYMGTLSYEQFKKGVQIPCTCGKQATKYLQVESPFVMSAPPAQYELKHGFTTCASEYTGNYQCGHYKHITSKETLYCIDGALLTKSSEYKGPITDVFYKE
 NSYTTTIKPVYTKLDGVCTEIDPKLDNYKKDNSYFTEQPIDLVNPQYPNASFDFNFVCVNDIKFADDLNQLTG YKKPASRELKVTFFPDNGDVVAIDYKHYTPSFK
 KGAKLLHKPIVHVNNATNKATYKPNWTCIRCLWSTKPVETSNSEFVLDKSEDAQGMNDLACEDLKPVEEVENPTIQKDVLECNVKTTEVVGDII LKPANNSLKITEEV
 GHTDLMAYVDNSSLTIKKPNELSRVLGLTLATHGLAAVNSVDHPTVSTTNNVTRCLNRVCTNMYPTIITLLQLTCLVNLNVTGFI SAARQG
 NTVKSVGKFCLEASFNYLKNPNSKLINII IIFLLLSVCLGSLIYSTAALGVLSNLMGMSYCTGYREGYNSTNVTIATYCTGSI PCSVCLSGLDSDLTYPSELTIT
 ISSFKWDLTAFGLVAEWFLAYLLFRFFVVLGLAAIMQLFFSYFAVHPI SNWLMWLI INLVQMAPISAMVRMYIFFAFSYVYVWKS YVHVVDGCNSSTCMCYKRNATR
 VECTTIVNGVRSFVYVYANGGKFCKLHNWNCVNDTFCAGSTFISDEVARDLSLQFKRPINPTDQSSYIVDSVTVKNGSIHLYFDKAGKTYERHSLSHFVNLDNLRN
 NTKGSLPINIVDFDGKSNCKGASVYYSQMLQCPILLDDQALVDFDVGDAEVAVMKFDAYVNTFSSTFNVPMELKLTITLVAEAE LAKNVSLDNVLTGFI SAARQG
 FVDSDEVETKDVVECLKLSHQSDIEVTGDCSNMYLTYNKVENMTPRDLGACIDCSARHINAQVAKSHNIALIWNVKDFMSLSEQLRKQIRSAAKNNLPFKLTCAATTRQV
 VNVVTTKIALKGGKIVNWLKQLIKVTLVFLFVAIIFYLITPVHVMKHTDFSSSEIIGYKAI DGGVTRDIASDTCTCFANKHADDFDTWFSRGGSYTNDKACPLIAAVITR
 EVGFVVPGLPGTILRTTNGDFLHFLPRVFSAVGNICYTPSKLIEYTFDFAISACVLAECTIFKDGASGKVPYCYDTNVLEGSVAYESLRPDRVYVLMGDSIIQFPNTYLE
 GSVRVVTFDSEYCRHGTCESEAGVCSVTSGRWLVNNDYRSPLPGVDFGVDAVNLLTNMFTPLIQIPGALDI SASIVAGGIVAIIVVTCLAYYFMFRFAFGESHVAVF
 NTLFLMSFTVCLTPVYSFPLGVYSVIYLYLTFLYLTNDVSFLAHIQWVMFTPLVPFWITIAIYICISTKHFWFFSNYLRKRVFNGVSFSTFEAAALCTFLNKEMY
 LKLRSDVLLPLTQYNYRYLALYNYKYFSGAMDTSYREAAACCHLAKALNDFNSGSDVLYQPPQTSITSAVLQSGFRKMAFSPGKVEGCMVQVTCGTTTLNGLWLDVVY
 CPRHVICTSEDMLNPYEDLLIRKSNHNFVLQAGNVQLRVIGHSMQNCVLLKLVDTANPKTPKYKFVRIQPGQTFSLVACYNGSPSGVYQCAMRPNFTIKGSFLNGSCGS
 VGFNIDYDCVSFCYMHMELPTGVHAGTDLGNFYGPFVDRQTAQAAGTDTTITVNLVLAWLYAAVINGDRWFLNRFTTTLNDFNLVAMKYNIEPLTQDHVDILGLPSAQ
 GIAVLDMCASLKELLQNGMNGRTILGSALLEDEFTPFDDVRQCSGVTFQSAVKRTIKGTHHWWLLLTILTSLLVLVQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMFVK
 HKHAFLCLFLPLSLATVAYFNMVMPASWVMRMTWLDMDVDTLSGGFKLKDCVMYASAVVLLIIMLTARTVYDDGARRVWTLNMLVTLVYKYVYGNALDQAI SMWALI ISV
 TSNYSGVVTVMFLARGIVFMCVEYCPFIFFITGNTLQCI MLVYCFGLGYFCTCYFGLFCLLNRYFRLTLGVYDYLSTQEFYRMNSOGLLPKNSIDAFKLNILKLGVGK
 PCIKVATVQSKMSDVKCTSVLLSVLQQLRVESSSKLWAQCVQLHNDILLAKDTEAFKFMVSLSVLLSMQGAVDINKLCEMLDNRLTQA IASEFSSLSPSYAAFATA
 QEAYEQAVANGDSEVVLKLLKSLNVAKSEFDRDAAMQRKLEKMAQAMTQMYKQARSEDKRAKVTSAMQTMFLTMLRLKLDNALNNI INNARDGCVP LNI I PLTTAAKL
 MVVIPDYNTYKNTCDGTTFTYASALWEIQQVVDADSKI VQLSEISMDSNP LALWPLI VTLALRANSVAVKLQNNELSPVALRQMSCAAGTTQACTDDNALAYNTTKGGRF
 VLALLSDQLDKWARFPKSDGTGTIYTELEPPCRFVTDTPKGPVKYLYFIKGLNLRNRMVGLSLAATVRLQAGNATEVPANSTVLSFCAFVDAAKAYKDYLASGGQF
 ITNCVKMLCTHTGTGQAITVTPPEANMDQESFGGASCLLYCRCHIDHPNPKGFCDLKGYVQIPTTNCANDPVGFTLKNTVCTVCGMWKYGCSGCDQLREPLMQSDAQSF
 NGFAV

Replicase polyprotein RPP 1a. Replicase polyprotein RPP 1a, 4405 aa.

The longest n-mers are underlined.

In the RPP 1a molecule, we localized eleven 8-mers (Table 11) and more than a hundred 7-mers homologous to human proteins.

Some of the 8-mers are found in more than one human protein, some fold into long n-mers, for example EDIQLLKSAYENFNQH₁₁₂₆₋₁₁₄₁, EVEKGVLPQLEQPY₅₅₋₆₈ and SVEEVLSEARQHL₃₄₋₄₆.

In the RPP 1a molecule, 7-mers SCGNFKV₅₀₅₋₅₁₁ and AIFYLIT₂₇₈₅₋₂₇₉₁ are homologous to human olfactory receptor proteins 52N2₁₉₀₋₁₉₆ and 2W1₃₂₋₃₈, respectively. A heptamer LKTLSSL₁₅₅₆₋₁₅₆₂ is homologous to the human bitter taste receptor T2R55₁₈₁₋₁₈₇ (Fig. 2).

Replicase polyprotein RPP 1ab. This huge (7096 aa; the primary structure see in¹⁸) molecule contains 210 hepta- and octamers homologous to human proteins. Some of them fold into long (more than 15 aa) n-mers.

The possibility of the involvement of replicases in provoking an autoimmune response is debatable. Enzymes in general, and cell cycle enzymes in particular, are evolutionarily highly conserved. Fragments homologous to human proteins must be thrown in huge quantities into the gut lumen during the decay of any microorganism that dies there. It is possible that the interaction of replicases with the host's immune system obeys the laws other than for shorter proteins.

ORF6, ORF10, and ORF14. In these polypeptides (61, 38, and 73 aa, respectively), we did not find 7-/8-mers homologous to human proteins. When assessing the role of SARS CoV-2 proteins in mimicry and provoking an autoimmune response in humans, we considered the following parameters: (i) the number of homologous n-mers; (ii) the compactness of their arrangement in the SARS CoV-2 protein molecules; (iii) intradomain localization (external, transmembrane, internal) of the SARS CoV-2 proteins, and (iv) physiological functions that involve the homologous human proteins (Table 12).

Conclusions

Analysis of homology between the SARS CoV-2 and human proteins led us to the following conclusions. Some of the SARS CoV-2 proteins can be implicated in mimicry that can delay the response of innate immunity to the invasion of virus particles into the microorganism, and in provoking an autoimmune process that directs a part

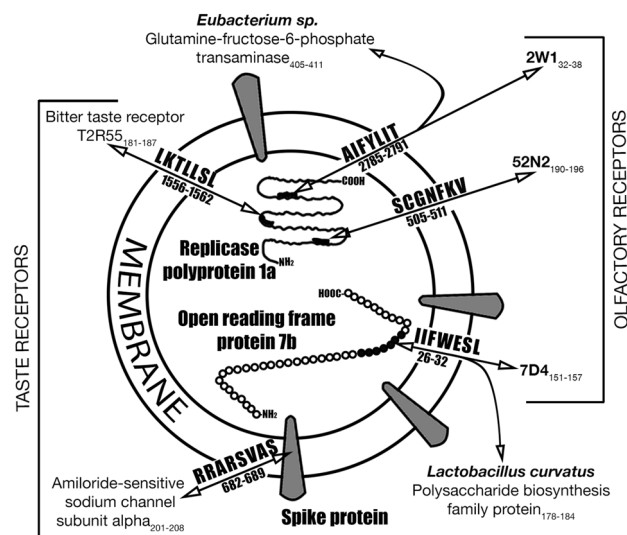


Figure 2. Some SARS CoV-2 hepta/octamers are homologous to human olfactory and taste receptor proteins. Homology to some proteins of commensal gut bacteria is also shown.

Goup of proteins	Protein	Mimicry	Autoimmune response	Comment
Structural	S	+++	+	Taste?—Amiloride-sensitive sodium channel subunit alpha ₂₀₁₋₂₀₈ Muscle contraction?—Unconventional myosin-XVI ₁₄₀₄₋₁₄₂₁
	E	—	+++	Gut microbiota?— <i>Lactobacillus paracasei</i> Digestion?—Cereals' proteins
	M	++	—	
	N	—	++	
Nonstructural	ORF3a	—	+	
	ORF6	—	—	No homology
	ORF7a	—	+	
	ORF7b	—	+	Smell?—Olfactory receptor 7D4 Gut microbiota?— <i>Lactobacillus curvatus</i>
	ORF8	—	++	
	ORF9b	—	++	Sperm capacitation?—Maestro heat-like repeat-containing protein family member 2B ₁₀₃₋₁₁₀
	ORF10	—	—	No homology
	ORF14	—	—	No homology
	RPP1a	—	?	Taste?—T2R55 receptor Smell?—Olfactory receptors 2W1 and 52N2 Gut microbiota?— <i>Eubacterium sp.</i>
	RPP1ab	—	?	

Table 12. Qualitative assessment of the possibility for the SARS CoV-2 proteins to be involved in the processes of mimicry and provoking an autoimmune response.

of the immune response to the proteins of a macroorganism (after the destruction of virus particles). Mimicry is probably more characteristic of the spike (S) protein, and the provocation of an autoimmune response seems to be a distinctive feature of the envelope (E) protein. The ORF7b protein may be involved in the impairment of olfactory receptors, and the S protein may be involved in taste perception dysfunction.

Drugs aimed at destructing or blocking these and alike regions in proteins of SARS CoV-2 and other viruses can enable the human immune system not to succumb to viral deception and destroy the invader shortly after its penetration into a macroorganism. It should also be borne in mind that drugs affecting such imitation regions can damage native proteins present of the human body. Destroying or blocking such regions can weaken the autoimmune response.

Data availability

The highest.

Code availability

Source code of Ouroboros (v. 0.5) is fully available at github. URL: <https://github.com/liquidbrainstrain/ouroboros>. Artwork: We used GIMP (Version 2.10.22) to create our artwork. The figures are completely original and have not been published anywhere.

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Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to A.M.

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