DOI: 10.56871/RBR.2024.63.31.001
УДК [616.2+616.34]-036.21+578.834.1+579.8+577.112+547.96

СТРУКТУРНЫЕ БЕЛКИ ДЕЛЬТА-ВАРИАНТА SARS COV-2: ГОМОЛОГИЯ С ОППОРТУНИСТИЧЕСКИМИ БАКТЕРИЯМИ

© Александр Тимурович Марьянович[1], Дмитрий Юрьевич Кормилец[2]

[1] Северо-Западный государственный медицинский университет им. И.И. Мечникова. 195067, г. Санкт-Петербург, Пискаревский пр., 47
[2] Военно-медицинская академия им. С.М. Кирова. 194044, Российская Федерация, г. Санкт-Петербург, ул. Академика Лебедева, 6

Контактная информация: Александр Тимурович Марьянович — д.б.н., профессор, заведующий кафедрой нормальной физиологии. E-mail: atm52@mail.ru ORCID: https://orcid.org/0000-0001-7482-3403 SPIN: 5957-2347

Для цитирования: Марьянович А.Т., Кормилец Д.Ю. Структурные белки дельта-варианта SARS CoV-2: гомология с оппортунистическими бактериями // Российские биомедицинские исследования. 2024. Т. 9. № 2. С. 5–17. DOI: https://doi.org/10.56871/RBR.2024.63.31.001

Поступила: 15.02.2024 **Одобрена: 04.04.2024** **Принята к печати: 20.05.2024**

Резюме. Способность SARS CoV-2 уклоняться от иммунного ответа можно считать общепризнанной. Гомология белков коронавируса и человека может быть одним из механизмов иммунного уклонения. Дельта-вариант обязательно имеет структурные особенности, которые объясняют его специфические свойства. Целью нашего исследования было выяснить, изменяют ли мутации, произошедшие в структурных белках дельта-варианта, его гомологию с белками, присутствующими в организме человека, то есть собственно человеческими, бактериальными и пищевыми. Используя инструменты биоинформатики, мы обнаружили гомологию на уровне гептамеров между структурными белками дельта-варианта и белками человека, а также белками некоторых условно-патогенных бактерий верхних дыхательных путей, легких и кишечника. Белки шиповый (S) и мембранный (M) дельта-варианта имеют большое количество сходств (гомологичных соответствий) с перечисленными белками, причем наибольшее количество — в случае мутации S:Δ156,157;R158G. Причина, по которой дельта-вариант SARS CoV-2 обладает специфическими характеристиками, и прежде всего повышенной летальностью, скорее всего, кроется в мутации в положениях 156–158 шипового белка.

Ключевые слова: SARS CoV-2, дельта-вариант, шиповидный белок, оппортунистические бактерии, гомология

SARS COV-2 DELTA VARIANT STRUCTURAL PROTEINS: HOMOLOGY WITH OPPORTUNISTIC BACTERIA

© Alexander T. Maryanovich[1], Dmitry Yu. Kormilets[2]

[1] North-Western State Medical University named after I.I. Mechnikov. 47 Piskarevskiy ave., Saint Petersburg 195067 Russian Federation
[2] Military Medical Academy named after S.M. Kirov. 6 Akademician Lebedev str., 194044 Saint Petersburg Russian Federation

Contact information: Alexander T. Maryanovich — Ph.D., D.Sc. (Biology), Professor, Head of Department of Normal Physiology. E-mail: atm52@mail.ru ORCID: https://orcid.org/0000-0001-7482-3403 SPIN: 5957-2347

For citation: Maryanovich AT, Kormilets DYu. SARS CoV-2 Delta variant structural proteins: homology with opportunistic bacteria. Russian Biomedical Research. 2024;9(2):5–17. DOI: https://doi.org/10.56871/RBR.2024.63.31.001

Received: 15.02.2024 **Revised: 04.04.2024** **Accepted: 20.05.2024**

Abstract. The capacity of SARS CoV-2 for immune evasion can be considered universally recognized. Coronavirus and human protein homology may be one of the mechanisms of immune evasion. Delta variant necessarily has structural features that explain its specific qualities. The aim of our study is to find out whether mutations in the structural proteins of Delta variant change its homology with proteins present in the human body, i.e. human, bacterial and dietary. Using bioinformatics tools we detected homology on the heptamer level between Delta variant structural proteins and human proteins as well as some opportunistic bacteria proteins of the upper respiratory tract, lung and gut. Delta variant spike (S) and membrane (M) proteins have a large number of similarities (homologous correspondences) with the listed proteins, with the S:Δ156,157;R158G mutation having the greatest amount. The reason why SARS CoV-2 Delta variant has specific characteristics, most importantly increased lethality, is most likely to be found in a mutation at positions 156–158 of spike protein.

Keywords: SARS CoV-2, Delta variant, spike protein, opportunistic bacteria, homology

INTRODUCTION

After a series of brilliant discoveries from Pasteur to Fleming and Waxman, mankind has learned to control most *bacterial infections.* Humans were able to create megalopolises with huge population densities. In response, nature had to put forward other limiting mechanisms less humanly controllable. The COVID-19 pandemic has become and will remain one of humanity's major concerns for the near future. The very important question is why and how this CoV could cause a pandemic [1]. Some mutation-induced structural substitutions in the N-terminal domain (NTD) of the SARS-CoV-2 S-protein lead to more efficient first contact and interaction with the upper airway epithelium [2].

The extraordinary virulence of Omicron variant (B.1.1.529) is now the main focus of researchers [3]. Nevertheless, it seems to us that in order to understand the causes of SARS CoV-2 *lethality*, the peculiarities of *Delta* variant (B.1.617.2) must be studied.

Using 3D models, the researchers can determine how the spike (S) protein binds to the ACE2 receptor [4]. The peculiarity of our approach is that we seek an explanation for the properties of coronavirus in the homology (commonality of short motifs) of virus proteins with human proteins. Recently we described dozens of homologous motifs in the primary structure of SARS CoV-2 and human proteins including proteins of olfactory and taste receptors [5]. Through mutations, the virus finds a way to avoid an immune response [6].

Molecular mimicry is considered a strategy used by many viruses to subvert and regulate antiviral immunity. For example, human cytomegalovirus has hijacked or developed a number of homologous sites that mimic immunomodulatory proteins encoded by the human body. These homologues encoded by the virus can contribute to the virus' evasion of immune clearance [7].

Following Joshua Lederberg's principle [8], we took into account not only proteins synthesized by the human body, but also those that originate from other genotypes and are constantly present in the macroorganism. These are the proteins of *commensal and opportunistic bacteria* of the upper respiratory tract, lung, oral cavity, and GI tract. We also analyzed the most common dietary proteins that are almost constantly present in the gut, namely those of the six world's most important cereal crops, i.e., Asian *rice Oryza sativa*, common wheat *Triticum aestivum*, maize *Zea mays*, common bean *Phaseolus vulgaris,* barley *Hordeum vulgare*, and sorghum *Sorghum bicolor*. We believed that the homology of the virus proteins with those of the named bacteria and cereals helps coronavirus to avoid or reduce the primary immune response.

THE AIM OF OUR STUDY

The aim of our study is to find out whether mutations in the structural proteins of SARS CoV-2 Delta variant change its homology with proteins present in the human body, i.e. human, bacterial and dietary.

RESULTS

Spike glycoprotein

Wuhan-Hu spike glycoprotein (S protein) molecule consists of 1273 amino acid residues. In Delta variant, as a result of two deletions (E_{156}Δ and F_{157}Δ), S protein consists of 1271 amino acid residues and contains seven substitutions in nine positions, namely $T_{19}R$, $G_{142}D$, $R_{158}G$, $L_{452}R$, $T_{478}K$, $P_{681}H$, and $D_{950}N$, numeration as in Wuhan-Hu variant [9].

S protein Delta variant, 1271 aa

MFVFLVLLPLVSSQCVNLRTRTQLPPAYTNSFTRGVYYP
DKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTNGT
KRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQ
SLLIVNNATNVVIKVCEFQFCNDPFLDVYYHKNNKSWMES
GVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREF
VFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINI
TRFQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRT
FLLKYNENGTITDAVDCALDPLSETKCTLKSFTVEKGIYQTSN
FRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRIS
NCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSF
VIRGDEVRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNNLD
SKVGGNYNYRYRLFRKSNLKPFERDISTEIYQAGSKPCNG
VEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPAT
VCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQF
GRDIADTTDAVRDPQTLEILDITPCSFGGVSVITPGTNTSNQ
VAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGC
LIGAEHVNNSYECDIPIGAGICASYQTQTNSRRRARSVAS
QSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTK
TSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQD
KNTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRS
FIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICAQKFN
GLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAA
LQIPFAMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIG
KIQDSLSSTASALGKLQNVVNQNAQALNTLVKQLSS

**NFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSL
QTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVDF
CGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFTTAPAI
CHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNT
FVSGNCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKN
HTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNES
LIDLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCC
MTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHYT**

Hereinafter, motifs homologous with human proteins [5] are highlighted in red font. Amino acid residues substituted as a result of mutations are highlighted in large letters. The N-terminal domain (NTD$_{14-303}$) is highlighted in green. Receptor-binding domain (RBD$_{317-539}$) is in gray italics. Receptor-binding motif RBM$_{436-506}$ is underlined. Heptapeptide repeat sequence 1 (HR1$_{910-982}$) is highlighted in blue. As a result of the double deletion Δ$_{156,157}$, starting from G$_{156}$, the numbering of positions in Delta variant does not correspond to the numbering in Wuhan-Hu.

Delta variant, as mentioned above, has a mutation S:P$_{681}$H. The S protein motif SPRRARS$_{680-686}$ homologous with a human protein has been replaced by a heptamer SHRRARS$_{678-684}$, which has no homologues in mammals (Table 1).

Table 1

Homology of a SARS CoV-2 S protein to a human protein

Mutation	Wuhan-Hu			Delta		
P$_{681}$H*	S protein heptamer	Species	Homologous protein heptamer	S protein heptamer	Species	Homologous protein heptamer
	SPRRARS$_{680-686}$*	*Homo sapiens*	Hermansky-Pudlak syndrome 1 protein$_{258-264}$	SHRRARS$_{678-684}$	No homological heptamers in commensal	

*In Wuhan-Hu and Delta variants, the position numbering differs after position 156 as a result of the Δ156,157 deletions.

The heptamers of S protein that are homologous with the proteins of some commensal and opportunistic bacteria are listed in Table 2.

Table 2

The heptamers of S protein homologous with the proteins of some commensal and opportunistic bacteria

Mutation	Wuhan-Hu				Delta			
	S protein heptamer	Species	Homologous protein heptamer	Localization in the human body	S protein heptamer	Species	Homologous protein heptamer	Localization in the human body
T$_{19}$R	VNLTTRT$_{16-22}$	*Escherichia coli BCE011_MS-01*	Uncharacterized protein$_{23-29}$	gut	VNLRTRT$_{16-22}$	*Streptococcus mitis SK597 TnpX; Streptococcus salivarius (strain CCHSS3)*	Site-specific recombinase$_{275-281}$	nasopharynx, oral cavity, throat
	NLTTRTQ$_{17-23}$	*Enterococcus faecalis*	Helicase, RecD/TraA family$_{755-761}$	gut	NLRTRTQ$_{17-23}$	*Subdoligranulum variabile*	Putative hydrolase$_{34-40}$	gut
G$_{142}$D*	NDPFLGV$_{137-143}$	No homological heptamers in commensal or opportunistic bacteria			NDPFLDV$_{137-143}$	*Pasteurella multocida subsp. multocida str*	Release factor glutamine methyltransferase$_{20-26}$	lung
Δ156, 157; R158G	EFRVYSS$_{156-162}$	No homological heptamers in commensal or opportunistic bacteria			ESGVYSS$_{154-160}$	*Lachnospiraceae bacterium 7_1_58FAA*	Uncharacterized protein$_{126-132}$	gut
						Escherichia coli UMEA 3609-1	Valine–tRNA ligase$_{320-326}$	gut
	FRVYSSA$_{157-163}$	No homological heptamers in commensal or opportunistic bacteria			SGVYSSA$_{155-161}$	*Fusobacterium sp. oral taxon 370 str. F0437*	Hep/Hag repeat protein (Fragment)$_{47-53}$	oral cavity
	RVYSSAN$_{158-164}$	*Bifidobacterium animalis subsp. lactis CNCM I-2494*	Fibronectin-binding protein$_{191-197}$	gut	GVYSSAN$_{156-162}$	*Bacillus sp. NRRL B-14911*	Methylmalonyl-CoA mutase$_{565-571}$	?

Endind of the table 2

Mutation	Wuhan-Hu				Delta			
	S protein heptamer	Species	Homologous protein heptamer	Localization in the human body	S protein heptamer	Species	Homologous protein heptamer	Localization in the human body
						Lactobacillus farraginis JCM 14108	D-alanyl-D-alanine carboxypeptidase$_{149-155}$	gut
						Fusobacterium nucleatum subsp. polymorphum F0401	Uncharacterized protein$_{234-240}$	oral cavity
						Prevotella saccharolytica F0055	Carbohydrate binding domain protein$_{715-721}$	oral cavity, upper respiratory tract, gut
						human gut metagenome	Glycoside hydrolase, family 25 (Fragment)$_{395-401}$	gut
L$_{452}$R	No homological heptamers in commensal or opportunistic bacteria							
T$_{478}$K*	No homological heptamers in commensal or opportunistic bacteria							
P$_{681}$H*	NSPRRAR$_{679-685}$	No homological heptamers in commensal or opportunistic bacteria			NSHRRAR$_{677-683}$	*Clostridium clostridioforme*	Uncharacterized protein$_{116-122}$	gut
D$_{950}$N*	KLQDVVN$_{947-953}$	*Prevotella salivae F0493*	Peptidase M16 inactive domain protein$_{918-924}$	oral cavity, gut	KLQNVVN$_{945-951}$	*Leptotrichia buccalis (strain ATCC 14201 / DSM 1135 / JCM 12969 / NCTC 10249)*	GCN5-related N-acetyltransferase$_{115-121}$	oral cavity
	DVVNQNA$_{950-956}$	No homological heptamers in commensal or opportunistic bacteria			NVVNQNA$_{948-954}$	*Prevotella multisaccharivorax DSM 17128*	Anaerobic ribonucleoside-triphosphate reductase$_{114-120}$	oral cavity, gut

*The same mutation has occurred in Omicron variant.

The heptamers of S protein that are homologous with the most common cereal proteins are listed in Table 3.

Table 3

The heptamers of S protein homologous with the most common cereal proteins

Mutation	Wuhan-Hu			Delta		
	S protein heptamer	Species	Homologous protein heptamer	S protein heptamer	Species	Homologous protein heptamer
T$_{19}$R	SQCVNLT$_{13-19}$	*Oryza sativa*	Leucine Rich Repeat family protein, expressed$_{520-526}$	SQCVNLR$_{13-19}$	No most common cereal sample	
	VNLTTRT$_{16-22}$	*Oryza sativa BCE011_MS-01*	Uncharacterized protein$_{23-29}$	VNLRTRT$_{16-22}$	No most common cereal sample	
	LTTRTQL$_{18-24}$	*Triticum aestivum*	Uncharacterized protein$_{888-894}$	LRTRTQL$_{18-24}$	No most common cereal sample	
L$_{452}$R	LYRLFRK$_{452-458}$	*Oryza sativa subsp. indica*	Putative uncharacterized protein$_{157-163}$	RYRLFRK$_{450-456}$	No most common cereal sample	
		Zea mays	Putative NAC domain transcription factor superfamily protein (Fragment)$_{100-106}$			

Endind of the table 3

Mutation	Wuhan-Hu			Delta		
	S protein heptamer	Species	Homologous protein heptamer	S protein heptamer	Species	Homologous protein heptamer
$T_{478}K^*$	sTPCNGV$_{477\text{-}483}$	No most common cereal sample		sKPCNGV$_{475\text{-}481}$	*Phaseolus vulgaris*	Uncharacterized protein$_{59\text{-}65}$
	sPRRARS$_{680\text{-}686}$	*Oryza sativa subsp. japonica*	Os02g0817400 protein (Fragment)$_{1\text{-}7}$	sHRRARS$_{678\text{-}684}$	*Oryza sativa subsp. japonica*	Expressed protein$_{296\text{-}302}$
		Zea mays	Uncharacterized protein$_{58\text{-}64}$		*Oryza sativa subsp. japonica*	Uncharacterized protein$_{616\text{-}622}$
					Hordeum vulgare	Predicted protein (Fragment)$_{16\text{-}22}$
	PRRARSV$_{681\text{-}687}$	*Oryza sativa subsp. japonica*	Putative uncharacterized protein$_{118\text{-}124}$	HRRARSV$_{679\text{-}685}$	No most common cereal sample	
		Zea mays	Uncharacterized protein$_{94\text{-}100}$			
$D_{950}N^*$	**ALGKLQD$_{844\text{-}950}$**	*Hordeum vulgare var. distichum*	Uncharacterized protein$_{123\text{-}129}$	ALGKLQN$_{842\text{-}848}$	No most commoncereal sample	
	LGKLQDV$_{945\text{-}951}$	*Hordeum vulgare var. distichum*	Uncharacterized protein$_{96\text{-}102}$	LGKLQNV$_{843\text{-}849}$	No most common cereal sample	
		Oryza sativa subsp. indica	Uncharacterized protein$_{248\text{-}254}$			
		Zea mays	Protein lap4$_{233\text{-}239}$			
			Golgi SNAP receptor complex member 1$_{75\text{-}81}$			
	GKLQDVV$_{946\text{-}952}$	*Zea mays*	Uncharacterized protein$_{388\text{-}394}$	GKLQNVV$_{844\text{-}850}$	No most common cereal sample	

*The same mutation has occurred in Omicron variant.

The heptamers of S protein that are homologous with some virus proteins are listed in Table 4.

Table 4

The heptamers of S protein homologous with some virus proteins

Mutation	Wuhan-Hu			Delta			Comment
	S protein heptamer	Other virus	Homologous protein heptamer	S protein heptamer	Other viruses	Homologous protein heptamer	
$P_{681}H$	QTQTNSP$_{675\text{-}681}$	*Human immunodeficiency virus 1*	Protease (Fragment)$_{2\text{-}7}$	QTQTNSH$_{673\text{-}679}$	No virus proteins homology		Homology with HIV-1 has disappeared
$D_{950}N^*$	LQDVVNQ$_{948\text{-}954}$	No virus proteins homology		LQNVVNQ$_{946\text{-}952}$	*Human immunodeficiency virus 1*	Envelope glycoprotein (Fragment)$_{71\text{-}77}$	Homology with HIV-1 has appeared

* The same mutation has occurred in Omicron variant.

Membrane protein

There are four mutations known in the membrane (M) protein Delta variant, namely A_2S, $F_{28}L$, $V_{70}L$, and $I_{82}T$ [10].

M protein Delta variant, 222 aa
MSDSNGTITVEELKKLLEQWNLVIGFLLLTWICLLQFAYANR
NRFLYIIKLIFLWLLWPVTLACFVLAALYRINWITGGIATAMACLV

GLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRP
LLESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSY
YKLGASQRVAGDSGFAAYSRYRIGNYKLNTDHSSSSDNIALLVQ

The heptamers of M protein that are homologous with the proteins of the commensal and opportunistic bacteria are listed in Table 5.

Table 5

The heptamers of M protein homologous with the proteins of the commensal and opportunistic bacteria

Mutation	Wuhan-Hu				Delta			
	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body
A$_2$S	MADSNGT$_{1-7}$	No homological heptamers in commensal or opportunistic bacteria			MSDSNGT$_{1-7}$	No homological heptamers in commensal or opportunistic bacteria		
	ADSNGTI$_{2-8}$	*Lachnospiraceae bacterium 7_1_58FAA*	Uncharacterized protein$_{252-258}$	gut	SDSNGTI$_{2-8}$			
F$_{28}$L	LVIGFLF$_{22-28}$	*Enterococcus faecalis R508*	Putative ferrichrome transport system permease protein FhuG$_{203-206}$	gut	LVIGFLL$_{22-28}$	*Eubacterium ventriosum ATCC 27560*	Putative K(+)-stimulated pyrophosphate-energized sodium pump$_{573-579}$	gut
						Enterococcus caccae ATCC BAA-1240	Uncharacterized protein$_{104-110}$	gut
						Faecalibacterium sp. CAG:74	Binding-protein-dependent transport systems inner membrane component$_{86-92}$	gut
						Prevotella histicola F0411	Uncharacterized protein$_{15-21}$	gut
						Lachnospiraceae bacterium 2_1_58FAA	Uncharacterized protein$_{65-71}$	gut
						Escherichia coli ISC11	Putative cell envelope opacity-associated protein A$_{42-48}$	gut
	VIGFLFL$_{23-29}$	*Enterococcus flavescens ATCC 49996*	Uncharacterized protein$_{128-134}$	gut	VIGFLLL$_{23-29}$	*Prevotella sp. oral taxon 472 str. F0295*	Uncharacterized protein$_{178-184}$	gut
		Lachnospiraceae bacterium COE1	MATE efflux family protein112-118	gut		*Lactobacillus brevis ATCC 14869 = DSM 20054*	Potassium uptake protein, TrkH family$_{239-245}$	gut
						Lactobacillus antri DSM 16041	Transporter, major facilitator family protein$_{422-428}$	gut
						Enterobacter cloacae subsp. cloacae (strain ATCC 13047 / DSM 30054 / NBRC 13535 / NCDC 279-56)	Putative multidrug resistance protein MdtD$_{183-189}$	gut
						Lachnospiraceae bacterium 28-4	Uncharacterized protein$_{18-24}$	gut
	IGFLFLT$_{24-30}$	*Lachnospiraceae bacterium CAG:215*	Transporter$_{468-474}$	gut	IGFLLLT$_{24-30}$	*Lactobacillus paracasei subsp. paracasei Lpp126*	Oligopeptide transport system permease protein oppB$_{9-15}$	oral cavity
						Eubacterium nodatum ATCC 33099	TIGR02185 family protein$_{43-49}$	oral cavity
						Bacteroides uniformis dnLKV2	Uncharacterized protein$_{737-743}$	gut
						Escherichia coli 2845650	Uncharacterized protein$_{13-19}$	gut
						Prevotella sp. CAG:1320	Putative thiol:disulfide interchange protein DsbD$_{8-14}$	gut
						Enterococcus faecalis 06-MB-DW-09	Putative transmembrane permease MsmF$_{16-22}$	gut
	GFLFLTW$_{25-31}$	No homological heptamers in commensal or opportunistic bacteria			GFLLLTW$_{25-31}$	No homological heptamers in commensal or opportunistic bacteria		

Endind of the table 5

Mutation	Wuhan-Hu				Delta			
	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body
	FLFLTWI$_{26-32}$	No homological heptamers in commensal or opportunistic bacteria			FLLLTWI$_{26-32}$	No homological heptamers in commensal or opportunistic bacteria		
	LFLTWIC$_{27-33}$	No homological heptamers in commensal or opportunistic bacteria			LLLTWIC$_{27-33}$	*Peptoniphilus sp. oral taxon 375 str. F0436*	Na+/H+ antiporter family protein$_{105-111}$	gut
	FLTWICL$_{28-34}$	No homological heptamers in commensal or opportunistic bacteria			LLTWICL$_{28-34}$	No homological heptamers in commensal or opportunistic bacteria		
V$_{70}$L	CFVLAAV$_{64-70}$	*Enterobacter sp. Ag1*	Formate dehydrogenase-O subunit gamma$_{24-30}$	gut	CFVLAAL$_{64-70}$	No homological heptamers in commensal or opportunistic bacteria		
	FVLAAVY$_{65-71}$	No homological heptamers in commensal or opportunistic bacteria			FVLAALY$_{65-71}$	*Bacteroides dorei CL03T12C01*	HAD hydrolase, family IA$_{344-350}$	gut
	VLAAVYR$_{66-72}$	No homological heptamers in commensal or opportunistic bacteria			VLAALYR$_{66-72}$	*Bifidobacterium longum subsp. infantis (strain ATCC 15697 / DSM 20088 / JCM 1222 / NCTC 11817 / S12)*	Putative ABC transporter permease component$_{110-116}$	gut
						Haemophilus parainfluenzae ATCC 33392	ABC transporter, permease protein$_{121-127}$	upper respiratory tract, lung
	LAAVYRI$_{67-73}$	*Lachnospiraceae bacterium 3_1_57FAA_CT1*	Uncharacterized protein$_{130-136}$	gut	LAALYRI$_{67-73}$	*Acinetobacter sp. CIP 101966*	Uncharacterized protein$_{18-24}$	oral cavity
	AAVYRIN$_{68-74}$	*Lautropia mirabilis ATCC 51599*	Selenide, water dikinase$_{56-62}$	oral cavity, upper respiratory tract	AALYRIN$_{68-74}$	*Prevotella melaninogenica (strain ATCC 25845 / DSM 7089 / JCM 6325 / VPI 2381 / B282) GN=HMPREF0659_A647*	Hydrolase, NUDIX family$_{54-60}$	upper respiratory tract
		Lachnospiraceae bacterium JC7	Diguanylate cyclase (GGDEF) domain-containing protein (Precursor)$_{114-120}$	gut		*Lactobacillus ruminis (strain ATCC 27782 / RF3)*	Conserved hypothetical YitT family protein	gut
						Bacteroides nordii CL02T12C05	Uncharacterized protein$_{700-706}$	gut
	AVYRINW$_{69-75}$	No homological heptamers in commensal or opportunistic bacteria			ALYRINW$_{69-75}$	No homological heptamers in commensal or opportunistic bacteria		
	VYRINWI$_{70-76}$	No homological heptamers in commensal or opportunistic bacteria			LYRINWI$_{70-76}$	No homological heptamers in commensal or opportunistic bacteria		
I$_{82}$T	ITGGIAI$_{76-82}$	*Ruminococcus obeum ATCC 29174*	Ion channel$_{143-149}$	gut	ITGGIAT$_{76-82}$	*Enterococcus faecalis*	Dephospho-CoA kinase$_{7-13}$	gut
		Bacteroides sp. 3_1_19	Putative uncharacterized protein$_{158-164}$	gut		*Clostridium asparagiforme DSM 15981*	ABC transporter, permease protein$_{268-274}$	gut
	TGGIAIA$_{77-83}$	No homological heptamers in commensal or opportunistic bacteria			TGGIATA$_{77-83}$	*Veillonella sp. oral taxon 780 str. F0422*	PrpF protein$_{312-318}$	oral cavity
	GGIAIAM$_{78-84}$	*Enterobacteriaceae bacterium 9_2_54FAA*	Uncharacterized protein$_{270-276}$	gut	GGIATAM$_{78-84}$	No homological heptamers in commensal or opportunistic bacteria		
		Eubacterium sulci ATCC 35585	Peptidase, M20/M25/M40 family$_{136-142}$	gut				
		Lactobacillus brevis subsp. gravesensis ATCC 27305	Transporter, major facilitator family protein$_{421-427}$	gut				
	GIAIAMA$_{79-85}$	*Lachnospiraceae bacterium 10-1*	Uncharacterized protein$_{148-154}$	gut	GIATAMA$_{79-85}$	*Enterobacter aerogenes UCI 48*	Uncharacterized protein$_{320-326}$	gut
	IAIAMAC$_{80-86}$	No homological heptamers in commensal or opportunistic bacteria			IATAMAC$_{80-86}$	No homological heptamers in commensal or opportunistic bacteria		
	AIAMACL$_{81-87}$	No homological heptamers in commensal or opportunistic bacteria			ATAMACL$_{81-87}$	*Lactobacillus paracasei subsp. paracasei CNCM I-4649*	Class II aldolase/adducin family protein$_{101-107}$	oral cavity, gut
	IAMACLV$_{82-88}$	No homological heptamers in commensal or opportunistic bacteria			TAMACLV$_{82-88}$	No homological heptamers in commensal or opportunistic bacteria		

*The same mutation has occurred in Omicron variant.

Membrane protein

There are four mutations known in the membrane (M) protein Delta variant, namely A_2S, $F_{28}L$, $V_{70}L$, and $I_{82}T$ [10].

M protein Delta variant, 222 aa

MSDSNGTITVEELKKLLEQWNLVIGFLLLTWICLLQFAYANRNRFLYIIKLIFLWLLWPVTLACFVLAALYRINWITGGIATAMACLVGLMWLSYFIASFRLFARTRSMWSFNPETNILLNVPLHGTILTRPLLESELVIGAVILRGHLRIAGHHLGRCDIKDLPKEITVATSRTLSYYKLGASQRVAGDSGFAAYSRYRIGNYKLNTDHSSSSDNIALLVQ

The heptamers of M protein that are homologous with the proteins of the commensal and opportunistic bacteria are listed in Table 6.

Table 6

The heptamers of M protein homologous with the proteins of the commensal and opportunistic bacteria.

Mutation	Wuhan-Hu				Delta			
	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body
A_2S	MADSNGT$_{1-7}$	No homological heptamers in commensal or opportunistic bacteria			MSDSNGT$_{1-7}$	No homological heptamers in commensal or opportunistic bacteria		
	ADSNGTI$_{2-8}$	*Lachnospiraceae bacterium 7_1_58FAA*	Uncharacterized protein$_{252-258}$	gut	SDSNGTI$_{2-8}$			
$F_{28}L$	LVIGFLF$_{22-28}$	*Enterococcus faecalis R508*	Putative ferrichrome transport system permease protein FhuG$_{203-206}$	gut	LVIGFLL$_{22-28}$	*Eubacterium ventriosum ATCC 27560*	Putative K(+)-stimulated pyrophosphate-energized sodium pump$_{573-579}$	gut
						Enterococcus caccae ATCC BAA-1240	Uncharacterized protein $_{104-110}$	gut
						Faecalibacterium sp. CAG:74	Binding-protein-dependent transport systems inner membrane component$_{86-92}$	gut
						Prevotella histicola F0411	Uncharacterized protein $_{15-21}$	gut
						Lachnospiraceae bacterium 2_1_58FAA	Uncharacterized protein$_{65-71}$	gut
						Escherichia coli ISC11	Putative cell envelope opacity-associated protein A$_{42-48}$	gut
	VIGFLFL$_{23-29}$	*Enterococcus flavescens ATCC 49996*	Uncharacterized protein$_{128-134}$	gut	VIGFLLL$_{23-29}$	*Prevotella sp. oral taxon 472 str. F0295*	Uncharacterized protein$_{178-184}$	gut
		Lachnospiraceae bacterium COE1	MATE efflux family protein112-118	gut		*Lactobacillus brevis ATCC 14869 = DSM 20054*	Potassium uptake protein, TrkH family$_{239-245}$	gut
						Lactobacillus antri DSM 16041	Transporter, major facilitator family protein$_{422-428}$	gut
						Enterobacter cloacae subsp. cloacae (strain ATCC 13047 / DSM 30054 / NBRC 13535 / NCDC 279-56)	Putative multidrug resistance protein MdtD$_{183-189}$	gut
						Lachnospiraceae bacterium 28-4	Uncharacterized protein$_{18-24}$	gut
	IGFLFLT$_{24-30}$	*Lachnospiraceae bacterium CAG:215*	Transporter$_{468-474}$	gut[9	IGFLLLT$_{24-30}$	*Lactobacillus paracasei subsp. paracasei Lpp126*	Oligopeptide transport system permease protein oppB$_{9-15}$	oral cavity
						Eubacterium nodatum ATCC 33099	TIGR02185 family protein$_{43-49}$	oral cavity
						Bacteroides uniformis dnLKV2	Uncharacterized protein$_{737-743}$	gut
						Escherichia coli 2845650	Uncharacterized protein$_{13-19}$	gut
						Prevotella sp. CAG:1320	Putative thiol:disulfide interchange protein DsbD$_{8-14}$	gut
						Enterococcus faecalis 06-MB-DW-09	Putative transmembrane permease MsmF$_{16-22}$	gut
	GFLFLTW$_{25-31}$	No homological heptamers in commensal or opportunistic bacteria			GFLLLTW$_{25-31}$	No homological heptamers in commensal or opportunistic bacteria		

Endind of the table 6

Mutation	Wuhan-Hu				Delta			
	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body	M protein heptamer	Species	Homologous protein heptamer	Localization in the human body
	FLFLTWI$_{26-32}$	No homological heptamers in commensal or opportunistic bacteria			FLLLTWI$_{26-32}$	No homological heptamers in commensal or opportunistic bacteria		
	LFLTWIC$_{27-33}$	No homological heptamers in commensal or opportunistic bacteria			LLLTWIC$_{27-33}$	*Peptoniphilus sp. oral taxon 375 str. F0436*	Na+/H+ antiporter family protein$_{105-111}$	gut
	FLTWICL$_{28-34}$	No homological heptamers in commensal or opportunistic bacteria			LLTWICL$_{28-34}$	No homological heptamers in commensal or opportunistic bacteria		
V$_{70}$L	CFVLAAV$_{64-70}$	*Enterobacter sp. Ag1*	Formate dehydrogenase-O subunit gamma$_{24-30}$	gut	CFVLAAL$_{64-70}$	No homological heptamers in commensal or opportunistic bacteria		
	FVLAAVY$_{65-71}$	No homological heptamers in commensal or opportunistic bacteria			FVLAALY$_{65-71}$	*Bacteroides dorei CL03T12C01*	HAD hydrolase, family IA$_{344-350}$	gut
	VLAAVYR$_{66-72}$	No homological heptamers in commensal or opportunistic bacteria			VLAALYR$_{66-72}$	*Bifidobacterium longum subsp. infantis (strain ATCC 15697 / DSM 20088 / JCM 1222 / NCTC 11817 / S12)*	Putative ABC transporter permease component$_{110-116}$	gut
						Haemophilus parainfluenzae ATCC 33392	ABC transporter, permease protein$_{121-127}$	upper respiratory tract, lung
	LAAVYRI$_{67-73}$	*Lachnospiraceae bacterium 3_1_57FAA_CT1*	Uncharacterized protein$_{130-136}$	gut	LAALYRI$_{67-73}$	*Acinetobacter sp. CIP 101966*	Uncharacterized protein$_{18-24}$	oral cavity
	AAVYRIN$_{68-74}$	*Lautropia mirabilis ATCC 51599*	Selenide, water dikinase$_{56-62}$	oral cavity, upper respiratory tract	AALYRIN$_{68-74}$	*Prevotella melaninogenica (strain ATCC 25845 / DSM 7089 / JCM 6325 / VPI 2381 / B282) GN=HMPREF0659_ A647*	Hydrolase, NUDIX family$_{54-60}$	upper respiratory tract
		Lachnospiraceae bacterium JC7	Diguanylate cyclase (GGDEF) domain-containing protein (Precursor)$_{114-120}$	gut		*Lactobacillus ruminis (strain ATCC 27782 / RF3)*	Conserved hypothetical YitT family protein	gut
						Bacteroides nordii CL02T12C05	Uncharacterized protein$_{700-706}$	gut
	AVYRINW$_{69-75}$	No homological heptamers in commensal or opportunistic bacteria			ALYRINW$_{69-75}$	No homological heptamers in commensal or opportunistic bacteria		
	VYRINWI$_{70-76}$	No homological heptamers in commensal or opportunistic bacteria			LYRINWI$_{70-76}$	No homological heptamers in commensal or opportunistic bacteria		
I$_{82}$T	ITGGIAI$_{76-82}$	*Ruminococcus obeum ATCC 29174*	Ion channel$_{143-149}$	gut	ITGGIAT$_{76-82}$	*Enterococcus faecalis*	Dephospho-CoA kinase$_{7-13}$	gut
		Bacteroides sp. 3_1_19	Putative uncharacterized protein$_{158-164}$	gut		*Clostridium asparagiforme DSM 15981*	ABC transporter, permease protein$_{268-274}$	gut
	TGGIAIA$_{77-83}$	No homological heptamers in commensal or opportunistic bacteria			TGGIATA$_{77-83}$	*Veillonella sp. oral taxon 780 str. F0422*	PrpF protein$_{312-318}$	oral cavity
	GGIAIAM$_{78-84}$	*Enterobacteriaceae bacterium 9_2_54FAA*	Uncharacterized protein$_{270-276}$	gut	GGIATAM$_{78-84}$	No homological heptamers in commensal or opportunistic bacteria		
		Eubacterium sulci ATCC 35585	Peptidase, M20/M25/M40 family$_{136-142}$	gut				
		Lactobacillus brevis subsp. gravesensis ATCC 27305	Transporter, major facilitator family protein$_{421-427}$	gut				
	GIAIAMA$_{79-85}$	*Lachnospiraceae bacterium 10-1*	Uncharacterized protein$_{148-154}$	gut	GIATAMA$_{79-85}$	*Enterobacter aerogenes UCI 48*	Uncharacterized protein$_{320-326}$	gut
	IAIAMAC$_{80-86}$	No homological heptamers in commensal or opportunistic bacteria			IATAMAC$_{80-86}$	No homological heptamers in commensal or opportunistic bacteria		
	AIAMACL$_{81-87}$	No homological heptamers in commensal or opportunistic bacteria			ATAMACL$_{81-87}$	*Lactobacillus paracasei subsp. paracasei CNCM I-4649*	Class II aldolase/adducin family protein$_{101-107}$	oral cavity, gut
	IAMACLV$_{82-88}$	No homological heptamers in commensal or opportunistic bacteria			TAMACLV$_{82-88}$	No homological heptamers in commensal or opportunistic bacteria		

Nucleocapsid protein

Two mutations are known in the Delta variant nucleocapsid (N) protein, namely R$_{203}$M and D$_{377}$Y [11].

N protein Delta variant 419 aa

MSDNGPQNQRNAPRITFGGPSDSTGSNQNGERSGARSKQR
RPQGLPNNTASWFTALTQHGKEDLKFPRGQGVPINTNSSPDD
QIGYYRRATRRIRGGDGKMKDLSPRWYFYYLGTGPEAGLPYG
ANKDGIIWVATEGALNTPKDHIGTRNPANNAAIVLQLPQGTTLPK
GFYAEGSRGGSQASSRSSSRSRNSSRNSTPGSSMGTSPARM
AGNGGDAALALLLLDRLNQLESKMSGKGQQQQGQTVTKKSAA
EASKKPRQKRTATKAYNVTQAFGRRGPEQTQGNFGDQELIRQ
GTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTWLTYTGAI
KLDDKDPNFKDQVILLNKHIDAYKTFPPTEPKKDKKKKAYETQA
LPQRQKKQQTVTLLPAADLDDFSKQLQQSMSSADSTQA

The heptamers of N protein homologous with the proteins of some opportunistic bacteria and the most common cereals are listed in Table 7.

Table 7

The heptamers of N protein homologous with the proteins of some opportunistic bacteria and the most common cereals

Mutation	Wuhan-Hu				Delta			
	N protein heptamer	Species	Homologous protein heptamer	Localization in the human body	N protein heptamer	Species	Homologous protein heptamer	Localization in the human body
R$_{203}$M	STPGSSR$_{197-203}$	*Prevotella buccalis ATCC 35310*	NHL repeat protein$_{306-312}$	oral cavity	STPGSSM$_{197-203}$	No bacterial or cereal sample		
	TPGSSRG$_{198-204}$	No bacterial or cereal sample			TPGSSMG$_{198-204}$	*Bacteroides uniformis CAG:3*	Uncharacterized protein$_{128-134}$	gut
	PGSSRGT$_{199-205}$	*Zea mays*	Putative WRKY DNA-binding domain superfamily protein$_{78-84}$	gut	PGSSMGT$_{199-205}$	*Oryza sativa subsp. indica*	Putative uncharacterized protein$_{558-564}$	gut
		Sorghum bicolor	Putative uncharacterized protein Sb07g002490$_{27-33}$	gut				
	GSSRGTS$_{200-206}$	*Sorghum bicolor*	Putative uncharacterized protein Sb08g014350$_{176-182}$	gut	GSSMGTS$_{200-206}$	*Fusobacterium sp. CM21*	Permease family protein$_{294-300}$	oral cavity
	SSRGTSP$_{201-207}$	*Hordeum vulgare var. distichum*	Uncharacterized protein$_{267-273}$	gut	SSMGTSP$_{201-207}$	No bacterial or cereal sample		
		Oryza sativa subsp. japonica	Expressed protein$_{216-222}$	gut				
	SRGTSPA$_{202-208}$	No bacterial or cereal sample			SMGTSPA$_{202-208}$	No bacterial or cereal sample		
	RGTSPAR$_{203-209}$	*Oryza sativa subsp. japonica*	Os06g0523800 protein$_{118-124}$	gut	MGTSPAR$_{203-209}$	No bacterial or cereal sample		
D$_{377}$Y	DKKKKAD$_{371-377}$	*Prevotella sp. oral taxon 473 str. F0040*	Pseudouridine synthase, RluA family$_{295-301}$	oral cavity	DKKKKAY$_{371-377}$	*Lachnospiraceae bacterium 3-1*	Oligoendopeptidase F$_{439-445}$	gut
	KKKKADE$_{372-377}$	*Prevotella sp. oral taxon 473 str. F0040*	Pseudouridine synthase, RluA family$_{296-302}$	oral cavity	KKKKAYE$_{372-377}$	*Oryza sativa subsp. indica*	Putative uncharacterized protein$_{1090-1096}$	gut
		Enterococcus faecalis	Uncharacterized protein$_{396-402}$	gut				
	KKKADET$_{373-379}$	No significant sample			KKKAYET$_{373-379}$	*Bacillus infantis NRRL B-14911*	GntR family transcriptional regulator$_{2-8}$	?
	KKADETQ$_{374-380}$	No bacterial or cereal sample			KKAYETQ$_{374-380}$	No bacterial or cereal sample		
	KADETQA$_{375-381}$	*Homo sapiens*	Myopalladin$_{90-96}$	?	KAYETQA$_{375-381}$	No bacterial or cereal sample		
	ADETQAL$_{376-382}$	*Oryza glaberrima*	Uncharacterized protein (Fragment)$_{474-480}$	gut	AYETQAL$_{376-382}$	*Lachnospiraceae bacterium M18-1*	Uncharacterized protein$_{244-250}$	gut
	DETQALP$_{377-383}$	No bacterial or cereal sample			YETQALP$_{377-383}$	*Lachnospiraceae bacterium M18-1*	Uncharacterized protein$_{245-251}$	gut

As shown above, some of the mutations that occurred in the Delta variant increased the homology of its structural proteins with those of the opportunistic and some other bacteria. These data are summarized in Table 8.

Information about the effects that mutations in SARS CoV-2 Delta variant have on the homology between its structural proteins and human opportunistic bacteria proteins are summarized in Figure 1.

DISCUSSION

In Wunan-Hu variant, the S protein molecule contains dozens of heptamers homologous to human proteins. Their total length is 169 amino acid residues, or 13.3% of the S protein molecule total length [5]. For the sake of brevity, we suggest calling **ho**mologous **mot**ifs *homots*. For example, a SARS CoV-2 S protein human homot means a motif common for the S protein and any human protein. The same way "in SARS CoV-2 S protein, the motif SPRRARS is a human homot" means that motif SPRRARS is present in the S protein of coronavirus as well as in some human protein. The term *mimics*, proposed by Damoiseaux et al. [12], is close in meaning but less specific.

We assumed that the reason for the special qualities of SARS CoV-2 Delta variant should be sought in the greater homology of its proteins with those of the human body. However, we did not find any significant differences between Wuhan-Hu variant and Delta variant in their homology to human proteins.

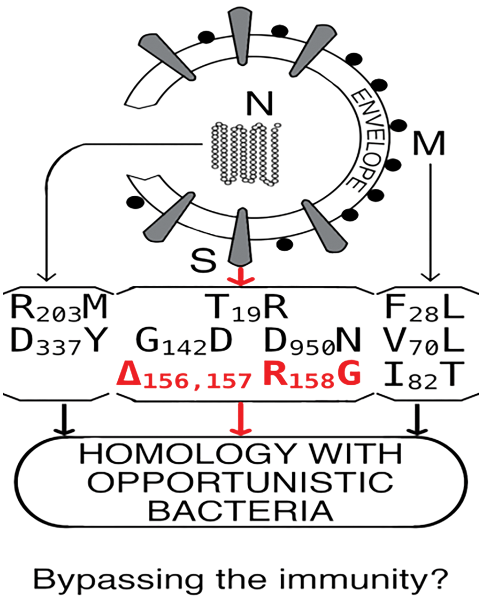

Fig. 1. The effect of mutations in SARS CoV-2 Delta variant structural proteins S, M, and N on their homology with human opportunistic bacteria. The most important mutation, in our opinion, is highlighted in red font

Delta variant stays on the nasal mucosal surface significantly longer than Wuhan-Hu variant (14 vs. 8 days) [13].

As has been already mentioned, we considered the human proteome in general as a set of proteins synthesized by the

Table 8

Mutational changes of homology SARS CoV-2 structural proteins with proteins of opportunistic bacteria and some other functionally significant proteins

Protein	Mutation	Increases homology with proteins of commensal or opportunistic bacteria, inhabitants of the oral cavity, upper respiratory tract or lung	Increases homology with proteins of gut commensal or opportunistic bacteria and/or the most common cereals	Increases homology with some other proteins
S (Table 2)	$T_{19}R$	+	+	
	$G_{142}D^{*}$	+	–	
	$\Delta_{156,157}$, $R_{158}G$	**+++**	**+++**	Homology with a protein of *Bacillus sp. NRRL B-14911* that can provoke autoimmune damage to the heart
	$L_{452}R$	–	–	
	$T_{478}K^{*}$	–	–	
	$P_{681}H$	–	–	
	$D_{950}N^{*}$	+	+	Homology with a protein of *Human immunodeficiency virus 1* (Table 4)
M (Table 6)	$A_{2}S$	–	–	
	$F_{28}L$	+	++	
	$V_{70}L$	++	++	
	$I_{82}T$	+	–	
N (Table 7)	$R_{203}M$	–	–	
	$D_{377}Y$	–	+	

*The same mutation has occurred in Omicron variant.

macroorganism itself, proteins of commensal and opportunistic bacteria, and the most common digestive proteins, therefore studying the homology of SARS CoV-2 Delta variant with all the listed types of proteins.

In S protein, mutations at the positions 19, 142, 156-158, and 950 created a number of heptamers homologous to proteins of bacteria, that are always present in the human nasopharynx, mouth, throat, upper respiratory tract, and lung (Table 2). It is possible that the presence of such homologous motifs allows Delta to bypass the innate immunity protection more successfully.

Mutations S:G$_{142}$D and S:D$_{950}$N are also found in Omicron variant, while the mutations S:T$_{19}$R and S:$\Delta_{156,157}$,R$_{158}$G are only present in Delta variant. These exclusive Delta variant mutations especially the ones at the positions 156-158 may be the reason for its specific qualities.

The L$_{452}$R and T$_{478}$K mutations did not affect the homology of S protein with proteins of opportunistic bacteria (Table 2).

In Delta variant, the positions where the most significant increase in homology occurred — S:$\Delta_{156,157}$;R$_{158}$G — are located in the N-terminus domain (NTD$_{14\text{-}303}$). So far, researchers have paid less attention to this domain than to the Receptor-binding domain (RBD$_{317\text{-}539}$). It is logically consistent to assume that in the S protein molecule one domain is responsible for binding to the receptor and other for structural mimicry and evasion.

The delta variant differs from the other SARS COV-2 variants in 14 positions. According to our data (Fig. 1), six of these alterations involved in the increase in the homology of coronavirus proteins with those of opportunistic bacteria. None of these six alterations are common to the Delta and non-VOC variants. This suggests that the increase in homology with proteins of opportunistic infections is specific to the Delta variant.

We are not yet able to analyze homology data for SARS CoV-2 S protein and the HIV-1 C protein (Table 4).

In M protein, the F$_{28}$L, V$_{70}$L, and I$_{82}$T mutations resulted in the emergence of heptamers homologous to proteins of numerous commensal and opportunistic upper respiratory and gut bacteria (Table 6). M protein is located on the outer side of the virion envelope [5], and these heptamers can participate in immune evasion.

In N protein (Table 7), the mutation N:R$_{203}$M resulted in the motif GSSMGTS$_{200\text{-}206}$ which is homologous to the Permease family protein$_{294\text{-}300}$ of *Fusobacterium nucleatum*, an opportunistic periodontal pathogen of the oral cavity [14]. The mutation M:D$_{377}$Y caused the following effects: (a) disappearance of the heptamer KADETQA$_{375\text{-}381}$, homologous to the human protein Myopalladin (MYPN$_{90\text{-}96}$), which is involved in communication between the sarcomere and the nucleus in cardiac and skeletal muscles [15]; and (b) emergence of KKKAYET$_{373\text{-}379}$, homologous to the heptamer GntR family transcriptional regulator$_{2\text{-}8}$ *Bacillus infantis*, which is involved in the provocation of immune myocardial disorder [16].

A recent review of the available evidence for immune mechanisms of cardiovascular damage COVID-19 has been presented [17]. N protein, located inside of the virion, should act at the later stages of the infectious process, for example, provoking an autoimmune response.

Of all the Delta variant mutations we studied, none caused an increase in the homology of the SARS CoV-2 S protein with proteins with the most common cereals (Table 3).

Natural selection fixes some substitutions in the primary structure of the protein molecules of viruses and eliminates others. One of the “aims” of selection might be immune evasion. A virus can achieve this by making the most functionally important parts of the protein molecule as similar as possible to the proteins permanently present in the host. Microorganisms, due to their genetic diversity and the huge size of their combined genome, provide more opportunities for viral mimicry than the macroorganism itself. Delta variant has increased homology of S and M proteins with proteins already familiar to human immunity, namely with opportunistic bacteria proteins.

The capacity of SARS CoV-2 for immune evasion can be considered universally acknowledged [3]. Coronavirus and human protein homology may be one of the mechanisms of immune evasion [5]. Delta variant necessarily has structural features that explain its specific qualities. Perhaps the reason is the homology of its proteins with those of commensal bacteria and opportunistic infections of the upper respiratory tract and lung. In this case, the S:$\Delta_{156,157}$;R$_{158}$G mutation deserves special attention. The reason why SARS CoV-2 Delta variant has these specific qualities, most importantly increased lethality, is most likely to be found in a mutation at positions 156-158 of spike protein. It has not yet been concluded whether the homology of Delta variant proteins with gut bacteria proteins and dietary protein is of any significance.

We hope that this preliminary study will open the door to further research into the immunology and bioinformatics.

METHODS

We used our original way of presenting the text search. The data were obtained from the Uniprot open-access protein database, in which the amino acid sequences of proteins are encoded by a one-letter code. We cut the primary structures of the coronavirus proteins into heptamers using the frameshift method and searched a separate database of 75777 molecules of human proteins [18]. This number is about three times the real number of all human proteins because of repetition and minor differences in the records. We looked for a full match of the 7-mer amino acid sequences in SARS CoV-2 proteins [19] with proteins of other organisms throughout the taxonomic range of evolution from bacteria and plants to humans. Heptamers were chosen as a criterion for homology because of the lack of matches in octamers and tens of thousands of matches in hexamers. In the case of matching heptamers, an alignment was performed on the matching site.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. А.Т. Марьянович и Д.К. Кормилец написали основной текст рукописи. А.Т. Марьянович и Д.К. Кормилец подготовили анализ данных. Авторы прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Данное исследование представляет собой инициативный проект авторов, финансируемый исключительно из их личных источников.

Заявление о доступности данных. Источником базы данных по 75 777 строкам белков человека является [18]. Источник базы данных объемом ок. 33 млн нитей всех видов белков [19].

Иллюстрации. Для создания наших иллюстраций мы использовали GIMP (версия 2.10.22). Рисунок полностью оригинальный и нигде не публиковался.

ADDITIONAL INFORMATION

Author contributions. A.T. Maryanovich and D.Yu. Kormilets wrote the main manuscript text. A.T. Maryanovich and D.Yu. Kormilets prepared data analysis. The authors read and approved the final version before publication.

Competing interests. The authors declare that they have no competing interests.

Funding: This research is an authors' initiative project funded exclusively from their personal sources.

Funding source. This study was not supported by any external sources of funding.

Data Availability Statement: The source of database of 75777 strings of human proteins is [18]. The source of database of approx. 33 mln strings of all species proteins is [19].

Artwork. We used GIMP (Version 2.10.22) to create our artwork. The figure is completely original and have not been published anywhere.

ЛИТЕРАТУРА / REFERENCES

1. Elrashdy F., Redwan E.M. & Uversky V.N. Why COVID-19 Transmission Is More Efficient and Aggressive Than Viral Transmission in Previous Coronavirus Epidemics? Biomolecules. 2020;10:1312. DOI: 10.3390/biom10091312.
2. Seyran M. et al. The structural basis of accelerated host cell entry by SARS-CoV-2. FEBS J. 2021;288:5010–5020. DOI: 10.1111/febs.15651.
3. Fang F.F. & Shi P.Y. Omicron a drug developer's perspective. Emerg Microbes Infect. 2022;11:208–211. DOI: 10.1080/22221751.2021.2023330.
4. Beaudoin C.A. et al. Predicted structural mimicry of spike receptor-binding motifs from highly pathogenic human coronaviruses. Comput Struct Biotechnol. J. 2021;19:3938–3953. DOI: 10.1016/j.csbj.2021.06.041.
5. Khavinson V. et al. Homology between SARS CoV-2 and human proteins. Sci Rep. 2021;11:17199. DOI: 10.1038/s41598-021-96233-7.
6. Kwarteng A. et al. Molecular characterization of interactions between the D614G variant of SARS-CoV-2 S-protein and neutralizing antibodies, A computational approach. Infect. Genet Evol. 2021;91:104815. DOI: 10.1016/j.meegid.2021.104815.
7. McSharry B.P., Avdic S. & Slobedman B. Human cytomegalovirus encoded homologs of cytokines, chemokines and their receptors, roles in immunomodulation. Viruses. 2012;4:2448–2470. DOI: 10.3390/v4112448.
8. Lederberg J. Infectious history. Science. 2000;288:287–293.
9. Planas D. et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature. 2021;596:276–280. DOI: 10.1038/s41586-021-03777-9.
10. Shen L. et al. Emerging variants of concern in SARS-CoV-2 membrane protein, a highly conserved target with potential pathological and therapeutic implications. Emerg Microbes Infect. 2021;10:885–893. DOI: 10.1080/22221751.2021.1922097.
11. Perez-Gomez R. The Development of SARS-CoV-2 Variants, The Gene Makes the Disease. J Dev Biol. 2021;9:58. DOI: 10.3390/jdb9040058.
12. Damoiseaux J. et al. Autoantibodies and SARS-CoV2 infection, The spectrum from association to clinical implication, Report of the 15th Dresden Symposium on Autoantibodies. Autoimmun Rev. 2021;21:103012. DOI: j.autrev.2021.103012.
13. Wang Y. et al. Transmission, viral kinetics and clinical characteristics of the emergent SARS-CoV-2 Delta VOC in Guangzhou. China Eclinical Medicine. 2021;40:101129. DOI: 10.1016/j.eclinm.2021.101129.
14. Dessì A., Bosco A., Pintus R., Orrù G. & Fanos V. Fusobacterium nucleatum and alteration of the oral microbiome, from pregnancy to SARS-COV-2 infection. Eur Rev Med Pharmacol Sci. 2021;25:4579–4596. DOI: 10.26355/eurrev_202107_26251.
15. Filomena M. C. et al. Myopalladin knockout mice develop cardiac dilation and show a maladaptive response to mechanical pressure overload. Elife. 2021;24:e58313. DOI: 10.7554/eLife.58313.
16. Massilamany C. et al. Whole genomic sequence analysis of, defining the genetic blueprint of strain NRRL B-14911, an emerging cardiopathogenic microbe. BMC Genomics. 2016;17(Suppl 7):511. DOI: 10.1186/s12864-016-2900-2.
17. Laino M. E. et al. Advanced Imaging Supports the Mechanistic Role of Autoimmunity and Plaque Rupture in COVID-19 Heart Involvement. Clin Rev Allergy Immunol. 2022;28:1–15. DOI: 10.1007/s12016-022-08925-1.
18. Proteomes — Homo sapiens (Human). URL: https //www.uniprot.org/proteomes/UP000005640 Homo sapiens, last change, 03 Sept 2020. (access: 24.04.2024)
19. Proteomes — Severe acute respiratory syndrome coronavirus 2 (2019-nCoV) (SARS-CoV-2). URL: https//www.uniprot.org/proteomes/UP000464024 SARS-COV-2, last change, 20 Aug 2020. (access: 24.04.2024)