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The Relationship between the Glycosilation of the Sars-Cov-2 Spike Protein and ABO System Blood Groups

Leonardo Ferreira Oliveira

ABSTRACT

Throughout history, the ABO system has been used as an element for clinical reasoning to analyze the relationship of different blood groups with different pathologies. There is ample evidence on the association between SARS-CoV-2 infection and polymorphism in the ABO system. Bioinformatics has revolutionized the scientific world, allowing the systematic study of biomolecules. The present work aims to clarify the relationship between the glycosition of the SARS-COV-2 spike protein and blood groups of the ABO system, using bioinformatics tools and systematic literary review. The SARS-CoV-2 spike protein is intensely glycosylated and plays a key role in the success of viral fixation, entry and fusion of the virus membrane into host cells. The N-glycans in this protein are related to the proper folding of proteins and also to the escape of innate and adaptive immune responses. It can be seen that the glycosylation of the spike protein is extremely important for SARS-Cov-2 to perpetuate its cycle and, probably, that is the explanation of the relationship with susceptibility related to groups in the ABO system.

Keywords: ABO. Glycosylation. Spike. SARS- CoV-2.

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SUMMARY

Throughout history, the ABO system has been used as an element for clinical reasoning to analyze the relationship of different blood groups with different pathologies. There is ample evidence on the association between SARS-CoV-2 infection and polymorphism in the ABO system. Bioinformatics has revolutionized the scientific world, allowing the systematic study of biomolecules. The present work aims to clarify the relationship between the glycosition of the SARS-COV-2 spike protein and blood groups of the ABO system, using bioinformatics tools and systematic literary review. The SARS-CoV-2 spike protein is intensely glycosylated and plays a key role in the success of viral fixation, entry and fusion of the virus membrane into host cells. The N-glycans in this protein are related to the proper folding of proteins and also to the escape of innate and adaptive immune responses. It can be seen that the glycosylation of the spike protein is extremely important for SARS-Cov-2 to perpetuate its cycle and, probably, that is the explanation of the relationship with susceptibility related to groups in the ABO system.

Keywords: ABO. Glycosylation. Spike. SARS-CoV-2.

I. INTRODUCTION

Bioinformatics has revolutionised biological and biomedical research as it allows researchers to systematically study genomes, the assemblage of RNA molecules and proteins. The wealth of data generated by genomics, transcriptomics and proteomics has enabled researchers to innovate and advance scientific knowledge [1]. Glycoproteomics is a branch of proteomics that identifies, catalogues and characterises proteins containing carbohydrates as post-translational modifications. Recently assays in glycoproteomics address the separation and enrichment of glycoproteins and glycopeptides, structural and functional analysis of glycoproteins and analysis of protein glycosylation sites [2].

Throughout history the ABO system has been used as an element for clinical reasoning, being employed for decades to analyse the relationship of the different blood groups with bacterial, viral infections [6; 7; 8; 9], caused by protozoa [10; 11; 12] and helminths [13; 14; 15], tumours [16; 17; 18; 19; 20] among others [21; 22].

The rapid global spread of SARS-CoV-2, the causative agent of coronavirus disease 2019 (COVID-19), has culminated in considerable morbidity and mortality, along with social and economic disruption worldwide [23].

Severe acute respiratory syndrome is a highly contagious disease with clinical symptoms of fever, dry cough, fatigue, and shortness of breath. Nucleic acid tests of respiratory tract samples and stool samples are the basis of laboratory confirmation of COVID-19, although serological tests are being used due to improved specificity and sensitivity. The production of IgM antibodies specific for SARS-CoV-2 commonly occurs about 3-5 days after the onset of symptoms, followed by the production of IgM antibodies [24]. The production of IgM antibodies specific for SARS-CoV-2 commonly occurs about 3-5 days after the onset of symptoms, followed by the production of IgG antibodies [24]. The existing evidence on the association between SARS-CoV-2 infection and ABO system polymorphism is preliminary and controversial [25]. However, meta-analysis studies [26; 27; 28; 29] and genome-wide association analysis have been able to elucidate the potential factors involved in the development of Covid-19 [30]. In addition, trials have sought to elucidate the relationship between ABO system antibodies and their influence on the interaction of SARS-CoV-2 and the host [31].

A group of researchers conducting a genetic study found that blood group O was associated with a lower risk of acquiring Covid-19 than non-O blood groups, while blood group A was associated with a higher risk than non-A blood groups. The authors ponder that one of the biological mechanisms justifying these findings relates to the development of neutralizing antibodies against protein-bound N-glycans [30].

Guillon et al. [32] hypothesized that since SARS-CoV replicates in cells that have the ability to synthesize ABO system epitopes, the S protein of virions produced by A or B individuals could be decorated with A or B carbohydrate epitopes, respectively. Thus natural anti-A or anti-B antibodies from individuals of blood groups O, B and A could bind to the S protein and interfere with the interaction with ACE2, thus preventing infection.

Based on the same assumption of the aforementioned authors, the present work aims to clarify the relationship between glycosylation of the spike protein of SARS-COV-2 and blood groups of the ABO system, using bioinformatics tools and systematic literature review.

II. MATERIALS AND METHOD

A bibliographical survey was conducted in PubMed using the descriptors in Health Sciences; ABO Blood Groups System, Coronavirus Infections, Glycosylation and Betacoronavirus, and their respective correlates in English. Articles describing the relationship between SARS-Cov-2 and ABO system blood groups were included, as well as papers referring to the theme of betacoronavirus protein glycosylation.

Free bioinformatics resources available on the internet were used. Two spike proteins, namely P59594 (SARS-Cov) and PoDTC2 (SARS-Cov-2), were selected from the Uniprot website (https://www.uniprot.org/). A three-dimensional structure of the protein sequences was produced using UCSF Chimera software, after previous identification and exclusion of signal peptide and transmembrane domains in TOPCONS website (https://topcons.cbr.su.se/).

The two proteins were also aligned using Uniprot resources, identifying glycosylation sites and similarity patterns between them. The analysis of O and N-glycosylation site prediction was performed in NetOGlyc 4.0 Server (http://www. cbs.dtu.dk/services/NetOGlyc/) and NetNGlyc 1.0 Server (http://www.cbs. dtu.dk/ services/Net NGlyc/), respectively.

III. RESULTS AND DISCUSSIONS

The most significant post-translational modification is glycosylation, which consists of the enzymatic addition of sugars to asparagine residues, called N-glycans, and/or serine and threonine residues, called O-glycans [33]. The heterogeneity related to protein glycosylation is related to the location of one or more sites where glycosylation occurs (macroheterogeneity), as well as due to the great variety and complexity of glycans that can be expressed in a given glycosylation site (microheterogeneity) [34]. Glycosylation can affect how a protein is secreted and packaged, as well as its stability, solubility and conformation, which culminates in biological activity and antigenicity [35].

The set of the great variety of glycans in an organism is called glycomome. Glycans participate in the regulation of cellular and humoral immune responses, including the constitution of MHC antigens and immune cell receptors, participation in endocytosis and the functions of immunoglobulins. In addition, some glycan motifs act as hazard-associated molecular or pathogen-associated molecular patterns patterns. Thus, glycosylation participate in the processes of diapedesis and chemotaxis, pathogen

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recognition, activation of immune cells as well as immunosuppression [33; 36].

The antigens of the ABO system represent a classic example of glycosylated proteins. The antigenicity of this system is attributed to the terminal sugars present in glycoproteins on the surface of blood cells, tissues and in secretions. The variety of phenotypes of the antigens of this system is conferred by the different genes that express glycosyltransferases encoded in the ABO locus that is located on the long arm of chromosome 9 (9q34.2) [37].

H-transferase (FUT1) is responsible for synthesising a structure known as the H antigen by adding a fucose to terminal galactose residues of oligosaccharide precursors. In epithelial tissues and salivary glands, a second fucosyltransferase (FUT2) synthesizes antigen H. In individuals of blood group A, B or AB, antigen H can be targeted by specific glycosyltransferases to form antigens A and B [38].

The glycosyltransferases of the ABO system, belong to the CAZy 6 family and are represented of more homologous group of enzymes that transfer distinct naturally occurring donor substrates, differing from each other by only four amino acids out of 354. Glycosyltransferase A (GTA) is an α -(1 \rightarrow 3)-N-acetylgalactosaminyltransferase (EC 2.4.1.40) transfers GalNAc from UDP-GalNAc to antigen H , producing antigen A. Glycosyl tranferase B (GTB), on the other hand, is an α -(1 \rightarrow 3)-galactosyltransferase (EC 2.4.1.37transfers Gal from UDP-Gal, also to antigen H, producing antigen B [38].

The ABO system antibodies are absent at birth and can be detected after a few months of life. Heteroimmunization is responsible for the appearance of these antibodies, mainly due to contact with microorganisms of the intestinal bacterial flora. These antibodies are potent IgM and/or IgG, capable of agglutinating red blood cells and of activating the complement cascade, causing intravascular hemolysis [39].

Although the mechanism of ABO blood type in COVID-19 infection has not yet been elucidated,

esearch related to other viruses may direct towards clarification. Since SARS-Cov and SARS-Cov-2 have similar nucleic acid sequence and also exhibit the same binding tropism to ACE2, comparing them may advance scientific knowledge [29].

The P59594 protein (FIGURE 1A) originating from SARS-Cov with 1255 amino acid residues and PoDTC2 (FIGURE 1B) protein from SARS-Cov-2 with 1273 amino acid residues, present 207 similar positions, making an identity of 75.881%, both with 22 possible glycosylation sites (FIGURE 2). The analysis performed on glycosylation prediction servers showed agreement with Uniport site alignment with the same amount of N-glycosylation sites (FIGURE 3A and 3B). O-glycosylation prediction showed three probable glycosylation sites for SARS-Cov-2 protein, and one site for SARS-Cov.

Guillon et al, [32] used a cellular model of adhesion to investigate the effect of natural antibodies of the ABO system on the interaction and blockade of SARS-CoV spike protein and angiotensin-converting enzyme 2. For this, an eGFP (green fluorescent protein) labelled spike protein at the C-terminus was expressed in CHO co-transfected with an $\alpha_{1,2}$ -fucosyltransferase and a GTA to co-express the ectodomain of the spike glycoprotein and the A antigen on the cell surface. It was observed that the S/ECA2 protein-dependent adhesion of these cells to a cell line expressing ACE2 was specifically inhibited by monoclonal or natural human anti-A antibodies, indicating that these antibodies can block the interaction between the virus and its receptor, providing protection.

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source: prepared by the author

Figurae 1: Three-dimensional structure of SARS-Cov and SARS-Cov-2 spike proteins

The spike protein of SARS-CoV-2 is highly glycosylated and plays a key role in the successful viral attachment, entry and membrane fusion of the virus to host cells. This protein plays a key role in the host immune response and is therefore the main target of research for vaccine production [40].

The N-glycans in the spike protein are related to proper protein folding as well as initiation by host proteases. In addition, these glycans may protect antigenic sites, preventing recognition by defence cells and antibodies. Thus glycosylation may allow coronavirus to evade innate and adaptive immune responses [41].

P0DTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1	MFVFLVLLPLVSSQCVNLTTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFL MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFL **:**::* *.*. :: * * * * * * *******::****: ******	56 60
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	57 61	PFFSNVTWFHAIHVSGT <mark>N</mark> GTKRFDNPVLPFNDGVYFASTEKSNIIRGWIFGTTLDSKTQS PFYSNVTGFHTINHTFGNPVIPFKDGIYFAATEKSNVVRGWVFGSTMN <mark>N</mark> KSQS **:*** **:::::::::::::::::::::::::::::	116 113
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	117 114	LLIVN <mark>N</mark> ATNVVIKVCEFQFCNDPFLGVYYHKN <mark>N</mark> KSWMESEFRVYSSAN <mark>N</mark> CTFEYVSQPFL VIII <mark>NN</mark> STNVVIRACNFELCDNPFFAVSKPMGTQTHTMIFDNAFNCTFEYISDAFS ::*:**:*****:.*:*:*:*:*:*	176 169
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	177 170	MDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQGFSALEPLVDLPIGINIT LDVSEKSGNFKHLREFVFKNKDGFLYVYKGYQPIDVVRDLPSGFNTLKPIFKLPLGINIT :*:. *.****:******* **:: :*. : **::*****.**.:*::*::*****	236 229
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	237 230	RFQTLLALHRSYLTPGDSSSGWTAGAAAYYVGYLQPRTFLLKYNENGTITDAVDCALDPL NFRAILTAFSPAQDIWGTSAAAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPL .*:::*:	296 283
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	297 284	SETKCTLKSFTVEKGIYQTSNFRVQP <mark>IES</mark> IVRFPNITNLCPFGEVFNATRFASVYAWNRK AELKCSVKSFEIDKGIYQTSNFRVVPSGDVVRFPNITNLCPFGEVFNATKFPSVYAWERK :* **::*** ::*********** *: .:**********	356 343
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	357 344	RISNCVADYSVLYNSASFSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVRQIAPGQTG KISNCVADYSVLYNSTFFSTFKCYGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTG :*************	416 403
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	417 404	KIADYNYKLPDDFTGCVIAWNSNNLDSKVGGNYNYLYRLFRKSNLKPFERDISTEIYQAG VIADYNYKLPDDFMGCVLAWNTRNIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSPD ************************************	476 463
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	477 464	STPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVVLSFELLHAPATVCGPKKSTNLVKN GKPCTP-PALNCYWPLNDYGFYTTTGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKN **:***:*** *.*** *.**************	536 522
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	537 523	KCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSFGGVS QCVNFNFNGLTGTGVLTPSSKRFQPFQQFGRDVSDFTDSVRDPKTSEILDISPCSFGGVS :************************************	596 582
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	597 583	VITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHV VITPGTNASSEVAVLYQDVNCTDVSTAIHADQLTPAWRIYSTGNNVFQTQAGCLIGAEHV *******	656 642
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	657 643	NNSYECDIPIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPT DTSYECDIPIGAGICASYHTVSLLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPT :.************************************	716 698
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	717 699	NFTISVTTEILPVSMTKTSVDCTMYICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDK NFSISITTEVMPVSMAKTSVDCNMYICGDSTECANLLLQYGSFCTQLNRALSGIAAEQDR **:**:***::***::****:****************	776 758
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	777 759	NTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKRSFIEDLLFNKVTLADAGFIKQ NTREVFAQVKQMYKTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAGFMKQ **:********	836 818
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	837 819	YGDCLGDIAARDLICAQKFNGLTVLPPLLTDEMIAQYTSALLAGTITSGWTFGAGAALQI YGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYTAALVSGTATAGWTFGAGAALQI **:**** ******************************	896 878
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	897 879	PFAMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNA PFAMQMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNA ***********************************	956 938
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	957 939	QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAA QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAA	1016 998
P0DTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1017 999	EIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNFT EIRASANLAATKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFT	1076 1058
P0DTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1077 1059	TAPAICHDGKAHFPREGVFVSNGTHWFVTQRNFYEPQIITTDNTFVSGNCDVVIGIVNNT TAPAICHEGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNT ******::**::***	1136 1118
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1137 1119	VYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNES VYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNES	1196 1178
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1197 1179	LIDLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKF LIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCGSCCKF	1256 1238
PODTC2 P59594	SPIKE_SARS2 SPIKE_SARS	1257 1239	DEDDSEPVLKGVKLHYT DEDDSEPVLKGVKLHYT	1273 1255

Source: Adapted by authors

Figure 2: Alignment of spike proteins P59594 and PoDTC2

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Α	SeqName Positio		sitior	n Potential		l Jury agreement	N-Glyc result		
	sp P59594	SPIRE	SARS	29	NYTO	0.7751	(9/9)	+++	
	sp P59594	SPIKE	SARS	65	NVTG	0.8090	(9/9)	+++	
	sp P59594	SPIKE	SARS	73	NHTP	0.4327	(6/9)	1 <u>-</u>	
	en 050504	SPIER	CADC	100	NESO	0 6081	(7/9)		
	ap D50504	CDIPP	CADC	118	MICT	0 4711	14/91		
	ap DE0E04	CDTUP	CADC	110	NCTN	0. 2020	(9/9)		
	sp_P39394	SPIKE	SARS	119	NOTE	0.7039	(9/9)		
	sp_P59594	SPIKE	SARS	150	NCTE	0.5000	(1/9)	+	
	sp_P59594	SPIKE	SARS	221	NITN	0.7517	(9/9)	+++	
	sp_P59594	SPIKE	SARS	269	NGTI	0.6910	(3/3)	++	
	sp_P59594	SPIKE	SARS	318	NITN	0.6414	(9/9)	++	
	sp_P59594	SPIKE	SARS	330	NATK	0.6062	(8/9)	+	
	sp_P59594	SPIKE	SARS	357	NSTF	0.5746	(8/9)	+	
	sp_P59594	SPIKE	SARS	589	NASS	0.5778	(6/9)	+	
	sp_P59594	SPIKE	SARS	602	NCTD	0.6882	(9/9)	++	
	sp_P59594	SPIKE	SARS	691	NNTI	0.4604	(5/9)	-	
	sp P59594	SPIKE	SARS	699	NFSI	0.5357	(7/9)	+	
	sp P59594	SPIKE	SARS	783	NFSQ	0.6348	(9/9)	++	
	sp P59594	SPIKE	SARS	1056	NFTT	0.4342	(5/9)	20	
	SD P59594	SPIKE	SARS	1080	NGTS	0.5806	(7/9)	+	
	SD P59594	SPIKE	SARS	1116	NNTV	0.5106	(5/9)	+	
	sp P59594	SPIRE	SARS	1140	NHTS	0.3739	(9/9)	<u> </u>	
	an DEGEGA	CDTUP	SADS	1155	MASU	0 4001	(8/9)	-	
	SI1 P 19 194	SPIRE.			10.00				
	sp_P59594 sp_P59594	SPIKE	SARS	1176	NESL	0.6796	(9/9)	++	
	sp_P59594 sp_P59594 SeqName	SPIKE	SARS	1176 Pote	NESL mtial	Jury N	(9/9) -Glyc	++	
	sp_P59594 sp_P59594 SeqName	SPIKE	SARS	1176 Pote	NESL mtial	Jury Nagreement re	(9/9) -Glyc esult	++	 - -
	sp_P59594 sp_P59594 SeqName sp_P0DTC2	Posi	SARS ition	1176 1176 Pote	NESL mtial	Jury N- agreement re	(8/9) -Glyc esult (8/9)	++	 - -
	sp_P59594 sp_P59594 	SPIKE Posi SPIKE S	SARS ition SARS2 SARS2	1176 Pote	NESL mtial NLTT NVTW	Jury N- agreement re 0.6606 0.7820	(8/9) (9/9) 	++ +	
	sp_P59594 sp_P59594 	SPIKE Posi SPIKE S SPIKE S SPIKE S	SARS ition SARS2 SARS2 SARS2	1133 1176 Pote	NESL mtial NLTT NVTW NGTK	Jury N- agreement re 0.6606 0.7820 0.7192	(8/9) 	++	 - -
	sp_P59594 sp_P59594 SeqName sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2	SPIKE Posi SPIKE S SPIKE S SPIKE S SPIKE S	SARS ition SARS2 SARS2 SARS2 SARS2 SARS2	1135 1176 Pote 17 61 74 122	NESL ential NLTT NVTW NGTK NATN	Jury N- agreement re 0.66006 0.7820 0.7192 0.6781	(8/9) (9/9) 	++ + ++++ +++ +	 - -
	sp_P59594 sp_P59594 SeqName sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2	SPIKE Posi SPIKE S SPIKE S SPIKE S SPIKE S	SARS ition SARS2 SARS2 SARS2 SARS2 SARS2 SARS2	1135 1176 Pote 17 61 74 122 149	NESL ential NLTT NVTW NGTK NATN NKSW	Jury N- agreement re 0.6606 0.7820 0.7192 0.6781 0.6318	(8/9) (9/9) 	++ +	
	sp_P59594 sp_P59594 SeqName sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2 sp_P0DTC2	SPIKE Posi SPIKE S SPIKE S SPIKE S SPIKE S SPIKE S	SARS SARS ition SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2	1133 1176 Pote 17 61 74 122 149 165	NESL ential NLTT NVTW NGTK NATN NKSW NCTF	Jury N- agreement re 0.6606 0.7820 0.7192 0.6781 0.6318 0.6220	(8/9) (9/9) -Glyc esult (8/9) (9/9) (9/9) (8/9) (7/9) (8/9)	*** *** ** * *	
	sp_P59594 sp_P59594 	SPIKE Posi SPIKE S SPIKE S SPIKE S SPIKE S SPIKE S SPIKE S	SARS SARS ition SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2	1133 1176 Pote 17 61 74 122 149 165 234	NESL mtial NLTT NVTW NGTK NATN NKSW NCTF NITR	Jury N- agreement re 0.6606 0.7820 0.7192 0.6781 0.6318 0.6220 0.7613	(8/9) -Glyc esult (8/9) (9/9) (9/9) (8/9) (7/9) (8/9) (9/9)	++ + +++ +++ + + + +	-
	sp_P59594 sp_P59594 	SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE SPIKE	SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2 SARS2	1133 1176 Pote 17 61 74 122 149 165 234 282	NASV NESL Initial NUTT NVTW NGTK NATW NKSW NCTP NITR NGTI	Jury N- agreement re 0.6606 0.7820 0.7192 0.6781 0.6318 0.6220 0.7613 0.7378	(8/9) (9/9) -Glyc esult (8/9) (9/9) (9/9) (8/9) (7/9) (8/9) (9/9) (9/9)	++ + + + + + + + + + + + + + + +	-
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Source: Adapted by authors

Figure 3a and 3b: Prediction of N-glycosylation in spike proteins P59594 and PoDTC2

According to Padhi et al. [42], when SARS-CoV-2 multiplies in host cells with its subsequent release to perpetuate the cycle, thus infecting new hosts, its proteins, especially spike, would have A and/or B antigens, depending on the blood group. Thus, as individuals of blood group O possess antibodies against antigens A and B, they would be able to protect, to a certain extent, from SARS-CoV-2 carrying A and/or B antigens, explaining the lower number of infected individuals in this group. Gérard et al. [43] postulate that group O as it predominantly presents anti-B and anti-A immunoglobulin of the IgG isotype, differently from groups A, B and AB where the IgM isotype predominates, would explain the fact that group O presents lower susceptibility when compared with the other non-A groups. The authors suggest that the presence of anti-A antibodies in the serum and more specifically of the IgG class should be considered a more significant factor than the blood group itself with regard to the relationship

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between COVID susceptibility to ABO blood groups.

IV. CONCLUSIONS

It can be inferred that glycosylation of the spike protein is extremely important for SARS-Cov-2 to evade immune responses and that it is probably the explanation for the relationship with susceptibility related to the ABO system groups. It is clear the importance of glycoproteomics and immunology knowledge in the search for both a vaccine and diagnostic tools, as well as the use of bioinformatics tools in the advancement of medical and biomedical sciences.

While the emergence of a new coronavirus puts the world under great pressure, the clarification of glycoproteins in the viral envelope opens up a wide range of possibilities for the application of lectins and glycosylation inhibitors that may participate in treatment and/or diagnosis.

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