COVID-19: Attacks Immune Cells and Interferences With Antigen Presentation Through MHC-Like Decoy System

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Summary: The high mortality of coronavirus disease 2019 is related to poor antigen presentation and lymphopenia. Cytomegalovirus and the herpes family encode a series of major histocompatibility complex (MHC)-like molecules required for targeted immune responses to achieve immune escape. In this present study, domain search results showed that many proteins of the severe acute respiratory syndrome coronavirus 2 virus had MHC-like domains, which were similar to decoys for the human immune system. MHC-like structures could bind to MHC receptors of immune cells (such as CD4+ T-cell, CD8+ T-cell, and natural killer-cell), interfering with antigen presentation. Then the oxygen free radicals generated by E protein destroyed immune cells after MHC-like of S protein could bind to them. Mutations in the MHC-like region of the viral proteins such as S promoted weaker immune resistance and more robust transmission. S 127-194 were the primary reason for the robust transmission of delta variants. The S 144-162 regulated the formation of S trimer. The mutations of RdRP: G671S and N: D63G of delta variant caused high viral load. S 62-80 of alpha, beta, lambda variants were the important factor for fast-spreading. S 616-676 and 1014-1114 were causes of high mortality for gamma variants infections. These sites were in the MHC-like structure regions.

Key Words: CD4⁺ T-cell, CD8⁺ T-cell, NK-cell, lymphopenia, delta variant, neutralizing antibody, N-terminal supersite

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BACKGROUND

The lymphopenia of coronavirus disease 2019 (COVID-19) patients includes CD4⁺ T cells, CD8⁺ T cells, B cells, and natural killer (NK) cells, with the damage of CD8⁺ T cells being more significant.^{1,2} No obvious virus infection is detected in lymphocytes and mesenchymal cell.³ Lymphopenia at the initial appearance of COVID-19 is associated with poor prognosis.⁴ Lymphopenia and its severity are reliable predictors of the clinical outcome of COVID-19, including mortality, intensive care needs, and oxygen requirements.⁴ Besides, the high fatality rate of COVID-19 is related to the poor performance of major histocompatibility complex (MHC) II and the low coverage

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of MHC II.⁵ The quality of MHC II presented by T cells is an essential prerequisite for T-cell-dependent antibody production. The binding capacity of MHC I epitope load and severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) peptide affects the immunity of T cells to infection.⁶ Therefore, MHC presentation is closely related to lymphopenia of COVID-19.

Lymphopenia, cell degeneration, necrosis, and atrophy are found in SARS and COVID-19 patients.7 The sort of lymphopenia and apoptosis between SARs and COVID-19 patients appears different. Namely, lymphopenia in SARs patients precedes apoptosis, while apoptosis in COVID-19 patients precedes lymphopenia.8 The frequency and activation of SARS-COV-2 specific CD8+ T cells increase during severe illness, highlighting differences in T-cell responses associated with disease progression.⁹ The number of regulatory T cells (Treg) has nothing to do with the severity of the disease, suggesting that T-cell exhaustion occurs in a process independent of Treg.¹⁰ SARS-COV-2 generates reactive oxygen species (ROS) through the combination of E protein and heme,¹¹ in which hydroxyl free radicals can directly destroy the cell membrane and cause damage to immune cells. Immune cells would be directly attacked along the route of antigen recognition and antigen presentation. So, CD4⁺ T cells, CD8⁺ T cells, and NK cells are most likely to be destroy and apoptosis in this link of binding to MHC molecules.

Mononuclear macrophages ingest antigens and process them into antigen peptides. Then antigen peptides are combined with surface MHC molecules and are expressed on the cell surface, effectively presenting antigens to helper T lymphocytes. B lymphocytes also have a similar antigen presentation effect. T cells combine with MHC II/antigen to activate B cells. While the BCR of the memory B-cell binds to a specific antigen, the antigen is endocytosed by the B-cell. After these antigens are cut into fragments, they return to the cell membrane in a state combined with MHC molecules.¹² T cells express CD4 or CD8 co-receptors. They recognize non-polymorphic regions of MHC protein on target cells and can bind to partial MHC protein regions.¹³ Helper T cells express CD4 and recognize MHC class II proteins, while cytotoxic T cells express CD8 and recognize MHC class I proteins.¹³ NK cells express inhibitory receptors (KIR) of MHC class I molecules. These inhibitory receptors include the human KIR [killer cell immunoglobulin (Ig)-like receptor].14 Another function of NK cells is recognizing and eliminating cells that cannot express their MHC class I molecules.¹⁵ It is interesting to note that, individuals with specific MHC alleles are less susceptible to severe forms of malaria.¹³ It means that the combination of immune cells and MHC is closely related to the susceptibility of certain diseases.

The MHC class II transactivator CIITA induces cell resistance to the Ebola virus and SARS-like coronavirus.¹⁶ However, the apparent CD4 conserved residues at the

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receptor-binding domain (RBD)-S1 site of SARS-COV-2 interrupt the CD4-MHC-II interaction for adaptive immune activation.¹⁷ The immunity of CD8⁺ T cells to SARS-COV-2 is related to the severity of COVID-19 and virus control. SARS-COV-2 evades CD8⁺ T-cell surveillance by mutation of the MHC I restricted epitope of CD8⁺ T cells.¹⁸ Mutant peptides exhibit reduced or abolished MHC I binding, which is related to the loss of recognition and functional response of CD8⁺ T cells isolated from human leukocyte antigen (HLA)-matched COVID-19 patients. However, the proportion of interferon-y-producing cells in SARS-COV-2 specific CD8⁺ T cells expressing PD-1 is higher than that of PD-1 cells in multimer⁺ cells. The SARS-COV-2 specific CD8⁺ T cells expressing PD-1 are not exhausted and function normally.¹⁹ It meant SARS-COV-2 had evolved an MHC-like structure that could bind to the MHC receptor of immune cells. Immune cells that could not attach to the MHC-like form of the virus had survived.

Some viruses have acquired inhibitors that target the MHC class I antigen presentation pathway.²⁰ The cytomegalovirus (CMV) and herpes family encode a series of key molecules required for a targeted immune response.²¹ All aspects of acute and chronic CMV disease may be controlled by antibodies, NK, and other cells of the innate immune system, as well as CD8⁺ T and CD4⁺ T-cell.²² About half of the identified genes in CMV²³ and beta herpes virus²⁴ have HCMV homologs.²² The m144²⁵ and m145 family of CMV (m17, m145-m158),²² m157,²⁶ UL37²⁷ are all MHC I-like molecules. The Ly49H NK-cell activation receptor recognizes m157.²⁸ Ly49 receptor binds m157 glycoprotein encoded by mouse CMV (MCMV).²¹ Human CMV(HCMV) UL18 binds inhibitory leukocyte immunoglobulin-like receptor R-1.²⁹ Human CMV express and distribute a complete library of immune evasion factors for a single MHC class I target.³⁰ Human CMV encodes glycoproteins homologous to MHC class I.³¹ The MHC class I homologs encoded by human CMV binds to endogenous peptides.³²

Many viruses have evolved surprising strategies to interfere with the MHC class I antigen presentation pathway.³³ After the initial NK response,³⁴ the host will produce adaptive $CD8^+$ T³⁵ and $CD4^+$ T³⁶ cellular responses. Viral MHC class I molecules allow evasion of NK-cell effector responses in the body²⁶ and contribute to immune evasion.²² Many studies have shown that MHC class I virus proteins interfere with infected cells recognizing, antigen processing, and presentation.²² The specific recognition of MHC by inhibitory KIR provides excellent protection against a decoy molecule of virus evolution.³⁷ The diversity of the receptor system may be the result of this specific interaction between MHC and KIR molecules. However, NK cells in severely ill patients with COVID-19 are severely depleted. The protective function of inhibitory KIR shows signs of failure. It shows that some regions of human MHC have an irreplaceable role. The MHC-like structures of the virus were precisely in these areas. If a mutation site was in the MHC-like domain, the mutation enhanced the MHC decoy function. In other words, the human immune system hard to neutralize these MHC-like sites by producing antibodies. Otherwise, the antibodies could also bind to MHC proteins. Then the antibodies would affect normal MHC antigen presentation function, causing autoimmune diseases.

The N-terminal domain (NTD) of the S protein and the S2 membrane fusion region may be MHC-like structural sites for the challenging battle between the immune system

and the virus. Most antibodies that recognize the SARS-CoV-2 S protein are directed against the RBD.³⁸ Analysis of the human monoclonal antibody (mAb) library in the sera of convalescent patients showed that most anti-S antibodies recognize RBD, and a small portion of antibodies recognizes NTD.³⁹ Some NTD-targeted mAbs can effectively inhibit SARS-CoV-2 infection in vitro; in vivo, the immune system uses neutralization and Fc-mediated effector function activities.⁴⁰ Fc receptor cells generally include B cells, killer cells, and macrophages. Compared with neutralizing RBD targeting antibodies that recognize multiple nonoverlapping epitopes, effective NTD targeting neutralizing antibodies appear to target a single supersite:⁴¹ N17, N74, N122, and N149. However, popular variants will partially or completely escape the neutralization mediated by human mAbs targeting the antigen supersite (site i).³⁹ The variants include B.1.1.7, B. 1.35, and P.1 pedigree. It is difficult for immune system antibodies to neutralize part of the mutation sites in the NTD and the fusion region of the S2 membrane.

In this present study, we used the domain search method to find that many proteins of the SARS-COV-2 virus have MHC-like structures. It indicates that SARS-COV-2 interferes with antigen presentation and attacks immune cells through the MHC-like systems. The SARS-COV-2 virus protein with MHC-like forms could interfere with the antigen presentation response by binding to the MHC receptor of immune cells. The SARS-COV-2 virus employees the MHClike structures of the S protein as bait. After the SARS-COV-2 S protein binds to CD4⁺ T, CD8⁺ T, and NK cells, the oxygen free radicals (ROS) generated by the E protein destroys these immune cells, resulting in a decrease in the number of lymphocytes. Through the analysis of the MHClike enhanced regions of existing popular variants, we found that: 127-194 and 144-162 areas of S MHC-like of delta variants were in the NTD; the 62-80 regions of S MHC-like of alpha, beta, lambda variants were also in the NTD; the 616-676 and 1014-1114 regions of S MHC-like of gamma variants were in the S2 membrane fusion region.

METHODS

Data Set

The Sequences of SARS-COV-2 Proteins

The SARS-COV-2 protein sequences came from the NCBI database. Including: S, E, N, M, ORF3a, ORF8, ORF7a, ORF7b, ORF6, ORF10, ORF1ab.

MHC-Related Sequence

We downloaded 18,112 protein sequences of MHCrelated from the UniProt data set and searched keyword was "MHC." The MHC-related sequences were compared with the viral proteins to search for the conserved domains.

Localized MEME Tool to Scan for Conserved Domains

The analysis steps are listed as follows:

- (1) Download MEME from the official website and subsequently install in the virtual machine Ubuntu operating system. The virtual machine was VM 15.2.
- (2) Download the SARS-COV-2 protein sequence from NCBI official website.
- (3) Download the FASTA format sequence of MHCrelated from Uniprot official website, respectively. The search keyword was "MHC."

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- (4) For each sequence in all MHC-related protein, paired with each SARS-COV-2 protein sequence to generate fasta format files for MEME analysis.
- (5) For the files generated in Step 4, a batch of 50,000 was used to create several batches. It was considered as the limited space of the virtual Ubuntu system.
- (6) In Ubuntu, searched the conserved domains (E-value < = 0.05) of SARS-COV-2 protein and MHC-related with MEME tools in batches.
- (7) Collected the result files of conserved domains. Find the domain name corresponding to the motif from the UniProt database.
- (8) We analyzed the domains' activity of the each SARS-COV-2 protein according to the characteristics of the MHC-related protein domains.

RESULTS

We downloaded MHC-related sequences from the UniProt database. Then compared these sequences with the SARS-COV-2 protein sequences to find the domains related to MHC function. We merged the motif sequences according to the domains of the search results. Both MHC 1 and MHC 2 structures include Ig-like and MHC domains. If a viral protein could bind to the antigen peptide like the MHC protein, the viral protein would have both domains.

SARS-COV-2 Virus Proteins Had Ig-Like Domains

Ig-like domains are involved in multiple functions, including cell-to-cell recognition, cell surface receptors, muscle structure, and the immune system. We first listed Ig-like domains of viral proteins in Table 1. Table 1 shows the structural proteins (S, E, N, M) and nonstructural proteins (ORF3a, ORF6, ORF7a, ORF7b, ORF8, ORF10, ORF1ab) of SARS-COV-2 all have Ig-like domains. Ig-like (IPR032165) is a domain composed of ~100 residues. Smaller domains (74-90 residues) are observed in several Ig-related molecules (CD2, CD4). The Ig-like motifs of ORF10, E, some subprotein of ORF1ab are the short. ORF7a Ig-like A, ORF8 Ig-like A, ORF3a Ig-like C, N Ig-like B and C, M Ig-like A and C, S Iglike B and H, 3'-to-5' exonuclease C, 3'-to-5' exonuclease C, helicase B motifs are longer. The Ig-like structures may help the receptor of CD4+ T, CD8+ T, and NK-cell recognize the MHC-like area of the viral proteins.

SARS-COV-2 Virus Proteins had MHC Domains

We listed MHC-like domains of viral proteins in Table 2. Table 2 shows that the structural proteins (S, E, N, M) and nonstructural proteins (ORF3a, ORF6, ORF7a, ORF7b, ORF8, ORF10, ORF1ab) of SARS-COV-2 have MHC_Ilike_Ag-recog domains. Many proteins have the MHC_II_alpha and MHC_II_beta domains. N, ORF10, ORF3a, 2'-Oribose methyltransferase, nsp10, nsp6, S and have MHC2interact domains. N, ORF10, ORF3a, ORF8, ORF7b, 2'-O-ribose methyltransferase, nsp6, and S have MHCassoc_trimer domain. ORF10, ORF3a, 3'-to-5' exonuclease, nsp4 has MHC_I_2 domain. S has the MHC_I_C domain.

We downloaded the functional descriptions of the relevant domains from the InterPro database.

The members of MHC_I_2 (PF14586) are called retinoic acid-inducible proteins. They are ligands that activate the immune receptor NKG2D. NKG2D is widely expressed on NK cells, T cells, and macrophages. MHC_I_C (PF06623) represents the C-terminal region of MHC class I antigen. MHC_I-like_Ag-recog (IPR011161) is an MHC class I antigen recognition sample. Class I MHC glycoproteins are expressed on the surface of all somatic nucleated cells, except neurons. MHC class I receptors present peptide antigens synthesized in the cytoplasm, including self-peptides (offered for self-tolerance) and foreign peptides (such as viral proteins). These antigens are produced by degraded protein fragments transported by the TAP protein (antigenic peptide transporter) to the endoplasmic reticulum, where they can bind to MHC I molecules and then transport them to the cell surface through the Golgi apparatus. MHC class I receptors display antigens recognized by cytotoxic T cells that can destroy virus-infected or malignant (self-peptide excess) cells. CD8⁺ T toxic cells and NK cells can recognize class I MHC proteins.

MHC_II_alpha (SM00920) is the alpha domain of class II histocompatibility antigen. MHC_II_beta (SM00921) is the beta domain of class II histocompatibility antigen. Class II MHC glycoproteins are expressed on the surface of antigen-presenting cells, including macrophages, dendritic cells, and B cells. MHC II protein presents extracellular peptide antigens derived from foreign substances such as bacteria. Proteins from pathogens are degraded into peptide fragments within the antigen-presenting cells. These fragments are sequestered into endosomes to bind to MHC class II proteins before being transported to the cell surface. MHC class II receptors display antigens for recognition by helper T cells and Inflammatory T cells. CD4⁺T helper cells recognize MHC class II proteins.

MHC2-interact (PF09307) is the interaction domain of class II invariant chain-related peptides and MHC2. Members of this family are found in class II invariant chainrelated peptides. They are required for binding to the class II MHC in the MHC class II processing pathway. MHCassoc_trimer (PF08831) is an invariant chain trimerization domain related to class II MHC. The folding and positioning of MHC class II heterodimers require class II-related consistent chain peptides. This domain participates in the trimerization of the ectoderm and interferes with DM/class II binding. The trimeric protein forms a cylindrical shape, which is considered necessary for the interaction between the invariant and class II molecules.

We noticed that S protein could form a trimer structure and had three MHCassoc_trimer domains: MHCassoc_ trimer A, B, and C. MHCassoc_trimer A is in S1 protein, but MHCassoc_trimer B and C in S2 protein. It represents that MHCassoc_trimer plays an important role in the formation of S protein trimer.

MHC-like Structures Had a Decoy Function Against the Immune System

Previous analysis shows that structural proteins and nonstructural proteins can bind to T (CD4⁺ T and CD8⁺ T) and NK immune cells through MHC-like structures. The binding prevented the MHC receptors of immune cells from securing to MHC, causing interference in antigen presentation. In addition, E protein generates oxygen free radicals (ROS) after attaching to heme, and the hydroxyl free radicals directly damaged cell membranes.¹¹ After CD4⁺ T, CD8⁺ T, and NK cells were bound to the MHC-like structure of S protein, the hydroxyl free radicals generated by E protein destroyed these immune cell membranes. It caused immune cells to die because of oxidative stress. For these two reasons, the MHC-like structure of the SARS-COV-2 virus protein had a decoy function against immune cells.

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Protein	Alias	Motif	Start	End
5	Α	WFHAIH	64	69
	В	KVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEY	129	170
	С	DCTMYIC	737	743
	D	MQMAYR	900	905
	Е	YHLMSFPQSAPHG	1047	1059
	F	HVTYVPAQEKNFTTAPAICHDGKAHFPRE	1064	1092
	G	THWFVTQRNFYEPQI	1100	1114
	Н	DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKGCCSCGSCCKFDEDDSEPVLKGVKLHY	1199	1272
E	Α	AILTALRLCAYCCNIVNVSLVKPSFYVYSRVKNLNSSRVPD	32	72
M	Α	WICLLQFAYANRNRFLYIIKLIFLWLLWPVTLACFVLAAVYRINWITGGIAIAMACLV	31	88
	В	MWSFNPE	109	115
	С	HHLGRCDIKDLPKEITVATSRTLSYYKLGASQRVAGDSGFAAYSRYRIGNYKLNTDHSSSSDNIA	154	218
N	Α	QGLPNNTASWFTALTQHGKED	43	63
	В	DQIGYYRRATRRIRGGDGKMKDLSPRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHIG	82	147
	С	LIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGTW	291	330
	D	FKDQVILLNKHIDAYKTFPPTE	346	367
ORF3a	Α	MDLFMR	1	6
	В	ASKIITLKKRWQ	59	70
	С	YLYALVYFLQSINFVRIIMRLWLCWKCRSKNPLLYDANYFLCWHTNCYDYCIPYNS	107	162
	D	EHDYQIGGYTEKWESGVKDCVVLHSYFTSDYYQ	181	213
	E	HVTFFIYNKIVDEPEEHVQIHTIDGSSGVVNPVMEPIYD	227	265
ORF6	A	MFHLVDFQVTIAEILLIIMRTFKVSIWNLDYIINLIIKNLSKSLTENKYSQLDEEQPMEID	1	61
ORF7a	А	MKIILFLALITLATCELYHYQECVRGTTVLLKEPCSSGTYEGNSPFHPLADNKFALTCFSTQFAFACPDGVKHVYQL- RARSVSPKLFIRQEEVQELYSPIFLIVAAIVFITLCFTL	1	116
ORF7b	Α	MIELSLIDFYLCFLAFLLFLVLIMLIIFWFSLELQDHNETCHA	1	43
ORF8	А	MKFLVFLGIITTVAAFHQECSLQSCTQHQPYVVDDPCPIHFYSKWYIRVGARKSAPLIELCVDEAGSKSPIQYI- DIGNYTVSCLPFTINCQEPKLGSLVVRCSFYEDFLEYHDVRV	1	116
ORF10	Α	MGYINVFAFPFTIYSLLLCRMNSRNYIAQVDVVNFNLT	1	38
nsp2	Α	IDTKRGVYCCREHEHEIAWYTERSEKSYELQTPF	42	75
	В	CDHCGETSWQTGDFVKATCE	143	162
1sp3	Α	SHMYCSFY	100	107
	В	EDDYQGKPLEFGATSAALQPEEEQEEDW	134	161
	С	SEYTGNYQCGHYKHITSKE	1007	1025
	D	HKPIVWH	1169	1175
	Е	HFISNSWLMWLIINLVQM	1539	1556
	F	YYVWKSYVHVVDGCNSSTCMMCYKRNRATRVE	1573	1604
	G	SHNIALIWNVKDFMSLSEQLRKQIRSAAKKNNLPF	1888	1922
1sp4	Α	MRFRRAFGEYSH	302	313
	В	FLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRRV	359	402
nsp6	Α	YFNMVYMPASWVMRIMTWLDM	80	100
nsp10	Α	SCCLYCRCHIDHPNPKGFCDLKGKYVQIPTTC	72	103
	В	CTVCGMWKGYGCSCDQ	117	132
RNA-dependent RNA polymerase	Α	RYFKYWDQTYHPNCVNCLDDRCI	285	307
	В	FYGGWHNMLKTVYSDVENPHLMGWDYPKCDRAMPNMLRIM	594	633
	С	SRYWEPEFYEAMYTPH	913	928

173 191 154 168 48 88 48 88 140 151 140 151 223 300 485 500 488 516 468 516

2'-O-ribose methyltransferase	A	EHSWNADLYKLMGHFAWWT	173
3C-like proteinase	V	YDCVSFCYMHHMELP	154
3'-to-5' exonuclease	A	DMTYRLISMMGFKMNYQVNGYPNMFITREAIRHVRAWIG	48
	В	PPPGDQFKHLIP	140
	U	TYACWHHSIGFDYVYNPFMIDVQQWGFTGNLQSNHDLYCQVHGNAHVASCDAIMTRCLAVHECFVKRVDWTIEYPIIG	223
	D	RHHANEYRLYLDAYNM	485
helicase	A	MPLSAPTLVPQEHYVRITG	233
	в	SAQCFKMFYKGVITHDVSSAINRPQIGVVREFLTRNPAWRKAVFISPYN	468
Ig indicates immunoglobulin; SAR:	-COV-2	, severe acute respiratory syndrome coronavirus 2.	

We noticed that N protein could form a multimer, S protein could form a trimer structure, and E could form a pentameric channel structure. The ORF3a protein and ORF8 protein can form a dimer structure, respectively. The dimer of ORF3a protein (or ORF8 protein) has a groove structure. The Ig-like sites of the ORF3a protein do not fully overlap with the MHC-like areas (Tables 1, 2). However, Table 2 shows that the MHC II and MHC I of ORF3a are located at the "CWKCR" heme-binding area⁴² and upstream and downstream. But the sites of MHC structures are not near the groove structure on the ORF3a crystal structure view (PDBID: 6xdc). Therefore, ORF3a is unlikely to have the ability to bind antigen peptides.

The Ig-like structure of the transmembrane protein ORF8 overlaps with the MHC-like system. The dimer of ORF8 has no rod-like structure. Table 2 and the crystal structure view of ORF8 (PDBID: 7jtl) show that the MHC II and MHC I structures of ORF8 include sites near the groove structure. Therefore, ORF8 may trapp antigen peptides through the MHC structure and interfering with antigen presentation. Besides, ORF8 captures MHC-1 and reroutes to autophagosomes for degradation.43 Table 2 indicates that the MHC I-like domain of ORF8 is MHC_Ilike_Ag-recog. ORF8 also has the MHCassoc_trimer domain. The MHC II-like domain of ORF8 overlaps with the MHC_I-like_Ag-recog and MHCassoc_trimer structures. So ORF8 may trap MHC I by MHC_I-like_Ag-recog and MHCassoc_trimer domains. Therefore, the MHC-like system of ORF8 has a decoy function for MHC I or antigen peptides.

MHC-like Enhanced Regions of S Protein Mutation

If the S mutation site was in the MHC-like domain, the mutation enhanced the MHC decoy function. Then the human immune system hard to neutralize these MHC-like sites by producing antibodies. Otherwise, it would affect the normal MHC antigen presentation function by combing MHC and the antibodies. On the basis of this principle, we analyzed several significant variants that were now popular to determine the MHC-like enhanced region of the S protein.

SARS-COV-2 Delta Variant

The B.1.617.2/Delta variant is highly confluent, especially in infected hamsters more pathogenic than the prototype SARS-COV-2.⁴⁴ The virus is more infectious and directly reduces the efficacy of antibodies produced by infection and vaccines. It is the most prevalent and difficult mutant virus strain in the world.

B.1.617.2/Delta variant mutation sites include:⁴⁵ T19R, G142D, E156G, F157 Δ , R158 Δ , L452R, T478K, D614G, P681R, D950N. Table 3 shows that G142D, E156G, F157 Δ , and R158 Δ are all in the MHC_II_alpha A, MHC_II_beta B, MHC_I-like_Ag-recog B domains. Both G142D and E156G are in the MHC_I_2 A domain. E156G, F157 Δ , and R158 Δ are all located in the MHC-soc_trimer A domain. Other mutation sites are not in the MHC-like domain. These four MHC-like domains are highly overlapping. Combining these four MHC-like domain sites, the MHC-like enhanced distribution area of B.1.617.2/Delta variant S protein is 127–194. It is in the NTD (14–305 residues, the S1 protein region).⁴⁶ Among them, MHCassoc_trimer (144–162) plays an essential role in forming S trimer. The MHC-like enhanced distribution area of the S protein

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ABLE 2	MHC domains'	motifs of SARS-COV-2 virus proteins
	wine domains	

Protein	Domain	Alias	Motif	Start	End
S	MHC_I_2	А	CEFQFCNDPFLGVYYHKNNKSWMESE	131	156
		В	WPWYIW	1212	1217
	MHC_I_C	А	KWPWYIWLGFIAGLIAIVMVTIMLCCM	1211	1237
	MHC II alpha	А	CEFOFCNDPFLGVYYHKNNKSWMESEFRVYSS	131	162
		B	OIPFAMOMAYR	895	905
		Č	L GK YFOYIK WPWYIWI GFIAGI IAIVMVTIMI CCMTSCCSC	1203	1243
	MHC II beta	~	WEHAILWSCHNGTWEED	64	1245
	MIIC_II_Octa	л р		127	170
		В	VIK VCEFQFCNDPFLGVYYHKNNKSWMESEFKVYSSANNCIFEYVSQPFLMD	127	1/8
		C	FAMQMAYKFN	898	907
		D	KMSECV	1028	1033
		E	YVPAQEKNFTTAPAICHDGKAHFPREGVFVSNGTHWFVTQR	1067	1107
		F	DLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCSCLKG	1199	1264
			VTWEIA AH	(2)	(0)
	MHC_1-like_Ag-recog	A		62	69
		в	VIKVCEFQFCNDPFLGVYYHKNNKSWMESEFRVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVF	127	194
		С	RFASVYAWNRKRISNCVADYSVLYNSASFSTFKCYGV	346	382
		D	SNKKFLPFQQFGRDIADTTDAVRDPQTLE	555	583
		E	NCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNSYECDIPIGAGICASYQT	616	676
		F	IPFAMQMAYR	896	905
		G	RAAEIRASANLAATKMSECVLGOSKRVDFCGKGYHLMSFPOSAPHGVV	1014	1114
			FLHVTYVPAOEKNFTTAPAICHDGKAHFPREGVFVSNGTHWFVTORNFYEPOI		
		н	OPELDSEK FELDKY	1142	1155
		T	ESEIDI OEL GEVEOVIEWDWVIWI GEIAGI IAIVMVTIMI COMTSCOSOL EGOCOCOSOCE EDEDDSEDVI EGVEL HVT	1105	1273
	MUC2 internet	1	ESTIDEVELOR TEQTIX WI WITWEDT AGEIATVM V HWIECCWITSCESCERGCESCOSCERT DEDDSET VEROVREITT I	1078	12/3
	MHC2-Interact	A	AFAICHDONANFFRE	1078	1092
		В	WPW YIW	1212	1217
		С	IVMVIIMLCCMTSCCSCLKGCC	1227	1248
	MHCassoc_trimer	A	YYHKNNKSWMESEFRVYSS	144	162
		В	AHFPREGVFVSNGTHW	1087	1102
		С	ELGKYEQYIKWPWYIW	1202	1217
E	MHC_II_alpha	Α	TLAILTALRLCAYCCNIVNVSLVKPSFYVYSRVKNLN	30	66
	MHC II beta	А	FVVFLLVTLAILTALRLCAYCCNIVNVSLVKPSFYVYSRVKNLNSSRVPD	23	72
	MHC I-like Ag-recog	A	ALRI CAYCCNI	36	46
	MHCassoc trimer	A .		40	16
м	MHC II alpha	^		159	167
111	MHC_H_apita	A		138	107
	MHC_II_beta	A	EELKKLLEGWN Charles Herry	11	21
		В	SMWSFNPE1N	108	11/
		С	HHLGRCDIKDLPKETIVATSRTLSYYKLGASQRVAGDSGFAAYSRYRIGNYKLNTDHSSSSDN	154	216
	MHC_I-like_Ag-recog	A	GHHLGRCDIKD	153	163
N	MHC_II_alpha	Α	DQIGYYRRATRRIRGGDGKMKDLSPRWYFYYLGTGPEAGLPYGANKDGIIWVATEGALNTPKDHI	82	146
		В	TDYKHWPQIAQFAPSASAFFGMSRIGMEVT	296	325
	MHC_II_beta	Α	SWFTALTQHGKEDLKFPRGQGVPIN	51	75
		В	QIGYYRRATRRIRGGDGKMKDLSPRWYFYYLGTGPEA	83	158
			GLPYGANKDGIIWVATEGALNTPKDHIGTRNPANNAAIV		
		С	EQTQGNFGDQELIRQGTDYKHWPQIAQFAPSASAFFGMSRIGMEVTPSGT	280	369
			WLTYTGAIKLDDKDPNFKDQVILLNKHIDAYKTFPPTEPK		
	MHC_I-like_Ag-recog	Α	RRPQGLPNNTASWFTALTQHGKEDL	40	64
		В	DDQIGYYRRATRRIRGGDGKMKDLSPRWYFYYLGTGPEAGLPYGA	81	172
		C	NKDGIIWVATEGALNTPKDHIGTRNPANNAAIVLQLPQGTTLPKGFY	201	271
		C	LIKUU I DI KUUNUKIA ALAANA ALAANA YTGAIKI DDK DPNFK DOVILI NK HIDA YK TFPPTFPK K D	291	3/1
	MHC2-interact	А	RWYFYYI	107	113
	MHCassoe trimer	A	WYEVVI	107	113
OP E2a	MHC 1.2	A .		110	113
UKF3a	MIIC_I_2	A	NEY KRIWIKUW LOW DIN MY CHWY CDREWNIDD DYD ANWEL CHWITNIGYDY CIDYAU	119	151
	MHC II alpha	A	KHMREWEEWKEENKNPLEYDANYELCWHENCYDYCTPYN	122	161

MRC Jelic Agency B MRC Jel		MHC_II_beta	A	MDLFMR	1	6	1
NIR., Jail., J			В	NFVRIMKLWLCWKCKSKNPLLYDANYFLCWHINCYDYCIP	119	159	nn
0 0		MHC_I-like_Ag-recog	A	INF V KIIMKL WLUWKUKSKNPLL Y DAN Y FLUWH I NUYDYUPY VNIK IVDEDEELIVOILI	118	247	ür
NHC-lates: NHC-lates: 114 CM 114 CM <td< td=""><td></td><td></td><td>Б</td><td></td><td>255</td><td>247</td><td>lot</td></td<>			Б		255	247	lot
MHConsegner NMELWICKEGSESP 134 145 150 150 08F6 MHC Hagha A DPOTTAFUL HARTENSWEN DUTINI HENSESITTENKYSQ 164 161		MHC2 interact		NEV MEE VELCWHTNC	257	152	he
Initial and a private sector (C) Initial and a private private sector (C) Initial and pri		MHC2-Interact	A	IT LCWITINC IMPI WI CWK CPSK ND	145	133	
ORFG MICL IL phan A DEPOYTAGE TEXES INVESSION DEPOYTAGE TEXES INTERVESSO Instrume Instrum Instrum Instrum		WITCassoc_triller	R	DANVELOWHTNOVDVOIDVN	124	150	
OND MEC JLSA	OP E6	MHC II alpha	Б Л	DANTITLEWITTNETDTEITTN DEOVTIAEII I IIMPTEK VSIWNI DVIINI IIKNI SKSI TENK VSO	142	51	0
MILC: Lake Agences A METEL Construction of the Co	OKI 0	MHC II bata	A .	MEHI VDEOVTIA EH I HMD TEV VSIWNI DVHNI HVNI SV SI TENV V	0	40	5
MACL, Carbon, C		MHC_Like Agreeg	A	METHLYDEQVIIAEILLIIWIKTEKYSIWINLDTIINLIIKINLSKSLTEINKT MEHLVD	1	49	ne
ORF7a MHCL Lighta YEASSET INCLUSATION OF A CONTRESSET ACTION OF A CONTRESSE		MITC_1-like_Ag-recog	A		1	51	4
ONE IN MICLIDUM A OTFULLEDCSSTFEMPLANELALEROPENDELYAANVEL 25 700 700 MICLIDUM A OTFULLEDCSSTFEMPLANELROPENDELYAANVEL 15 36 36	OPE7a	MHC II alpha	Б А	VECNODEL	21	31	, ⁶
MHCLDika A Orientation (Minor Marker	ORF/a	MHC_II_alpha	A	I EUNSFEIT	40	4/	Z
MHC_LBLe_Ag-scoog A CEDITIONECTING 1000000000000000000000000000000000000		MHC_II_beta	A	GIIVLLKEPCSSGIYEGNSPFHPLADNKFALICFSIQFAF	26	110	h
MIC_INSC.92000 A CRUMMENTON 10 30 </td <td></td> <td>MUC Libe As man</td> <td></td> <td>ACPDGVKHVYQLKAKSVSPKLFIKQEEVQELYSPIFLIVAAIVFI</td> <td>15</td> <td>26</td> <td>d l</td>		MUC Libe As man		ACPDGVKHVYQLKAKSVSPKLFIKQEEVQELYSPIFLIVAAIVFI	15	26	d l
0 RF7b MIC_Lista A 0 PM PT 0 P		MITC_1-like_Ag-recog	A		13	20	er
ORF?b MHC II. Jupba C OWNER/IN/ DWE/LIKE OWNER/IN/ COMPARIANCE OWN			Б	I EGN5FF HFLADNK	40	33	ų
ORF 70 MILC LUB93 A DUTATULUT DUTATULU	0057	MUC II alala	Ċ		6/	/5	≥
MHC, Likk, Agercog A C I LAPLE LIVIENILITY NATHORNAL PROPERTY IN A PROP	ORF/b	MHC_II_alpha	A	DHNETCHA	36	43	P
MHC Lake Agrees A MILL HAT LIFL VILMULTWYSLEUDINST. UTA 9 4.3 00 ORF8 MHC Lake Inner A MILL VILL INTERCES USSCT CHUPY VDDPCPHIFYSK WIRVGARKSAPLIEL 11 3.6 ORF8 MHC Like Inner A TTVAAFHIGES USSCT CHOPY VDDPCPHIFYSK WIRVGARKSAPLIEL 10 5.4 MHC Like Inner A TTVAAFHIGES USSCT CHOPY VDDPCPHIFYSK WIRVGARKSAPLIEL 10 5.4 MHC Like Inner A DDPCONST VSCL PETINC 16 3.6 3.6 ORF10 MHC Like Inner A DDPCONST VSCL PETINC USSCT CHOPY VDDPCONT VSCL PETINC 18 3.4 ORF10 MHC Like Inner A DDPCONST VSCL PETINC USSCT CHOPY VDDPCONT VSCL PETINC USSCT CHOPY VDDPCONT VSCL PETINC USSCT CHOPY VDDPCONT VSCL PETINC VS		MHC_II_beta	A	CFLAFLLFLVLIMLIIFWFSLELQDHNEICH	12	42	
MHC II. John A MLID WISLELQDINK ICH J <t< td=""><td></td><td>MHC_I-like_Ag-recog</td><td>A</td><td>FYLCFLAFLLFLVLIMLIIFWFSLELQDHNEICHA</td><td>9</td><td>43</td><td>õ</td></t<>		MHC_I-like_Ag-recog	A	FYLCFLAFLLFLVLIMLIIFWFSLELQDHNEICHA	9	43	õ
OKPS MHC LL apha A TIVAAPHQESLQSC10P(QP)VIDDPCPHIFYSKW1RVGAKKSAPLIEL 11 38 NHC LL beta TVAAPHQESLQSC10P(QP)VVDDPCPHIFYSKW1RVGAKKSAPLIEL 12 9 VDBAGSK90(DIDGNTYSCLPTINC 10 54 56 VDBAGSK90(DIDGNTYSCLPTINC 10 54 56 VDBAGSK90(DIDGNTYSCLPTINC) 13 36 VDSCDPTINC) 13 36 ORF10 MHC L3 A OPFTIYSLLCRMNSRNYLQVDVVN 13 36 MHC L1 A MCYDINCAPPTIYSLLCRMNSRNYLQVDVVN 1 36 36 MHC L3 A MCYDINCAPPTIYSLLCRMNSRNYLQVDVVNN 1 36 36 MHC L1 A MCYDINCAPPTIYSLLCRMNSRNYLQVDVVNN 1 38 36 mg2 MHC L3 MGVINNCAPPTIYSLLCRMNSRNYLQVDVVNN 1 38 36 mg2 MHC L3 MCYDINCAPPTIYSLLCRMNSRNYLQVDVVNN 1 38 36 mHC L1 kas Agreccog A DYRCNYCREHEHEMYTTRSESYEDTPT 16 37 37 mHC L1 kas Agreccog <		MHCassoc_trimer	A	MLIIFWFSLELQDHNETCH	24	42	23
MRC_LLbsta A TVAAFHQEESLQSCTQHQPY/VDDPCPHIFYSKWYIRVOARKSAPLEL 90 COREJO MRC_Lbisc_Agencog A ITTVAAFHQEESLQSCTQUQPY/VDDPCPHIFYSKWYIRVOARKSAPLEL 61 74 DECASCKSPQUIDIONTTSCLPTIN DECASCKSPQUIDIONTTSCLPTINSLUC 63 74 DECASCKSPQUIDIONTSCLPTINSLUC A 74 74 DECASCKSPQUIDIONTSCLPTINSLUC 74 74 74 MICC_Like.Agencog A DEPCASCHONTON 74 74 MICC_Like.Agencog A DEPCASCHONTON 74 74 MICC_Like.Agencog A MCPTINILLCRMNSRNYLQVDVVNPNLT 7 75 MICC_Like.Agencog MCGYINCAFPETTYSLLICCMNSRNYLQVDVVNPNLT 1 78 msp2 MICC_Like.Agencog MCGYINCAFPETTYSLLICRMNSRNYLQVDVVNPNLT 12 76 MICC_Like.Agencog DEFMGRIRSVYPASPRICOMCISTLMKCDHCGETSWQT 14 77 MICC_Like.Agencog E DEFMGRIRSVYPASPRICOMCISTLMKCDHCGETSWQT 13 160 MICC_Like.Agencog C CPACINSEVGPCHERLAWTERSEKSPELQTPF 44 77 msp3 <t< td=""><td>ORF8</td><td>MHC_II_alpha</td><td>A</td><td>TTVAAFHQECSLQSCTQHQPYVVDDPCPIHFYSKWYIRVGARKSAPLI</td><td>11</td><td>58</td><td></td></t<>	ORF8	MHC_II_alpha	A	TTVAAFHQECSLQSCTQHQPYVVDDPCPIHFYSKWYIRVGARKSAPLI	11	58	
MHC_1-like_Agreeog A TUTVAHRYGESUPPTING 10 54 DEAGSKSPQ/TDG B DEAGSKSPQ/TDG 63 76 C NTVSCLPTINGCEPK 78 94 ORF10 MHC_1-like_Agreeog A DDPC/HFYSRW/TQ/DDVVN 34 45 MHC_1-Like_Agreeog A MCNNEAPPTTTYSLLCERMSSEN/TAQVDVVN 1 36 34 MHC_1-Like_Agreeog A MCNNEAPPTTTYSLLCERMSSEN/TAQVDVVNNENT 1 36 34 mg2 MHC_1-Like_Agreeog A MCNNEAPPTTTYSLLCERMSSEN/TAQVDVVNENT 1 36 mg2 MHC_1-Like_Agreeog A MCNNEAPPTTYSLLCERMSSEN/TAQVDVVNENT 1 37 mg2 MHC_1-Like_Agreeog A DTKROWCCREHEHEJAWTTRSEKSYELOTFF 36 66 60 MHC_1-Like_Agreeog B DEMGROWSWYNENPECNOMCISTINKCDHCGETSWOT 11 31 17 mg3 MHC_1-Like_Agreeog C CPCACHINSEQPETINKCDHCGETSWOT 113 117 115 mg4 MCL1-Like_Agreeog N NTKROWCCREHEREIAWTTRSEKSYELOTFF<		MHC_II_beta	А	TVAAFHQECSLQSCTQHQPYVVDDPCPIHFYSKWYIRVGARKSAPLIEL	12	90	
MHC_Like_Agreeog A TITVAAFIQCESLQSCTQUQPVVVDDPCPHIFYSKWYIRVGARKS 10 54 DEAGKSKPIQVID G3 76 94 ORF10 MHCassoc_trimer A DPCTPITNCQEPK 78 94 ORF10 MHCassoc_trimer A APPTTYSLLCRMSRNYIAQVDVVN 8 34 MHC_Like_Agreeog A APPTTYSLLCRMSRNYIAQVDVVNPNLT 1 38 MHC_Like_Agreeog A MGVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 36 MHC_Like_Agreeog A MGVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 36 MHC_Like_Agreeog A MGVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 37 msp2 MHC_Lipha A GVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 37 msp3 MHC_Lipha A GVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 37 msp3 MHC_Lipha A GVINVEAPPTTYSLLCRMSRNYIAQVDVVNPN 1 38 msp3 MHC_Lipha A DIKRCWYCCREHEIELAWYTRSRNYLGVDVCNPT 1 38 msp3 MHC_Liblac_Agreeog				CVDEAGSKSPIQYIDIGNYTVSCLPFTINC			
B DEAGSSPIQYDI 63 76 C NYTSCLPFTNCQEPK 78 94 ORF10 MHC3soc_trimer A DDPCPHFYSLUCRNNSRNYLQQDDVN<		MHC_I-like_Ag-recog	А	ITTVAAFHQECSLQSCTQHQPYVVDDPCPIHFYSKWYIRVGARKS	10	54	
ORF10 MHCasso_trimer A DOPCPHIPYSKW 34 45 ORF10 MHC_L2 A APPTTVSLLLCRMNSRNYIAQVDVVN 8 34 MHC_L1bela A MCPINPFAPPTTVSLLLCRMNSRNYIAQVDVVNFNLT 1 35 MHC_L1bela A MCPINPFAPPTTVSLLLCRMNSRNYIAQVDVVNFNLT 1 36 MHC_L1chika_Aprecog A MCPINPFAPPTTVSLLLCRMNSRNYIAQVDVVNFN 1 36 mBC_L1dpha A MCPINPFAPPTTVSLLLCRMNSRNYIAQVDVVNFN 1 36 mBC_L1dpha A MCPINPFAPPTTVSLLLCRMNSRNYIA 1 35 mBC_L1dpha A DTKRGYVCCRHHEHEJAW 46 60 MHC_L1beta B DTKRGYVCCRHHEHEJAWYTERSEKSYELQTFFE 41 77 MHC_L1beta B DTKRGYVCCRHHEMYTERSEKSYELQTFFE 41 77 MHC_L1beta B DTKRGYVVPASPNECNOMCLSTLMKCDHCGETSW 10 209 mp3 MHC_L1beta DYRHYTRSFKKGAKLIHKYTKPNTWC 10 109 119 mp3 MHC_L1beta C C SARHIN 116			В	DEAGSKSPIQYIDI	63	76	
MHCasoc_triner A DDPCPHIPYSKW 34 45 ORF10 MHC_L1_2 A APFTTYSLLCRMNSRNYLQQDDVVNFNLT 8 34 MHC_Hick_Apercor A MCYINYFAPFTTYSLLLCRMNSRNYLQQDDVVNFNLT 1 35 MHC_2-interact A MCYINYFAPFTTYSLLLCRMNSRNYLQUDVVNFN 1 36 mHC_2-interact A MCYINYFAPFTTYSLLLCRMNSRNYLQUDVVNFN 1 37 mHC_1L_sha_Apercor A MCYINYFAPFTTYSLLCRMNSRNYLQUDVVNFN 1 38 mHC_1L_sha A RGYUCCREHEHELAWYTENSEKSYELQTPF 43 75 MHC_1L_ban B DGFMGRIRSYYPASPNECQMCLSTLMKCDHCGETSWQT 44 77 MHC_1L_ban A DGFMGRIRSYYPASPNECQMCLSTLMKCDHCGETSWQT 11 31 mHC_1L_ban C CCARCHENERGYUPASPNECQMCLSTLMKCDHCGETSWQT 115 1107 mmp3 MHC_1L_ban A DGYHYTPASPNECQMCLSTLMKCDHCGETSW 115 1107 mp3 MHC_1L_ban A SHYHTYPSKKGAKLHKPHYWHYNANTKATYKPNTWC 152 166 MHC_1L_ban C CAR			С	NYTVSCLPFTINCQEPK	78	94	
ORF10 MHC_L2 A A PFPTTYSLLCEMNSRNIAQVDVVN S S S MHC_L1beta A MGYINVFAPPTTYSLLCRMNSRNYIAQVDVVNFNLT 1 38 mhC_Like_Agrecog A MGYINVFAPPTTYSLLCRMNSRNYIAQVDVVNFNLT 1 38 mhC_siencat A MGYINVFAPPTTYSLLCRMNSRNYIA 1 38 msp2 MHC_Lighba A MGYINVFAPPTTYSLLCRMNSRNYIA 1 38 msp2 MHC_Lighba A MGYINVFAPPTTYSLLCRMNSRNYIA 46 66 MHC_Lighba A DGYGORTHENELWYTERSEKSYELOTPFE 41 75 MHC_Libka DGYGORTRNYPASPNECNOMCLSTLMKCDHCGETSWO 112 184 mHC_Like_Agrecog B FDTKRGVYCCREHEHELWYTERSEKSYELOTPFEI 112 184 mp3 MHC_Like_Agrecog C CPACHNSEVGPENDUCISTLMKCDHCGETSW 112 113 1197 mp3 MHC_Like_Agrecog A DYENTYFFEKGAKLLHKRYWWWINNATNKATYKPNTWC 113 113 1137 mp3 MHC_Like_Agrecog C CASARIIN 74 ASMY		MHCassoc_trimer	Α	DDPCPIHFYSKW	34	45	
MHC_IL_beta A MCVINVFAPFTTYSLLLCRMSRNYLQVDVVNFNLT 1 38 MHC_IL_blcA_Agreeog A MCVINVFAPFTTYSLLLCRMSRNYLQVDVVNFNL 1 99 msp2 MHCO_interate A MCVINVFAPFTTYSLLLCRMSRNYLQVDVVNFNL 1 98 msp2 MHCO_interate A MCVINVFAPFTTYSLLLCRMSRNYLA 1 1 98 msp2 MHC_IL_bata A MCVINVFAPFTTYSLLLCRMSRNYLA 46 60 MHC_IL_bata A MCVINVFAPFTTYSLLLCRMSRNYLA 46 60 MHC_IL_bata A MCVINVFAPFTTYSLLLCRMSRNYLA 45 70 MHC_IL_bata B DGFMGRIRSVYPVASPRCOMCLSTLMKCDHCGETSWQT 11 151 171 MHC_IL_bata A FDITKROVYCCREHHELAWYTERSEKSYELQTPFE 41 171 112 182 MHC_ILik_Agreeog A FDITKROVYCCREHHELAWYTERSEKSYELQTPFE 11 100 100 100 100 100 100 100 100 100 100 100 115 115 115 115 115 115 115 115 116 100 116 100 1	ORF10	MHC_I_2	А	AFPFTIYSLLLCRMNSRNYIAQVDVVN	8	34	
mBC_14lkc_Agreeog A MCVINVFAPFTTYSLLLCR/MSRNYLAQVDVVNFN 1 36 nsp2 MICCastoc_trimer A MCVINVFAPFTTYSLLLCR/MSRNYLAQVDVVNFN 1 28 nsp2 MICCastoc_trimer A MCVINVFAPFTTYSLLLCR/MSRNYLA 1 28 mBC_11_alpha A MCVINVFAPFTTYSLLLCR/MSRNYLA 1 37 MIC_11_beta A DCFMCRERSVEPVASPNEC/MCCCEFEHELEWYTERSEKSVELOTPFE 43 75 MIC_11_beta B DCFMCRERSVEPVASPNEC/MCCCEFEHELEWYTERSEKSVELOTPFE 41 77 MIC_14lic_Agreecog A FIDTKROVYCCREHELEWYTERSEKSVELOTPFE 41 77 MIC_14lic_Agreecog C CPACINSVEPVASPNEC/MONCLSTLMKCDCHCGETSWOT 11 318 1197 nsp3 MIC_11beta, A DYKHYTESFKAVHFISNSWLMWLIINLVQMAPISAMVRMY1 153 1197 110 <t< td=""><td></td><td>MHC_II_beta</td><td>А</td><td>MGYINVFAFPFTIYSLLLCRMNSRNYIAQVDVVNFNLT</td><td>1</td><td>38</td><td></td></t<>		MHC_II_beta	А	MGYINVFAFPFTIYSLLLCRMNSRNYIAQVDVVNFNLT	1	38	
MHC2-interaid A MGYINVFAPPFTTYSLLLCRMNSRNYIA 1 92 msp2 MHC ILabpha A MGYINVFAPPFTTYSLLLCRMNSRNYIA 46 60 msp2 MHC ILabpha A MGYINVFAPPFTTYSLLLCRMNSRNYIA 43 75 MHC ILabpha A DTKRGVYCCREHEHEIAWYTERSEKSYELOTPF 114 153 75 MHC J-like, Agrecog A FIDTKRGVYCCREHEHEIAWYTERSEKSYELOTPFEI 112 114 175 MHC J-like, Agrecog C FIDTKRGVYCCREHEHEIAWYTERSEKSYELOTPFEI 112 112 114 175 MHC J-like, Agrecog C CPACHNEGOFEN 112 114 175 112 114 175 MHC J-like, Agrecog C CPACHNEGOFENLAEYIN 110		MHC_I-like_Ag-recog	А	MGYINVFAFPFTIYSLLLCRMNSRNYIAQVDVVNFN	1	36	
msp2 MHC.susc., timer A MGYINYFA.PFTVISLLCRMNSRNYIA 1 28 msp2 MHC.IL.abin A RGYYCCREHEHELAW 43 75 MHC.IL.beta B DGYRGRISVYPVASPNECNQMCLSTLMKCDHCGETSWQT 14 153 MHC.IL.beta B DGYMGRISVYPVASPNECNQMCLSTLMKCDHCGETSWQT 11 153 MHC.IL.beta B DGYMGRIGSVYPVASPNECNQMCLSTLMKCDHCGETSW 11 184 MHC.IL.beta B DGYMGRIGSVYPVASPNECNQMCLSTLMKCDHCGETSW 11 184 MHC.IL.beta B C CPACHNSEVGPVASPNECNQMCLSTLMKCDHCGETSW 11 181 msp3 MHC.IL.beta C CPACHNSEVGPHSLAEYIN 190 209 msp3 MHC.IL.beta B DYKHYPYSPKKGAKLLHKPIVHVNNATNKATYKPNTWC 153 187 msp3 MHC.IL.beta C CSARHIN 186 182 1606 MHC.IL.beta C CSARHIN 190 209 123 1606 MHC.IL.beta B OPEEEOEDCEEEEF 99 123 1606 MHC.IL.beta C CSARHIN 584 568 MHC.I.Beta, Agrecog D VCRCLW 110 1106 MHC.I.Beta, Agrecog B VCRCLW 14		MHC2-interact	Α	MGYINVFAFPFTIYSLLLC	1	19	
nsp2 MHC_ILpha A RGYYCCREHEHLAW 46 60 MHC_ILbeta B DGFMGRIRSVYPVASPNECNQMCLSTLMKCDHCGETSWQT 41 75 MHC_ILbeta B DGFMGRIRSVYPVASPNECNQMCLSTLMKCDHCGETSWQT 41 153 MHC_ILbeta A FIDTKRGYYCCREHEHLAWYTERSEKSYELQTPFEI 41 76 MHC_ILbeta A FIDTKRGYYCCREHEHLAWYTERSEKSYELQTPFEI 41 77 MHC_ILbeta A FIDTKRGYYCCREHEHLAWYTERSEKSYELQTPFEI 41 77 MHC_ILbeta A C CPACINEKGARCHENYPNSPNECNQMCLSTLMKCDHCGETSW 12 184 MHC_ILbeta A DYKHYTPSFKKGAKLLHKPIVMYNNATNKATYKPNTWC 115 197 197 NBC INCLFNEXOFPENSLACKSVPNASSVENWVNNATNIKKSVHVNNATNKATYKPNTWC 158 1606 198 197 NHC_ILbeta B INQLFSVFAVHFISNSWLMWLIINLVQMAPISAMVRMYI 158 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 152 1606 156		MHCassoc_trimer	А	MGYINVFAFPFTIYSLLLCRMNSRNYIA	1	28	
MHC_IL_beta A DTK.RGYYCCREHEHEIAWYTERSEKSYELQTPF 43 75 MHC_LLbeta B DGRMQRIRSYYPASPNECNQMCLSTLMKCDHCGETSWOT 114 177 MHC_Like_Agrecog A FIDTKRGYYCCREHEHEIAWYTERSEKSYELQTPFEI 112 184 MHC_Like_Agrecog B KLDGPMGRIRSYYPASPNECNQMCLSTLMKCDHCGETSW 112 184 MHC_Like_Agrecog C CPACHNSEVOPASPNECNQMCLSTLMKCDHCGETSW 1153 1197 nsp3 MHC_Like_Agrecog C CPACHNSEVOPASPNECNQMCLSTLMKCDHCGETSW 1153 1197 msp3 MHC_Like_Agrecog C CPACHNSEVOPASPNECNQMCLSTLMKCDHCGETSW 1153 1197 msp3 MHC_Like_Agrecog C CPACHNSEVOPASPNECNQMCLSTLMKCDHCGENSW 1153 1197 MHC_Like_Agrecog MHC_HIKe_Agrecog G DYKHYTPSFKGAKLHKPIVWHYNNATNKATYKPNTWC 1153 1153 MHC_Like_Agrecog A SHWYCSYYPDEDEEEGDCEEEEF 1153 1153 1154 MHC_Like_Agrecog G VERCLW NHCHUPHYNTHAUNUNYNNYNYNYNYNYNYNYNYNYNYNYNYNYNYNYNYN	nsp2	MHC_II_alpha	А	RGVYCCREHEHEIAW	46	60	
MHC_U_beta B DGFMGRIRSYYPVASPNECNQMCLSTLMKCDHGGETSWQT 114 153 MHC_bike_Agrecog A FIDTKRGYYCQCEHHEHENYYTERSEKSYELQTPFEI 41 77 mHC_bike_Agrecog B KLDGFMGRIRSYYPVASPNECNQMCLSTLMKCDHCGETSW 112 184 orgGDFVKATCEFCGTENLTKEGATTCGYLPQNA 112 184 113 1197 mhC_bike_Agrecog C CPCHNSEVOPENSLAEVHN 190 209 mHC_like_Agrecog A DYKHYTBFSKGAKLLHKPIVWHVNNATNKATYKPNTWC 153 1197 mHC_like_Agrecog MHC_like_Agrecog C CPCHNSEVOPENSLAEVHN 153 1666 mHC_like_Agrecog A DYKHYTBFSKGAKLLHKPIVWHVNNATNKATYKENTWC 153 1666 153 1697 mHC_like_Agrecog A SHMYCSPYPDEDEEGDCEEEFF 99 123 161 153 161 MHC_like_Agrecog D WCRCLW 154 568 154 568 154 568 MHC_like_Agrecog D WCRCLW 154 153 159 154 153 159	-	MHC_II_beta	А	DTKRGVYCCREHEHEIAWYTERSEKSYELQTPF	43	75	
MHC_l-like_Agrecog A FIDTKRGYYCREHEHELAW'TERSEKSYELQTPFEI 41 77 MHC_l-like_Agrecog B KLDGFMGRIRSVYPVASPNECNQMCLSTLMKCDHCGETSW 12 184 nsp3 MHC_l-like_Agrecog C CPACHNSEVGPTKASPNECNQMCLSTLMKCDHCGETSW 190 209 nsp3 MHC_l-like_Agrecog C CPACHNSEVGPTKASPNECNQMCLSTLMKEGATTCGYLPQNA 190 209 msp3 MHC_l_bike_Agrecog C CPACHNSEVGPTKASPNECNQMCYKRNATKYPNTWC 153 1197 msp3 MHC_l_beta B IMQLFFSYKKGAKLLHKPIVMHVNNATNKATYKPNTWC 153 166 MHC_l_beta B IMQLFFSYKWSYHVVDGCNSSTCMMCYKRNATRVECT 1876 1882 MHC_l-like_Agrecog A ASHMYCSFYPDEDEEEGDCEEEEF 190 190 MHC_l-like_Agrecog C NEQELIGTSWNLREMLAHAEETR 154 156 MHC_l-like_Agrecog F RSFYYNANGKGFCKLHNWNCVNCDT 1613 163 MHC_l-like_Agrecog F RSFYYNANGKGFCKLHNWNCVNCDT 164 377 MHC_l-like_Agrecog F RSFYYNANGKGFCKLHNWNCVNCDT 364		MHC_II_beta	В	DGFMGRIRSVYPVASPNECNQMCLSTLMKCDHCGETSWQT	114	153	
MHC_l-like_Ag-recog B KLDGFMGRIRSYYPASPNECNOMCLSTLMKCDHCGETSW 112 184 MHC_l-like_Ag-recog C CPACHNSEVGEFCGTENLTKEGATTCGYLPQNA 100 209 nsp3 MHC_l-like_Ag-recog C CPACHNSEVGEFLALEVHN 100 209 msp3 MHC_ll_beta A DYKHYTBFKKGAKLLHKPIVWHNNATNKATYKPNTWC 1153 1197 mHC_ll_beta B IMQLFSYFAVHFISNSWLMVLIINLVQMAPISAMVRMYI 1528 1606 MHC_ll_ke_Ag-recog A ASHMYCSYFYPDEDEEGDCEEEF 1876 1882 MHC_llike_Ag-recog B QFEEEQEEDW 152 161 MHC_llike_Ag-recog B QFEEEQEEDW 544 568 MHC_llike_Ag-recog B WCRCLW 190 1196 MHC_llike_Ag-recog B SWLMWLINLVQMAPISAMVRMYIFASFYYVW 152 161 MHC_llike_Ag-recog B WCRCLW 190 1196 190 1196 MHC_llike_Ag-recog F RSMUMVLINLVQMAPISAMVRMYIFASFYYVW 154 156 153 153 153 15		MHC_I-like_Ag-recog	А	FIDTKRGVYCCREHEHEIAWYTERSEKSYELQTPFEI	41	77	
MBC_like_Ag-recog C CPACHNSEVGPENLTKEGATTCGYLPQNA 90 209 nsp3 MHC_libeta A DYKHYTPSFKKGALLHKPIVWHVNNATNKATYKPNTWC 1153 1197 nsp3 MHC_libeta A DYKHYTPSFKKGALLHKPIVWHVNNATNKATYKPNTWC 1528 1606 MHC_libeta B IMQLFFSYFAVHFISNSWLMWLIINLVQMAPISAMVRMYI 1528 1606 MHC_like_Ag-recog A ASHMYCSFYPPDEDEEEGDCEEEEF 99 123 MHC_like_Ag-recog B OPEEQEEDW 152 161 MHC_like_Ag-recog C NEKQEIGTSWNLRMULINLVQMAPISAMVRMYIFASFYYVW 190 1196 MHC_like_Ag-recog B OPEEQEEDW 152 161 MHC_like_Ag-recog D WCIRCLW 190 1196 MHC_like_Ag-recog D WCIRCLW 163 1639 MHC_like_Ag-recog F RRSFYVANGGKGFCKLHNWNCVNCDT 163 1639 MHC_like_Ag-recog F RRSFYVANGGKGFCKLHNWNCVNCDT 364 377 MHC_like_Ag-recog A QWMVMFTPLVPFWITAYIICISTKHFYWFSNYLKRR		MHC_I-like_Ag-recog	В	KLDGFMGRIRSVYPVASPNECNQMCLSTLMKCDHCGETSW	112	184	
MHC_1-like_Ag-recog C CPACHNSEVGPEHSLAEYHN 190 209 nsp3 MHC_1Lbeta A DYKHYTPSFKKGAKLLHKPIVWHVNATNKATYKPNTWC 1153 1157 mRC_WS MHC_1Lbeta B IMQLFFSYFAVHFISNSWLMVLIINLVQMAPISAMVRMYI 1528 1666 MHC_1Lbeta B IMQLFFSYFAVHFISNSWLMVLIINLVQMAPISAMVRMYI 1528 1666 MHC_1Lbeta C CSARHN 1876 1882 MHC_1-like_Ag-recog A ASHMYCSFYPPDEDEEEEGDCEEEEF 99 123 MHC_1-like_Ag-recog C NEKQEILGTVSWNLEMLAHAEETR 190 196 MHC_1-like_Ag-recog D WCIRCLW 190 196 MHC_1-like_Ag-recog F RRSFYYANGGKGFCKLHNWNCVNCDT 1613 1637 nsp4 MHC_1_2 A QWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 364 401 MHC_1_like_Ag-recog F RRSFYYANGGKGFCKLHNWNCVNCDT 1613 1637 nsp4 MHC_1_like_Ag-recog A QWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 364 401 MHC_1_like_Ag-recog </td <td></td> <td> 0 0</td> <td></td> <td>QTGDFVKATCEFCGTENLTKEGATTCGYLPQNA</td> <td></td> <td></td> <td></td>		0 0		QTGDFVKATCEFCGTENLTKEGATTCGYLPQNA			
nsp3 MHC_IL_beta A DYK HYTPSFKK GAKLLHKPIVWHVNNATNKATYKPNTWC 1153 1197 nKCUWS IRCUWS IRCUWS<		MHC_I-like_Ag-recog	С	CPACHNSEVGPEHSLAEYHN	190	209	
Inclust	nsp3	MHC II beta	А	DYKHYTPSFKKGAKLLHKPIVWHVNNATNKATYKPNTWC	1153	1197	
MHC_II_beta B IMQLFFSYFAVHFISNSWLMWLIINLVQMAPISAMVRMYI FFASFYYYWKSYYHVVDGCNSSTCMMCYKRNATRVECT 1528 1606 MHC_II_beta C CSARHIN 1876 1882 MHC_I-like_Ag-recog A ASHMYCSFYPPDEDEEEGDCEEEEF 99 123 MHC_I-like_Ag-recog B QPEEEQEEDW 152 161 MHC_I-like_Ag-recog C NEKQEILGTVSWNLREMLAHAEETR 544 568 MHC_I-like_Ag-recog D WCIRCLW 190 1196 1196 MHC_I-like_Ag-recog F RNSFYYANGSGGFCKLHNWNCVNCDT 1613 1639 1639 nsp4 MHC_I-laipha A QWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 364 377 92 228 MHC_IL_alpha A GWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 364 377 92 228 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401 362 401	1			IRCLWS			
FFASFYYWKSYVHVVDGCNSSTCMMCYKRNRATRVECT FFASFYYWKSYVHVVDGCNSSTCMMCYKRNRATRVECT IB76 IB82 MHC_IIbeta C CSARHIN 1876 1882 99 121 MHC_IIbeta A ASHMYCSFYPPDEDEEEGDCEEEEF 99 121 111		MHC II beta	В	IMQLFFSYFAVHFISNSWLMWLIINLVQMAPISAMVRMYI	1528	1606	
MHC_II_beta C CSARHIN 1876 1882 MHC_I-like_Ag-recog A ASHMYCSFYPPDEDEEEGDCEEEEF 99 123 MHC_I-like_Ag-recog B QPEEEQEEDW 152 161 MHC_I-like_Ag-recog C NEKQEILGTVSWNLREMLAHAEETR 190 1190 1196 MHC_I-like_Ag-recog D WCIRCLW 1100 1196 154 1576 MHC_I-like_Ag-recog E SWLMWLIINLVQMAPISAMVRMYIFFASFYYW 1613 1639 1190 1196 MHC_I-like_Ag-recog E SWLMWLIINLVQMAPISAMVRMYIFFASFYYW 164 401 1544 1576 MHC_I-like_Ag-recog F RSFYYANGGKGFCKLHNWNCVNCDT 1613 1639 1613 1639 MHC_I_lealpha A QWMVMFTPLVPFWTIAYIICISTKHFYWFFSNYLKRR 364 377 MHC_I_lebta A EYCRHGTCER 129 228 129 228 129 228 129 228 129 228 129 228 129 228 129 228 129 </td <td></td> <td></td> <td></td> <td>FFASFYYVWKSYVHVVDGCNSSTCMMCYKRNRATRVECT</td> <td></td> <td></td> <td></td>				FFASFYYVWKSYVHVVDGCNSSTCMMCYKRNRATRVECT			
MHC_1-like_Ag-recogAASHMYCSFYPPDEDEEEGDCEEEEF99123MHC_1-like_Ag-recogBQPEEEQEEDW152161MHC_1-like_Ag-recogCNEKQEILGTVSWNLREMLAHAEETR544568MHC_1-like_Ag-recogDWCIRCLW119011901190MHC_1-like_Ag-recogESWLMWLIINLVQMAPISAMVRMYIFFASFYYVW15441576MHC_1-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDT16131639nsp4MHC_1_2AQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR364401MHC_1I_alphaAQWMVMFTPLVPFWI364377MHC_1I_betaBHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR362401MHC_1-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_1-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_1_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC II beta	С	CSARHIN	1876	1882	
MHC_1-like_Ag-recogBQPEEEQEEDW152161MHC_1-like_Ag-recogCNEKQEILGTVSWNLREMLAHAEETR544568MHC_1-like_Ag-recogDWCIRCLW119011901196MHC_1-like_Ag-recogESWLMWLIINLVQMAPISAMVRMYIFFASFYYVW1613163911901196MHC_1-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDT161316391190119611901196nsp4MHC_12AQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR36440136437721922821922821922821922821922821922821922840156240156240156240156356		MHC I-like Ag-recog	Ă	ASHMYCSFYPPDEDEEEGDCEEEEF	99	123	
MHC_1-like_Ag-recogCNEKQEILGTVSWNLREMLAHAEETRMHCMHC_1-like_Ag-recogDWCIRCLW11901196MHC_1-like_Ag-recogESWLMWLIINLVQMAPISAMVRMYIFFASFYYVW15441576MHC_1-like_Ag-recogFRRSFYVANGGKGFCKLHNWNCVNCDT16131639MHC_1-like_Ag-recogFRRSFYVANGGKGFCKLHNWNCVNCDT16131639MHC_1_like_Ag-recogFRRSFYVPW364401MHC_1_lebtaAQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR364377MHC_1_lebtaBHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR362401MHC_1-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_1-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_1_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC I-like Ag-recog	В	OPEEEOEDW	152	161	
MHC_1-like_Ag-recogDWCIRCLWInternational MathematicationMHC_1MHC_1-like_Ag-recogESWLMWLIINLVQMAPISAMVRMYIFASFYYVW15441576MHC_1-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDT16131639MHC_1-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDT16131639MHC_12AQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR364401MHC_11_betaAEYCRHGTCER219228MHC_11_betaBHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR362401MHC_1-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_1-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_11_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC I-like Ag-recog	Ē	NEKOEII GTVSWNI REMI AHAEETR	544	568	
nsp4MHC_1-like_Ag-recogESWLMWLIINLVQMAPISAMVRMYIFASFYYVW15441576CF-Like MHC_1-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDT1613163916131639nsp4MHC_1_2AQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR364401401MHC_1_alphaAQWMVMFTPLVPFWI364364377MHC_1L_betaAEYCRHGTCER219228MHC_1-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_1-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_1L_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC I-like Ag-recog	Ď	WCIRCLW	1190	1196	~
MHC_l-like_Ag-recogFRRSFYVYANGGKGFCKLHNWNCVNCDTIntoIntoIntoIntonsp4MHC_l2AQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR364401MHC_l1_alphaAQWMVMFTPLVPFWI364377MHC_l1_betaAEYCRHGTCER219228MHC_l-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_l-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_l1_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC I-like Ag-recog	Ē	SWLMWLJINLVOMAPISAMVRMYIFFASFYYVW	1544	1576	主
nsp4 MHC_IL_alpha A QWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 364 401 MHC_IL_alpha A QWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 219 228 MHC_IL_beta A EYCRHGTCER 219 228 MHC_IL_beta B HIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR 362 401 MHC_I-like_Ag-recog A PVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR 29 78 MHC_I-like_Ag-recog B FYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF 351 393 nsp6 MHC_IL_beta A QSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH 27 62		MHC I-like Ag-recog	Ē	RRSFYVYANGGKGECKLHNWNCVNCDT	1613	1639	<u> </u>
MHC_IL_alphaAQWMVMFTPLVPFWI364377MHC_IL_betaAEYCRHGTCER219228MHC_IL_betaBHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR362401MHC_I-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_I-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_IL_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762	nsp4	MHC I 2	A	OWMVMETPI VPEWITIA VIICISTK HEYWEESNVI K R R	364	401	Lik
MHC_IL_betaAEVCRIGTCER219228MHC_IL_betaBHIQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR362401MHC_IL-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_I-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_IL_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC II alpha	A	OWMVMFTPLVPFWI	364	377	e
MHC_IL_betaBHQWMVMFTPLVPFWITIAYIICISTKHFYWFFSNYLKRR26240190MHC_IL-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR2978MHC_I-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF351393nsp6MHC_IL_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC II beta	Δ	EVCRHGTCER	210	278	De
MHC_I-like_Ag-recogAPVHVMSKHTDFSSEIIGYKAIDGGVTRDIASTDTCFANKHADFDTWFSQR302401MHC_I-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF2978nsp6MHC_II_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC II beta	R	HIOWMVMETPI VPEWITIA VIICISTK HEVWEESNVI KRR	219	401	8
MHC_I-like_Ag-recogBFYLTNDVSFLAHIQWMVMFTPLVPFWITIAYIICISTKHFYWF2576nsp6MHC_II_betaAQSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH2762		MHC Llike Agreeog	Δ	PVHVMSKHTDESSEIIGVK AIDGGVTR DIASTDTCEANKHADEDTWESOP	20	78	Ň
nsp6 MHC_II_beta A QSTQWSLFFFLYENAFLPFAMGIIAMSAFAMMFVKH 27 62		MHC Llike Agrees	P	EVI TNDVSELAHIOWMVMETDI VDEWITIA VIICISTK HEVWE	29	302	Š
	nen6	MHC II beto		Ο ΣΤΟΨΥΙ ΕΕΕΙ VENAEI DEAMGIIAMSAEAMMEVEH	551 77	575	ste
	nspo	WIIIC_II_Deta	л		27	02	3

Liu
and

Protein	Domain	Alias	Motif	Start	End
	MHC_II_beta	В	WVMRIMTWLDM	90	100
	MHC_I-like_Ag-recog	А	SWVMRIMTWLDM	89	100
	MHC2-interact	А	MVYMPASWVMRIMTWLDM	83	100
	MHCassoc_trimer	А	GTHHWL	9	14
nsp7	MHC_I-like_Ag-recog	Α	WAQCVQLHND	29	38
nsp8	MHC_I-like_Ag-recog	А	KSEFDRDAAMQRKLEKMADQAMTQMYKQARSEDKRAKVTSAMQTM	46	90
nsp10	MHC_II_beta	Α	NMDQESFGGASCCLYCRCHIDHPNP	62	86
	MHC_II_beta	В	WKGYGCSCDQLREPMLQ	123	139
	MHC_I-like_Ag-recog	А	TPEANMDQESFGGASCCLYCRCHIDHPN	58	85
	MHC2-interact	А	YCRCHIDHPNPKGFCD	76	91
RNA-dependent RNA polymerase	MHC_II_alpha	А	RKHTTCCSLSHRFYR	640	654
	MHC_II_alpha	В	YWEPEF	915	920
	MHC_II_beta	Α	ERLKLFDRYFKYWDQTYHPNCVNCLDDRCILH	278	309
	MHC_II_beta	В	YSDVENPHLMGWDYPKCDRAMPNMLRIMA	606	634
	MHC_II_beta	С	HPNQEYADVFHLYLQYIRKLHDELTGHMLDMYSVM	872	906
	MHC_II_beta	D	SRYWEPEFYEAMYT	913	926
	MHC I-like Ag-recog	А	SNYQHEETIYNLLKDCPAVAKHDFFKFRIDGDMVPHISRQRL	78	119
	MHC_I-like_Ag-recog	В	FDRYFKYWDQTYHPNCVNCLDDRCILH	283	309
	MHC_I-like_Ag-recog	С	KFYGGWHNMLKTVYSDVENPHLMGWDYPKCDRAMPNML RIMASLVLARKHTTCCSLSHRFYRLANECAQVLSEMVMCGGS	593	672
	MHC I-like Ag-recog	D	KCWTETDLTKGPHEFCSOHTMLVKOGDDY	798	826
	MHC_I-like_Ag-recog	Е	LMIERFVSLAIDAYPLTKHPNQEYADVFHLYLQYIRKLH DELTGHMLDMYSVMLTNDNTSRYWEPEFYEAMYTPHT	854	929
2'-O-ribose methyltransferase	MHC_II_alpha	А	TEHSWNADLYKLMGHFAWW	172	190
	MHC II beta	А	PREQIDGYVMHANYIFWRNT	215	234
	MHC I-like Ag-recog	А	HSWNADLYKLMGHFAWWT	174	191
	MHC I-like Ag-recog	В	PREQIDGYVMHANYIFWR	215	232
	MHC2-interact	А	MGHFAWWTAF	184	193
	MHCassoc trimer	А	MGHFAWW	184	190
3C-like proteinase	MHC II beta	А	YMHHMEL	161	167
1	MHC I-like Ag-recog	А	YDCVSFCYMHHME	154	166
3'-to-5' exonuclease	MHC_I_2	Α	CWHHSIGFDYVYNPFMIDVQQW	226	247
	MHC II beta	А	EGLCVDIPGIPKDMTYRRLISMMGFKMNYQVNGYPNMFITREEAIRHVRAWIGFDVEGCHATRE	36	99
	MHC II beta	В	CWHHSIGFDYVYNPFMIDVOOW	226	247
	MHC II beta	С	AVCRHHANEYRLYLDAYNMMISAGFSLWVYKQ	482	513
	MHC I-like Ag-recog	А	IPGIPKDMTYRRLISMMGFKMNYQVNGYPNMFITREEAIRHVRAWIGFDVEGCHATR	42	98
	MHC_I-like_Ag-recog	В	DTYACWHHSIGFDYVYNPFMIDVQWGFTGNLQS NHDLYCOVHGNAHVASCDAIMTRCLAVHECFVKRVDWTIEYPIIGDELKINAACRKVOHM	222	315
	MHC I-like Ag-recog	С	CRHHANEYRLYLDAYNMMISAGFSLWVYKOFDTYNLWNTF	484	523
endoRNAse	MHC I-like Ag-recog	A	RNLOEFKPRSOMEIDFLELAMDEFIERYKLEGYAFEHI	198	235
helicase	MHC I-like Ag-recog	A	RPFLCCKCCYDHVISTSH	22	39
	MHC I-like Ag-recog	В	EPEYFNSVCRLMKTIGPDMFLGTCRR	418	443
	MHC I-like Ag-recog	č	R EFL TR NPA WR K AVEISPY NSONA	497	520

MHC indicates major histocompatibility complex; SARS-COV-2, severe acute respiratory syndrome coronavirus 2.

Domain	Alias	Start	End	T19R	G142D	E156G	F157Δ	R158Δ	L452R	T478K	D614G	P681R	D950N
MHC_I_2	А	131	156		V	V							
	В	1212	1217										
MHC_I_C	Α	1211	1237										
MHC_II_alpha	Α	131	162		V	V	V	V					
-	В	895	905										
	С	1203	1243										
MHC_II_beta	Α	64	80										
	В	127	178		V	V	V	V					
	С	898	907										
	D	1028	1033										
	E	1067	1107										
	F	1199	1264										
MHC_I-like_Ag-recog	Α	62	69										
	В	127	194		V	V	V	V					
	С	346	382										
	D	555	583										
	E	616	676										
	F	896	905										
	G	1014	1114										
	Н	1142	1155										
	Ι	1195	1273										
MHC2-interact	Α	1078	1092										
	В	1212	1217										
	С	1227	1248										
MHCassoc_trimer	Α	144	162			V	V	V					
	В	1087	1102										
	С	1202	1217										

has MHC-I_like and MHC-II_like functions, so it can also bind to CD4+ T, CD8+ T, NK cells.

SARS-COV-2 Gamma Variant

The seropositivity rate of SARS-COV-2 antibody is very high. There is a greater chance of infectivity and death. The S mutation sites of Gamma variants are:^{47,48} L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I, V1176F. Table 4 shows that D138Y is in the MHC_I_2 A, MHC_II_alpha A, MHC_II_beta B, and MHC_I-like_Ag-recog B domains. R190S, H655Y and T1027I are in MHC_I-like_Ag-recog B, E, G domains, respectively. Compared with the B.1.617.2/Delta variant, the MHC-like domain of the S protein of the SARS-COV-2 Gamma variant has two mutation points, H655Y, and T1027I. It shows that Gamma variant S participates in receptor-binding H655Y and participates in membrane fusion T1027I in the MHC-LIKE region. Therefore, the infection rate and mortality of Gamma variants are high. However, the Gamma variant does not have a mutation site located in the MHCassoc_trimer domain. It may not enhance the immune escape of the regulatory region of the S trimer. Therefore, the MHCassoc_trimer domain (144-162) is an important reason why the Delta variant spreads infection faster than the Gamma variant.

SARS-COV-2 Alpha Variant

B.1.1.7/Alpha variant has a more tremendous increase in the transmission rate than the earlier SARS-COV-2 virus. However, there is no significant difference in overall mortality. The mutation site of S in the B.1.1.7/Alpha variant is:⁴⁹ Δ69–70, Δ144, Δ145, N501Y, A570D, D614G, P681H,

T716I, S982A, D1118H. Table 5 shows that $\Delta 69-70$ is at MHC_II_beta A and MHC_I-like_Ag-recog A domains. $\Delta 144$ and $\Delta 145$ is in MHC_I_2 A, MHC_II_alpha A, MHC_II_beta B, MHC_I-like_Ag-recog B, MHCassoc_trimer A domains. A570D is in MHC_I-like_Ag-recog D domain. $\Delta 144$ and A570D are all in the S1 protein. There are no MHC-like domain mutations in the S2 protein. The mutation at position 144-145 is in the Alpha variant S. The mutation at position 156 is in the delta variant S. They are in the MHCassoc_trimer A domain. The mutations at position 144-162 may enhance the immune escape of the MHC-like region involved in receptor-binding and regulate trimer's formation.

SARS-COV-2 Beta Variant

The vaccine is effective against the B.1.351/Beta variant. The mutation sites of B.1.351/Beta variant S are:50 L18F, D80A, D215G, LAL241-243A, K417N, E484K, N501Y, D614G, A701V. Table 6 shows that D80A is in the MHC_II_beta A domains. Most of the other mutation sites are not in the MHC-like domains. It shows that most of the mutation sites do not affect the MHC-like domain.

Mutation sites G75V, T76I of the SARS-COV-2 C.37/ lambda⁵¹ variant are both in the MHC_II_beta A domain. So S 62-80 of SARS-COV-2 alpha, beta, lambda variants were the first MHC-like enhanced distribution area. The second MHC-like enhanced distribution area of S protein is 127-194, located in the NTD (14-305 residues) of S1 protein. MHCassoc_trimer (144-162) is a trimer of S Formation, which plays an important role. The third and fourth MHC-like enhanced distribution areas of S protein are MHC_I-like_Ag-recog E (616–676), MHC_I-like_Ag-recog G (1014–1114).

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Domain	Alias	Start	End	L18F	T20N	P26S	D138Y	R190S	K417T	E484K	N501Y	D614G	H655Y	T1027I	V1176
MHC I 2	А	131	156				V								
	В	1212	1217												
MHC_I_C	А	1211	1237												
MHC_II_alpha	А	131	162				V								
1	В	895	905												
	С	1203	1243												
MHC_II_beta	А	64	80												
	В	127	178				V								
	С	898	907												
	D	1028	1033												
	E	1067	1107												
	F	1199	1264												
MHC_I-like_Ag-recog	Α	62	69												
	В	127	194				V	V							
	С	346	382												
	D	555	583												
	E	616	676										V		
	F	896	905												
	G	1014	1114											V	
	Н	1142	1155												
	I	1195	1273												
MHC2-interact	A	10/8	1092												
	В	1212	1217												
MIG C	Ç	1227	1248												
MHCassoc_trimer	A	144	162												
	В	108/	1102												

Domain	Alias	Start	End	∆ 69–70	Δ144–Δ145	N501Y	A570D	D614G	P681H	T716I	S982A	D1118H
MHC I 2	А	131	156		V							
	B	1212	1217									
MHC I C	А	1211	1237									
MHC_II_alpha	А	131	162		V							
1	В	895	905									
	С	1203	1243									
MHC_II_beta	Α	64	80	V								
	В	127	178		V							
	С	898	907									
	D	1028	1033									
	E	1067	1107									
	F	1199	1264									
MHC_I-like_Ag-recog	Α	62	69	V								
	В	127	194		V							
	С	346	382									
	D	555	583				V					
	E	616	676									
	F	896	905									
	G	1014	1114									
	Н	1142	1155									
	Ι	1195	1273									
MHC2-interact	Α	1078	1092									
	В	1212	1217									
	С	1227	1248									
MHCassoc_trimer	Α	144	162		V							
	В	1087	1102									
	С	1202	1217									

MHC indicates major histocompatibility complex.

		-										
Domain	Alias	Start	End	L18F	D80A	D215G	LAL241–243∆	K417N	E484K	N501Y	D614G	A701
MHC_I_2	А	131	156									
	В	1212	1217									
MHC_I_C	Α	1211	1237									
MHC_II_alpha	Α	131	162									
	В	895	905									
	С	1203	1243									
MHC_II_beta	Α	64	80		V							
	В	127	178									
	С	898	907									
	D	1028	1033									
	E	1067	1107									
	F	1199	1264									
MHC_I-like_Ag-recog	А	62	69									
	В	127	194									
	С	346	382									
	D	555	583									
	E	616	676									
	F	896	905									
	G	1014	1114									
	Η	1142	1155									
	Ι	1195	1273									
MHC2-interact	Α	1078	1092									
	В	1212	1217									
	С	1227	1248									
MHCassoc_trimer	А	144	162									
	В	1087	1102									
	С	1202	1217									

write indicates major instocompationity complex.

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Mutations in MHC-Like Regions of RNA-Dependent RNA Polymerase and N Protein Causing High Viral Load of Delta Variant

The viral load of Delta variant patients is very high. It shows that the replication activity of the Delta variant of the SARS-COV-2 virus is very active. The viral proteins directly related to viral replication activities are orf1ab and N proteins. We searched the orf1ab and N protein mutation sites of five variants of Alpha, Beta, Gama, Delta, and Lambda from "CORONAVIRUS CORONAVIRUS ANTIVIRAL & RESISTANCE DATABASE" (https:// covdb. stanford. edu/ page/ mutation-viewer). Then compared with Table 2 to find the MHC-like enhanced region sites of orf1ab and N proteins (Table 7). Table 7 shows that the orflab and N protein mutation sites of Alpha, Beta, and Gama variants are not in the MHC-like region. The N protein mutation site of the Lambda variant is also not in the MHC-like area. However, the mutation sites of Delta (orflab and N protein) and Lambda (orflab protein) are in the MHC-like region. The RdRP: G671S mutation site of Delta variant orf1ab is at MHC_I-like_Ag-recog C. The nsp3:F1569V of Delta variant orf1ab is at MHC II beta B and MHC I-like Agrecog E. The D63G of Dalta variant N is in MHC_II_beta A, MHC_I-like_Ag-recog A. Both N and RNA-dependent RNA polymerase are directly related to virus replication. In addition, the interaction between N and Nsp3 is essential for connecting the viral genome for processing. So, Table 7 indicates that the mutations of RdRP : G671S and N : D63G enhanced the immune escape ability of the Delta variant virus during the replication process. Therefore, the replication activity for this variant is very active.

DISCUSSION

Genetic Variation of MHC Protected Immune Cells

The MHC molecule is a cell surface protein complex encoded in the HLA locus.⁵² The genetic variation of the three MHC class I genes (HLA-A, -B, and -C genes) affect the susceptibility and severity of COVID-19 disease.⁵³ The HLA gene complex is closely linked to genes, and there is little exchange between homologous chromosomes. HLA loci located on the same chromosome constitute a closely linked gene group (including HLA-I and II genes), called haplotype or haplotype. A haplotype is inherited as a unit. To the offspring, it is called haplotype genetics. However, HLA haplotypes are not the main risk/protective factor for SARS-COV-2 infection or severity in the Israeli population.⁵⁴ It indicates that the genetic variation of MHC structure may protect immune cells that can bind to MHC to a certain extent.

In this present study, we found that many proteins of the SARS-COV-2 virus have MHC-like structures recognized by MHC receptors. CD4 or CD8 co-receptors expressed by T cells can bind to part of MHC proteins.¹³ The inhibitory receptors of NK cells can also bind to the MHC-1 receptor recognition structure. Therefore, the S protein of the SARS-COV-2 virus could bind to CD4⁺T, CD8⁺T, and NK cells through MHC-like structures. Then the ROS generated by the E protein destroyed these immune cells,¹¹ resulting in a decrease in lymphocytes. The genetic variation of HLA may produce MHC molecules that could not bind to the viral MHC-like structure. It was helpful for immune cells to evade the attachment and positioning of

TABLE 7	7. MHC-lik	e enhance	ement sites of orf1ab and N proteins	
Protein	Variant	Code	Mutation site	MHC-like enhancement site
orflab	Alpha Beta	B.1.1.7 B.1.351	nsp3:T1831, nsp3:A890D, nsp3:11412T, nsp6:SGF106-108, RdRp:P323L nsp2:T851, nsp3:K837N, 3CL:K90R, nsp6:SGF106-108, RdRP:P323L	
	Gama	P.1	nsp3:S370L, nsp3:K977Q, nsp6:SGF106-108, RdRP:P323L, nsp13: E341D	
	Delta	B .1.617.2	nsp3:A488S, nsp3:P1228L, nsp3:P1469S, nsp4:V167L, nsp4:T492l, nsp6:T77A, RdRP:P323L, RdRP: G67lS, nsp13:P77L, nsp14:A394V	RdRP: G671S (MHC_I-like_Ag-recog C)
	Lambda	C.37	nsp3:T4281, nsp3:P1469S, nsp3:F1569V, nsp4:L438P, nsp4:T492I, 3CL:G15S, nsp6:SGF106-108, RdRP: P323L	nsp3:F1569V(MHC_II_beta B, MHC_I-like_Ag- recog E)
z	Alpha	B .1.1.7	D3L, R203K, G204R, S235F	
	Beta	B .1.351	T205I	
	Gama	P.1	P80R, R203K, G204R	Ι
	Delta	B .1.617.2	D63G, R203M, G215G,D377Y	D63G (MHC_II_beta A, MHC_I-like_Ag-recog A)
	Lambda	C.37	P13L, R203K, G204R, G214C	
MHC	indicates m	najor histoco	mpatibility complex.	

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SARS-COV-2 MHC-like proteins. In this situation, the antigen presentation response would not be disturbed, and immune cells (such as CD4⁺T, CD8⁺T, NK cells) would be protected from the virus's ROS damage.

S Mutations in the MHC-Like Regions Promoted Weaker Immune Resistance and More Robust Transmission

If a mutation site was in the MHC-like domain, the mutation enhanced the MHC decoy function. It challenged the production of antibodies to neutralize these MHC decoy sites. If antibodies could attach to the MHC-like proteins, the antibodies could also bind to MHC proteins. Then the normal MHC antigen presentation function would be affected, and the body would appear autoimmune diseases. It is not a piece of good news for CD4⁺ T, CD8⁺ T, NK cells, and other immune cells that can bind to MHC. These immune cells could indiscriminately bind to MHC-like structures of the S protein, and were attacked by ROS from the E protein. Then the immune system could not effectively perform the antigen presentation for the SARS-COV-2 virus protein. It also could not produce the neutralizing antibody effectively. Moreover, the probability of infected cells was killed by immune cells would be significantly reduced.

This present study found that neutralizing antibodies were challenging to generated for mutations in S MHC-like regions 127-194 and 144-162. It occurred with delta variant infections. The delta variant was the SARS-COV-2 virus with a robust transmission. The S 62-80 mutations of SARS-COV-2 alpha, beta, lambda variants had a similar situation. McCallum et al³⁹ found R246A substitution reduces the binding of S2L28, S2M28, and S2X333. This substitution significantly affected the binding of S2X28 and mAb 4A8. The L18F, D80A, D253G/Y, or S255F variants only abolish the combination of S2L28 and NTD. The L18F substitution exists in B.1.351 and P. 1 pedigree. The Y144 deletion abolished the binding to S2M28, S2X28, S2X333, and 4A8 instead of S2L28. It explains that these mAbs have lost the ability to neutralize the B.1.1.7 S pseudovirus, which contains this deletion. The H146Y mutant reduces S2M28, S2X28, especially the combination of 4A8. The binding of all site i-specific NTD mAbs to B.1.351 NTD is abolished, and 4A8 does not recognize this NTD variant. The evidence indicates that the NTD variants located in MHC-like regions 127-194 and 144-162 enhance the immune escape of the virus and increase the efficiency of virus transmission.

We also found that the immune system was challenging to generate neutralizing antibodies against mutations in S MHC-like 616–676 and 1014–1114 regions. It happened to gamma variant infections. The gamma variant was the SARS-COV-2 virus that caused high mortality. Chen et al⁵⁵ find that specific mAbss have reduced or weakened neutralizing activity against B.1.351, B.1.1.28, B.1.617.1, and B.1.526 viruses in cell culture. And the neutralizing effect of antibodies against H655Y and T1027I mutation sites is not apparent.⁵⁵ It shows that the variants in MHC-like regions 616–676 and 1014–1114 also strengthen the immune escape of the virus, and enhance the virus's receptor engagement and membrane fusion ability.

CONCLUSION

The high mortality rate of COVID-19 is related to poor antigen presentation and lymphopenia. MHC genetic variations may protect immune cells. CMV and the herpes

family encode a series of MHC-like molecules required for targeted immune responses to achieve immune escape. This present study used bioinformatics methods to study whether the SARS-COV-2 virus proteins also had MHC-like structures. The domain search results indicate that MHC receptors could recognize many proteins of the SARS-COV-2 virus because of their MHC-like domains. The MHC-like structures were equivalent to bait against the human immune system. We believed that the SARS-COV-2 virus proteins with MHC-like structures could bind to the MHC receptor of immune cells to interfere with the antigen presentation response. After the S protein was bound to CD4⁺T, CD8⁺T, and NK cells through MHC-like structures, ROS generated by the E protein destroyed these immune cells, decreasing the number of lymphocytes. Mutations in the MHC-like region of the proteins such as S protein promoted weaker immune resistance and more robust transmission. The mutations in the S MHC-like 127-194 and 144-162 regions were the reason for the entire transmission of delta variant. It is worth noting that the 144-162 region regulates the formation of S trimer. Mutations in S MHC-like 62-80 of SARS-COV-2 alpha, beta, lambda variants were one important factor for fast-spreading. The mutations in the S MHC-like 616-676 and 1014-1114 regions were causes of high mortality for gamma variants infections. The mutations of RdRP : G671S and N : D63G of delta variant caused high viral load.

CONFLICTS OF INTEREST/FINANCIAL DISCLOSURES

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