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Multi Epitope Peptide Vaccine against Human Parvovirus B19 Using Immuno-Informatics Approaches

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Abstract **Introduction:** Human parvovirus B19 (B19V) is small non-enveloped, single-stranded DNA virus belong to genus Erythrovirus. B19V can cause erythema infectiosum (fifth disease), oligoarthritis, hydrops fetalis and a plastic crisis in patients with sickle cell anemia. A variety of vaccine strategies have been employed targeting immune responses. However their results were controversy with a limiting in availability of viral antigen. Since B19V replicates predominantly in erythroid progenitor cells of human bone marrow, this makes a peptide-based vaccines a promising strategy for development of vaccine against B19V with less allergenic and reactogenic responses. The aim of the present study was to design an efficient multi-epitope vaccine for human B19 virus using VP1 glycoprotein. **Material and method:** Thirty six sequences of VP1 glycoprotein were retrieved from NCBI database in December 2017 and aligned to determine the conservancy between the retrieved strains. The IEDB different analysis resources were used to predict epitopes that could act as promising peptides vaccine against parvovirus B19. The predicted epitopes were further assessed for population coverage against the whole world population. **Results:** The epitopes $_{214}$-PEVP-$_{217}$, $_{675}$-GLHQPPP-$_{681}$ and $_{554}$-SLRPGPVSQPYH-$_{565}$ were found to be the most potential epitopes against B cells. For the T cell three epitopes namely $_{155}$-FRYSQLAKL-$_{163}$, $_{302}$-CTISPIMGY-$_{310}$ and $_{316}$-YLDFNALNL-$_{324}$ showed high affinity to MHC-I alleles. The epitopes (core) $_{155}$-FRYSQLAKL-$_{163}$, $_{438}$-FYVLEHSSF-$_{446}$ and $_{404}$-WVYFPPQYA-$_{412}$ showed high affinity to interact with MHC-II alleles. $_{155}$-FRYSQLAKL-$_{163}$ and $_{438}$-FYVLEHSSF-$_{446}$ showed high coverage for whole world population with percentage of 99.73% and 94.85% respectively. **Conclusion:** This study proposed eight epitopes for B and T cells that could be a powerful multi epitope vaccine against B19V. Particular concern directed towards the epitope $_{155}$-FRYSQLAKL-$_{163}$ which demonstrated merits by reacting efficiently with both MHC-I and MHC-II alleles. Clinical trial is required to proof the efficacy of these epitopes as promising candidate vaccine against parvovirus B19.

Keywords: *Parvovirus B19, VP1 glycoprotein, NCBI, IEDB, Immunoinformatics*

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1. Introduction

Human parvovirus B19 (B19V) is a small, non-enveloped, single-stranded DNA virus, belongs to the genus Erythrovirus. The genus belongs to large family of Parvoviridae in which the word (parvum) means small. The family formed small capsids about 25 nm in diameter [1,2]. The first discovery of B19V was in 1975 and around 1980s scientist linked the B19V infection to certain disease like a plastic crisis and fifth disease (erythema infectiosum) [1,3,4]. B19V causes aplastic crisis in patients with shortened red cell survival due to induction of apoptosis in infected erythroid progenitors. Erythema infectiosum also known as slapped cheek (fifth disease). It can also causes oligoarthritis and hydrops fetalis or intrauterine death in infected fetuses [3,4]. The prevalence of B19V is highly common among children with sickle cell anemia and it leads to deaths due to acute and chronic anemia's (crisis episodes). Moreover the prevalence of B19V among pregnant women remains as a major cause of high maternal mortality especially in Sudan. [5,6,7]

Parvovirus B19 is transmitted by respiratory aerosol spread from individuals with acute infection, blood products and vertical transmission from mother to fetus. The majority of infections occur during childhood and the risk being greatest in the first two trimesters of pregnancy [1]. Regional epidemics occur during late winter and spring due to absence of a lipid envelope in the virus and their genomic stability which makes virus notoriously resistant to heat inactivation and solvent detergents [1,8,9,10]. This demonstrated seasonal variation in outbreak of the virus throughout the year and high prevalence among children and compromised and pregnant women [4,11,12].

The parvovirus B19 genome consists of a single

stranded linear molecule of 5596 nucleotides, composed of an internal coding sequence of 4830 nucleotides flanked by terminal repeat sequences of 383 nucleotides each. B19V contains two structural proteins, viral protein 1(VP1) and viral protein 2 (VP2). VP1differs from VP2 only in an N-terminal "unique region" composed of 227 additional amino acids which are mostly located outside the virion [1,2,13]. VP1 contains many linear epitopes recognized by neutralizing antibodies and accessible to antibody. This binding makes VP1 most fit capsid protein for designing a vaccine [1,14].

Till 1993 no human B19V vaccine is available. The development of such vaccine has been hampered by the limited availability of viral antigen since B19V replicates predominantly in Erythroid progenitor cells in human bone marrow. Moreover there is no convenient in vitro culture system available for routinely propagating large amounts of virus. However recently a recombinant design vaccine was established and their efficacy was controversial [15,16,17].

In this report we attempted to design a vaccine for human B19 virus using VP1 glycoprotein as an immunogen to invigorate protective immune response using immunoinformatics tools. The insilico prediction of epitopes for appropriate protein residues would help in production of peptide vaccine with intense immunogenic and insignificant allergenic impact that opposed to antibody creation that relies on biochemical examinations. The traditional vaccines can be costly, time consuming and not generally work. Moreover formulation of attenuated or inactivated form of microorganism contains a hundred of unnecessary proteins that induced immunity, allergenic or reactogenic responses [18,19,20].

2. Material and Methods

2.1. Protein Sequence Retrieval

A total of 36 strains of VP1 glycoprotein were retrieved from NCBI (https://www.ncbi.nlm.nih.gov/protein?term=Human+parvovirus+B19+VP1) in Dec 2017 from different parts of the word. The retrieved strains and their accession numbers were depicted in Table 1.

2.2. Phylogenetic Analysis

The retrieved sequences were subjected to phylogenetic analysis to determine the common ancestor of each strain using different tools from (http://www.phylogeny.fr) [21].

2.3. Determination of VP1 Conserved Regions

The retrieved sequences of VP1 strains were aligned to obtain conserved regions using multiple sequence alignment (MSA). Sequences were aligned with aid of the ClustalW as implemented in the BioEdit program, version 7.2.5 [22].

2.4. Epitopes Prediction

To detect the candidate epitopes from VP1 of Parvo virus B19, for B-lymphocytes and T-lymphocytes, several analysis prediction tools from Immune Epitope Database (IEDB) (http://www.iedb.org/) [22,23] were used.

2.4.1. B-cell Epitope Prediction

B cell epitope is the portion of an immunogen which interacts with B lymphocytes. B-lymphocytes upon exposure differentiated into plasma cells and memory cells. Thus B cells epitopes are shown to being accessible and antigenic [24]. Accordingly the classical propensity scale methods and hidden Markov model programmed software were used for the following aspects:

Table 1. The retrieved strains, accession numbers and area of collection. *Ref sequence

Accession number	Year of collection	Country
*AAV35057.1	2004	Germany
ABC87248.1	1998	Vietnam
ABC87243.1	2006	Vietnam
AAT67240.1	2004	Brazil
AKQ44382.1	2015	Brazil
AAB47464.1	1993	China
AAB47462.1	1994	China
AAB47460.1	1991	China
AAB47458.1	1992	Korea
AAB47456.1	1993	Japan
AAB47454.1	1993	USA(Georgia)
AAB47452.1	1994	USA(Alaska)
AAB47450.1	1988	USA(Virginia)
AAB47448.1	1991	United Kingdom
ALQ33061.1	2015	China
AIS74864.1	2014	USA
AIS74859.1	2013	USA
AIS74844.1	2014	USA(Kansas)
AIS74834.1	1994	USA(Colorado)
AII82175.1	2013	Germany
AII82172.1	2013	Germany(Bonn)
AAX83877.2	2005	Germany
AAS83528.2	2006	United Kingdom
ABB36730.2	2006	Ghana
ABB36727.2	2007	Ghana
ACJ61238.1	2008	Brazil
AAA83558.1	1995	USA
ACL36594.1	2008	USA
ABC02066.2	1998	Germany
AIK97781.1	1981	Japan
AIK97776.1	1987	Japan
AAC99438.1	1988	Japan
BAA90267.1	2004	Germany
AAT84710.1	2009	Belgium
AAT84707.1	2004	Japan
CBI63313.1	1999	Japan

2.4.1.1. Prediction of Linear B-cell Epitopes

BepiPred from immune epitope database (http://toolsiedb.ofg/bcell/) [25] was used as a linear B-cell epitopes prediction from the conserved region of VP1 glycoprotein with a default threshold value of 0.5.

2.4.1.2. Prediction of surface accessibility:-

Emini surface accessibility prediction tool of the immune epitope database (IEDB) was used

(http://tools.immuneepitope.org/tools/bcell/iedb) [26]. The surface accessible epitopes were predicted from the conserved region of VP1 glycoprotein with default threshold value 1.000.

2.4.1.3. Prediction of Epitopes Antigenicity

The kolaskar and tongaonker antigenicity method was used to determine the antigenic sites with a default threshold value of 1.025 (http://tools.immuneepitope.org/bcell/) [27].

2.4.2. T-cell Epitopes Prediction

2.4.2.1. MHC Class I Binding Predictions

Analysis of peptide binding to MHC class I molecules was assessed by the IEDB MHC-I prediction tool at (http://tools.iedb.org/mhci/n). MHC-I peptide complex presentation to T-lymphocytes underwent several steps. For instance the attachment of cleaved peptides to MHC-1 molecules was predicted by Artificial Neural Network (ANN) [28,29,30]. Also all epitopes lengths were set as 9 mers. Besides, all the conserved epitopes that bind to alleles at score equal to or less than 100 half-maximal inhibitory concentrations (IC-50) were selected for further analysis [31].

2.4.2.2. MHC Class II Binding Predictions

Analysis of peptide binding to MHC class II molecules was assessed by the IEDB MHC II prediction tool at (http://tools.immuneepitope.org/mhcii/) [32,33]. For MHC-II binding prediction, human allele references set were used. MHC class II groove has the ability to bind peptides with different lengths. Therefore for the analysis, the NN-align as prediction method from IEDB MHC-II prediction tool were used. It allows for identification of the MHC class II binding core and epitopes binding affinity All conserved epitopes that bind to many alleles at score equal or less than 500 half-maximal inhibitory concentrations (IC-50) were selected for further analysis.

2.5. Population Coverage Calculation

For the calculation of the population coverage for all potential MHC-I and II epitopes bindings, the IEDB tools (http://tools.iedb.org/tools/population/iedb_input) [34] was used. The VP1 glycoprotein of B19V was assessed for population coverage against the whole world with selected MHC-I and MHC-II interacted alleles.

2.6. Homology Modeling

Raptor X protein structure prediction server (http://raptorx.uchicago.edu/StructurePrediction/predict/) was used for creation the 3D structure of the VP1 glycoprotein of B19 virus. The reference sequence [AAV35057.1] was used as an input and Chimera 1.8 was used as a tool to visualize the selected epitopes belonging to B cell and T cell (MHC-I and MHC-II). Homology modeling was used for visualization of the surface accessibility of the B lymphocytes predicted candidate epitopes as well as for visualization of all predicted T cell epitopes in the structural level.

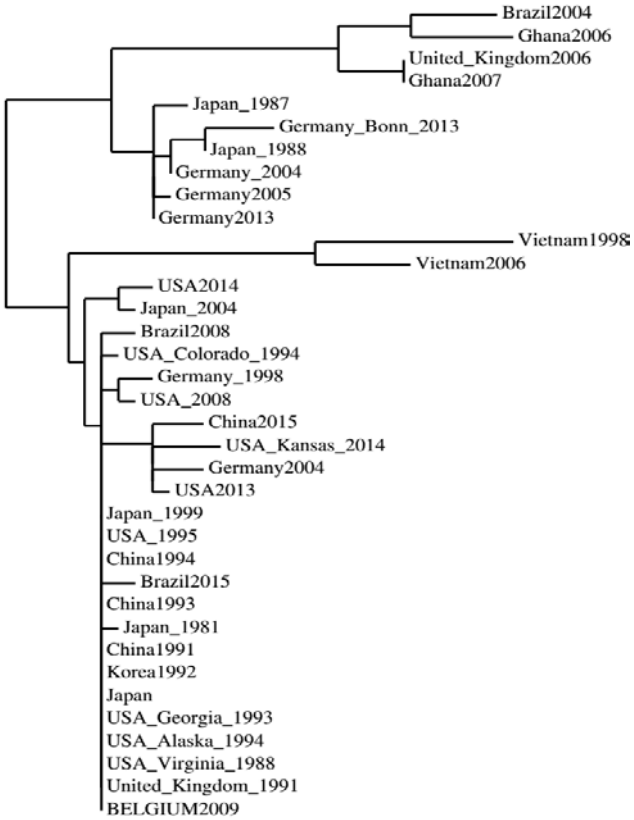

Figure 1. Cladogram showed the relationship between the different VP1 glycoprotein strains

3. Results

3.1. Phylogenetic Evolution of the Retrieved Strains

All retrieved strains were representing in phylogenic tree Figure 1. From the figure the Germany and Japan strains share common ancestor. Also Ghana, Brazil and United Kingdom shared common ancestor. Also in another site USA, Japan, China, Korea, German, United Kingdom and Belgium shared common ancestor.

3.2. Alignment

Multiple sequence alignment was represented in Figure 2. Sequence alignment showed that some regions were mutated region, and dots show the conservancy between different retrieved sequences of the strains.

3.3. Prediction of B-cell Epitope

The reference sequence of the viral protein (VP1) was subjected to Bepipred linear epitope, Emini surface accessibility and Kolaskar and Tongaonkar antigenicity methods in IEDB to predict the likelihood of specific regions in the protein that bind to B cell receptor, being in the surface and immunogenic respectively. The thresholds of Bepipred linear epitope, Emini surface accessibility and Kolaskar and Tongaonkar antigenicity were shown in Figure 3. For Bepipred linear epitope prediction

method, the average binding score of viral protein to B cell was 0.5. Fifty two epitopes were predicted as a linear epitopes and only 23 epitopes were conserved regions. Emini surface accessibility provided only thirteen epitopes that were potentially predicted on surface by passing the default threshold 1.000. Kolaskar and Tongaonkar antigenicity provided only eight epitopes that gave score above the default threshold 1.025. All the epitopes predicted by these different tools against B cell were provided in Table 2. Accordingly three conserved epitopes were successfully predicted to elicit the B cell lymphocytes since they were conserved among all retrieved strains, got higher score values in Emini surface accessibility and Kolaskar and Tongaonkar antigenicity prediction methods. These three epitopes were $_{214}$PEVP$_{217}$, $_{675}$GLHQPPP$_{681}$ and $_{554}$SLRPGPVSQPYH$_{565}$. The three dimension structural (3D) level of these epitopes was shown in Figure 4.

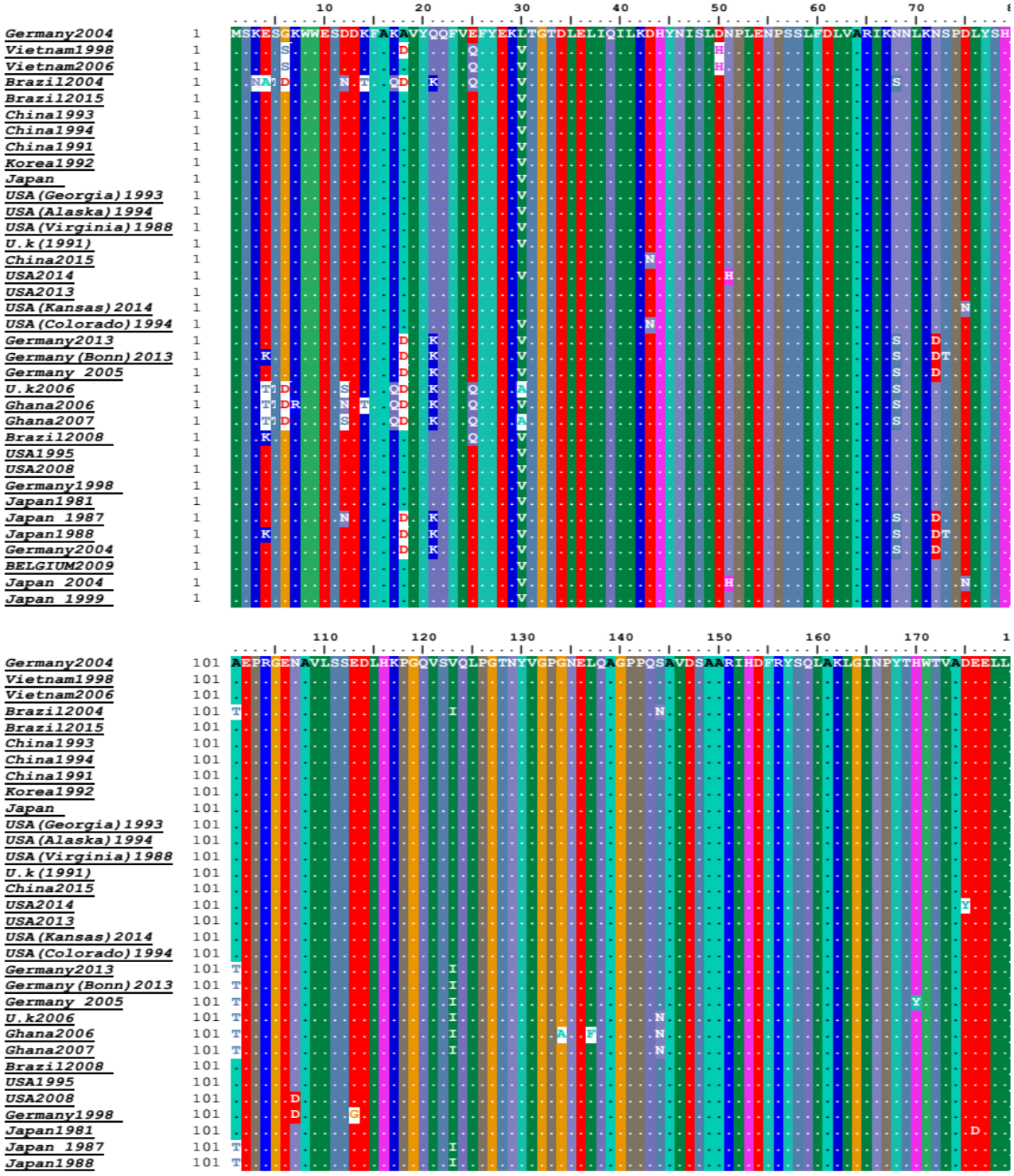

Figure 2. Multiple sequence alignment for a part of the retrieved strains for the most mutated regions. Dots showed the conservancy between the aligned sequences

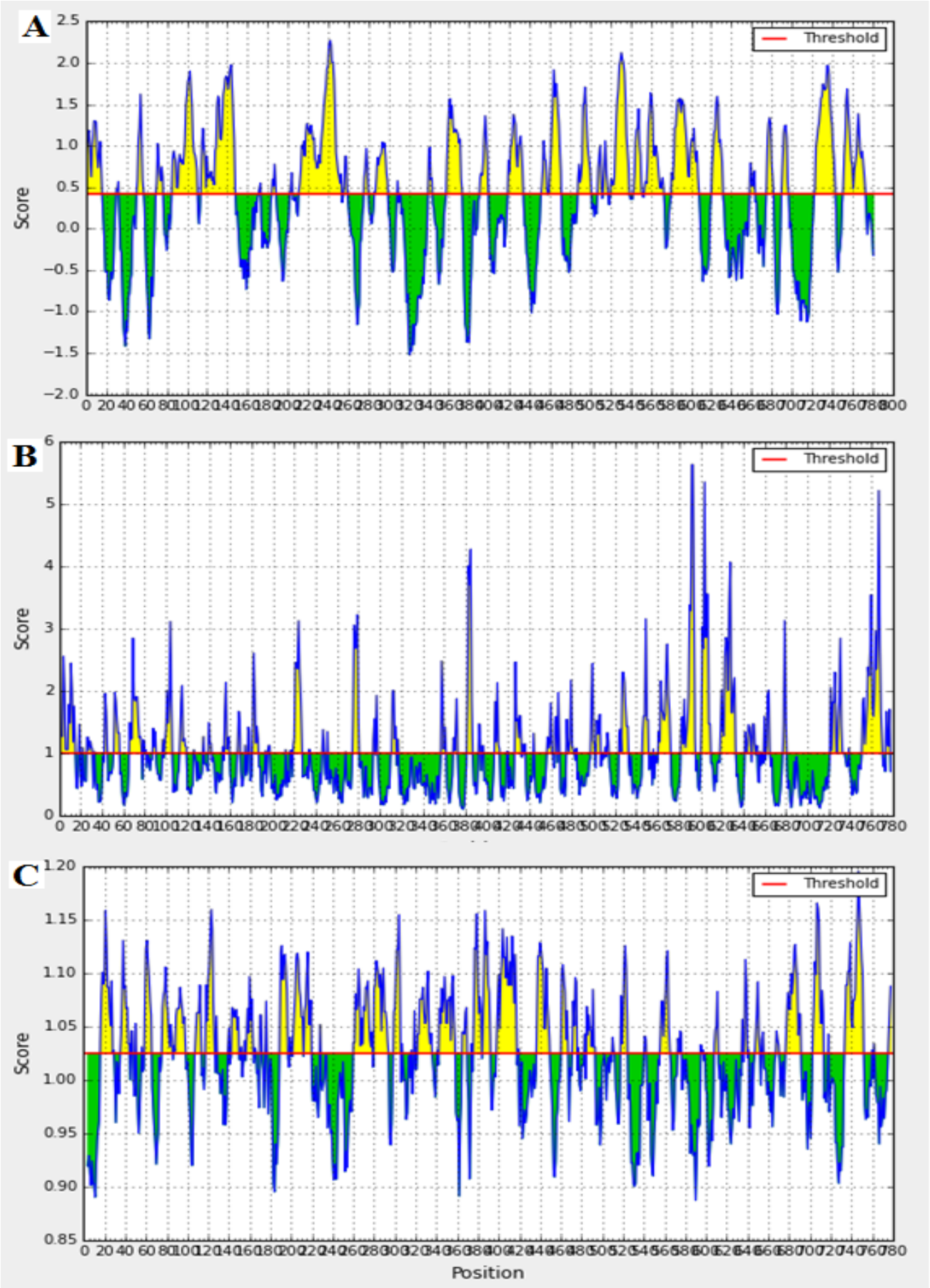

Figure 3. Prediction of B-cell epitopes by different IEDB scales (**A-** Bepipred linear epitope prediction, **B-** Emini surface accessibility, **C-** Kolaskar and Tongaonkar antigenicity prediction). Regions above threshold (red line) are proposed to be a part of B cell epitope while regions below the threshold (red line) are not

Table 2. B-cell epitopes prediction, the position of peptides is according to the position of amino acids in the VP1 of the B19V

Peptide	Start	End	Length	Emini [a]	Kolaskar [b]
KWWES	7	11	5	1.377	0.916
EPRGE	102	106	5	2.413	0.903
QLPGTN	124	129	6	1.052	0.981
QLPGTNYV	124	130	8	0.734	1.054
ETGF	185	188	4	0.745	0.931
PEVP	214	217	4	1.069	1.091
PSMTSVNS	226	233	8	0.789	0.999
GAGGGGSN	239	246	8	0.257	0.903
PAASSCHNASGKEA	286	299	14	0.417	1.022
DSKKLAS	427	433	7	1.607	1.009
SKKLAS*	428	433	6	1.241	1.033
LGVP	488	491	4	0.326	1.143
HAIQ	508	511	4	0.58	1.084
QNFMP	513	517	5	0.99	0.954
SLRPGPVSQPYH	554	565	12	1.296	1.073
WDTDKYV	567	573	7	1.582	1.001
QGVGRFP	596	602	7	0.531	1.025
PNKGTQQYTDQ	621	631	11	8.011	0.958
NLDDS	659	663	5	1.33	0.954
GLHQPPP	675	681	7	1.143	1.062
SGPIGG	691	696	6	0.292	0.975
RKATGRWNPQPGVYPP	724	739	16	3.418	0.993
EKPEELWT	766	773	8	2.5	0.95

*peptides revealed higher score if they were shorten in all tools.
a: default threshold value 1.000
b: default threshold value 1.025

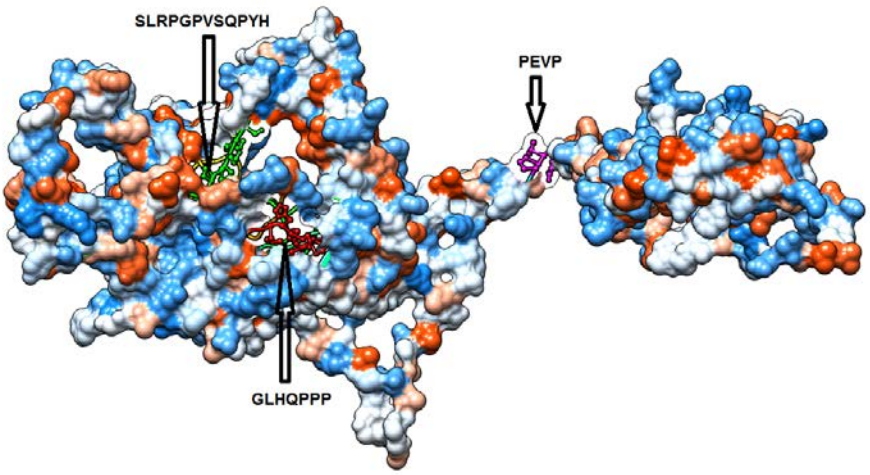

Figure 4. Position of proposed conserved B cell epitopes in structural level of VP1 protein of parvovirus B19. The three predicted epitopes were shown to interact with B cell and showed conservancy, surface accessibility and antigenicity using IEDB software

3.4. T lymphocytes Epitopes Binding Prediction

3.4.1. MHC-I Binding Predictions

The reference structural protein (VP1) was analyzed using IEDB MHC-1 binding prediction tool to predict T cell epitopes interacting with different types of MHC-I alleles. Thirty three conserved peptides were predicted to interact with different MHC-1 alleles. The peptide $_{155}$-FRYSQLAKL-$_{163}$ had higher affinity to interact with 6 alleles, followed by $_{302}$-CTISPIMGY-$_{310}$ that interacted with four alleles and $_{316}$-YLDFNALNL-$_{324}$ that interacted with only two alleles as shown in Table 3. These three epitopes and their positions in structural level of VP1 were shown in Figure 5. The thirty three conserved peptides and their interaction with different MHC-1 alleles were supplemented in an extra sheet 1.

Table 3. List of top epitopes that had binding affinity with MHC-I alleles. The position of peptides is according to position of amino acids in VPI protein of B19 V

Peptide	Start	End	Allele	IC50
FRYSQLAKL	155	163	HLA-B*27:05	17.35
			HLA-B*39:01	57.21
			HLA-C*06:02	29.82
			HLA-C*07:01	29.76
			HLA-C*07:02	79.84
			HLA-C*14:02	92.13
CTISPIMGY	302	310	HLA-A*11:01	84.4
			HLA-A*26:01	8.53
			HLA-A*26:01	8.53
			HLA-A*29:02	81.8
YLDFNALNL	316	324	HLA-A*02:01	23.31
			HLA-C*05:01	67.14

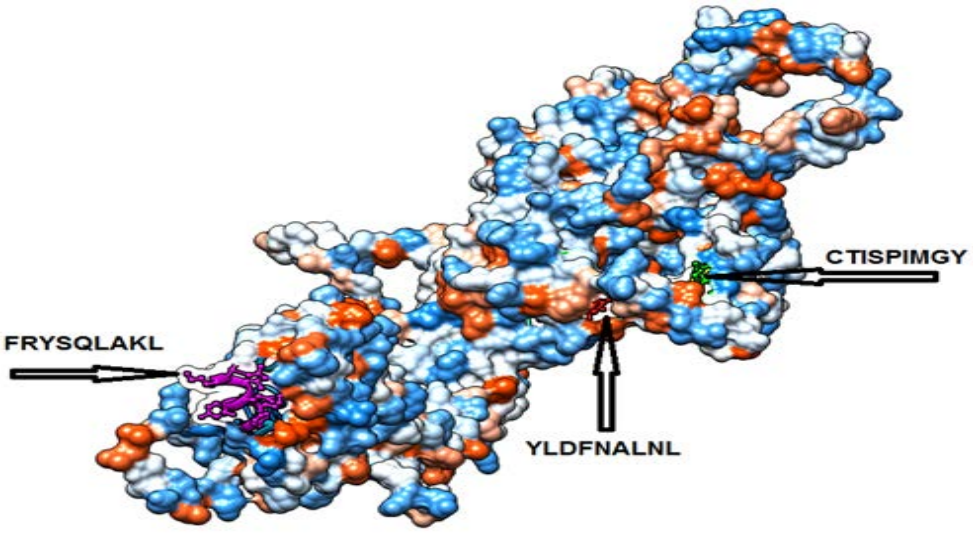

Figure 5. Position of proposed conserved T cell epitopes that interact with MHC-I in structural level of glycoprotein of VP1

3.4.2. MHC-II Binding Predictions

Seventy nine (79) conserved epitopes were predict from reference viral protein (VP1) which have ability to interact with MHC-II alleles. As shown in Table 4, three peptides (core) $_{155}$-FRYSQLAKL-$_{163}$, $_{438}$-FYVLEHSSF-$_{446}$ and $_{404}$-WVYFPPQYA-$_{412}$ demonstrated higher affinity to interact with MHC-II alleles. The three dimensional structural level (3D) of these epitopes within VP 1 protein was shown in Figure 6. The other core epitopes and their corresponding alleles that interacted with MHC-II were supplemented in an extra sheet- 2.

Table 4. List of top three epitopes that had binding affinity with the MHC Class II alleles .The position of peptides is according to position of amino acids in VPI protein of B19 V

Sequence Core	Peptide Sequence	Start	End	Allele	IC50
FRYSQLAKL	AARIHDFRYSQLAKL	149	163	HLADPA1*03:01/DPB1*04:02	14.7
				HLADPA1*01:03/DPB1*02:01	14.1
				HLADPA1*02:01/DPB1*01:01	7.6
				HLADPA1*03:01/DPB1*04:02	14.7
				HLADQA1*05:01/DQB1*03:01	141.5
				HLA-DRB1*01:01	16
				HLA-DRB1*03:01	375.8
				HLA-DRB1*04:01	301.1
				HLA-DRB1*04:05	137.2
				HLA-DRB1*07:01	9.5
				HLA-DRB1*08:02	263.9
				HLA-DRB1*09:01	26.4
				HLA-DRB1*11:01	110.6
				HLA-DRB1*13:02	460.2
				HLA-DRB3*01:01	257.1
				HLA-DRB5*01:01	20.8
	ARIHDFRYSQLAKLG	150	164	HLADPA1*01:03/DPB1*02:01	13.9
				HLADPA1*02:01/DPB1*01:01	7.6
				HLADQA1*05:01/DQB1*03:01	117.5
				HLA-DRB1*01:01	12.2
				HLA-DRB1*03:01	435.2
				HLA-DRB1*04:01	210.6
				HLA-DRB1*04:04	385.6
				HLA-DRB1*04:05	156.7
				HLA-DRB1*07:01	10.7
				HLA-DRB1*08:02	207.6
				HLA-DRB1*09:01	23.1
				HLA-DRB1*11:01	77.2
				HLA-DRB1*13:02	453.6
				HLA-DRB3*01:01	286.2
				HLA-DRB5*01:01	23.1
	RIHDFRYSQLAKLGI	151	165	HLADPA1*03:01/DPB1*04:02	7.5
				HLADPA1*01:03/DPB1*02:01	12.3
				HLADPA1*02:01/DPB1*01:01	7

Sequence Core	Peptide Sequence	Start	End	Allele	IC50
				HLADPA1*02:01/DPB1*05:01	414.6
				HLADPA1*03:01/DPB1*04:02	7.5
				HLADQA1*05:01/DQB1*03:01	122.9
				HLA-DRB1*01:01	8.7
				HLA-DRB1*03:01	338.1
				HLA-DRB1*04:01	175.6
				HLA-DRB1*04:04	247.9
				HLA-DRB1*04:05	133.8
				HLA-DRB1*07:01	7.7
				HLA-DRB1*08:02	194.7
				HLA-DRB1*09:01	17.5
				HLA-DRB1*11:01	29.1
				HLA-DRB1*13:02	334.1
				HLA-DRB3*01:01	253.8
				HLA-DRB5*01:01	20.1
	IHDFRYSQLAKLGIN	152	166	HLADPA1*03:01/DPB1*04:02	8
				HLADPA1*01:03/DPB1*02:01	14.6
				HLADPA1*02:01/DPB1*01:01	8
				HLADPA1*02:01/DPB1*05:01	444.5
				HLADPA1*03:01/DPB1*04:02	8
				HLADQA1*05:01/DQB1*03:01	104.7
				HLA-DRB1*01:01	7.7
				HLA-DRB1*03:01	353.3
				HLA-DRB1*04:01	195
				HLA-DRB1*04:04	238.5
				HLA-DRB1*04:05	146.7
				HLA-DRB1*07:01	8.6
				HLA-DRB1*08:02	288.4
				HLA-DRB1*09:01	14.6
				HLA-DRB1*13:02	323.5
				HLA-DRB3*01:01	272.4
				HLA-DRB5*01:01	21.3
	HDFRYSQLAKLGINP	153	167	HLADPA1*03:01/DPB1*04:02	10.8
				HLADPA1*01:03/DPB1*02:01	19
				HLADPA1*02:01/DPB1*01:01	12.9
				HLADPA1*03:01/DPB1*04:02	10.8
				HLADQA1*05:01/DQB1*03:01	120.4
				HLA-DRB1*01:01	11.2
				HLA-DRB1*04:04	224.3
				HLA-DRB1*04:05	211.1
				HLA-DRB1*07:01	11.8
				HLA-DRB1*08:02	381.5
				HLA-DRB1*09:01	16.9
				HLA-DRB5*01:01	33.2
	DFRYSQLAKLGINPY	154	168	HLADPA1*03:01/DPB1*04:02	16.2
				HLADPA1*01:03/DPB1*02:01	37.2
				HLADPA1*02:01/DPB1*01:01	29.4
				HLADPA1*03:01/DPB1*04:02	16.2
				HLADQA1*05:01/DQB1*03:01	274.7
				HLA-DRB1*01:01	15.7
				HLA-DRB1*04:04	208.2
				HLA-DRB1*04:05	125.9
				HLA-DRB1*07:01	17.1
				HLA-DRB1*09:01	20
				HLA-DRB5*01:01	51.9
	FRYSQLAKLGINPYT	155	169	HLADPA1*03:01/DPB1*04:02	122.8
				HLADPA1*01:03/DPB1*02:01	211.3
				HLADPA1*02:01/DPB1*01:01	142.6
				HLADPA1*03:01/DPB1*04:02	122.8
				HLA-DRB1*01:01	18.1
				HLA-DRB1*04:04	170.5
				HLA-DRB1*07:01	20.9
				HLA-DRB1*09:01	36.4
				HLA-DRB5*01:01	73.6

Sequence Core	Peptide Sequence	Start	End	Allele	IC50
FYVLEHSSF	ASEESAFYVLEHSSF	432	446	HLADPA1*01:03/DPB1*02:01	64.1
				HLA-DRB1*01:01	62.2
				HLA-DRB1*04:01	304.9
				HLA-DRB1*04:05	35.2
				HLA-DRB1*07:01	261.9
				HLA-DRB1*11:01	322.8
				HLA-DRB3*01:01	89.2
	SEESAFYVLEHSSFQ	433	447	HLADPA1*01:03/DPB1*02:01	51.8
				HLA-DRB1*01:01	26.5
				HLA-DRB1*04:05	24.5
				HLA-DRB1*11:01	133.2
				HLA-DRB3*01:01	57.4
	EESAFYVLEHSSFQL	434	448	HLADPA1*01:03/DPB1*02:01	30.7
				HLADPA1*02:01/DPB1*01:01	36.9
				HLA-DRB1*01:01	11
				HLA-DRB1*04:05	19.5
				HLA-DRB1*09:01	243.5
				HLA-DRB1*11:01	63
				HLA-DRB3*01:01	49
	ESAFYVLEHSSFQLL	435	449	HLA-DRB1*01:01	6.6
				HLA-DRB1*04:05	17.5
				HLA-DRB1*09:01	195.5
				HLA-DRB1*11:01	35.3
				HLA-DRB3*01:01	44
	SAFYVLEHSSFQLLG	436	450	HLA-DRB1*01:01	7.5
				HLA-DRB1*04:05	20.4
				HLA-DRB1*09:01	228
				HLA-DRB1*11:01	41.8
	AFYVLEHSSFQLLGT	437	451	HLA-DRB1*01:01	10.3
				HLA-DRB1*04:05	30.2
				HLA-DRB1*11:01	64
	FYVLEHSSFQLLGTG	438	452	HLA-DRB1*01:01	16.3
				HLA-DRB1*11:01	117.1
WVYFPPQYA	APELPIWVYFPPQYA	398	412	HLADPA1*01:03/DPB1*02:01	311.4
				HLA-DRB1*01:01	10.5
				HLA-DRB1*04:05	385.1
				HLA-DRB1*07:01	393.1
	PELPIWVYFPPQYAY	399	413	HLADPA1*01:03/DPB1*02:01	176.2
				HLADPA1*02:01/DPB1*01:01	170.8
				HLA-DRB1*01:01	6.6
				HLA-DRB1*04:05	340.2
				HLA-DRB1*07:01	390.6
	ELPIWVYFPPQYAYL	400	414	HLADPA1*02:01/DPB1*01:01	94.6
				HLA-DRB1*01:01	4.9
				HLA-DRB1*04:05	301
				HLA-DRB1*07:01	287.6
				HLA-DRB1*11:01	437.9
				HLA-DRB5*01:01	471.8
	LPIWVYFPPQYAYLT	401	415	HLADPA1*02:01/DPB1*01:01	55.4
				HLADQA1*05:01/DQB1*03:01	423.9
				HLA-DRB1*01:01	4.5
				HLA-DRB1*04:05	328.6
				HLA-DRB1*07:01	380.3
				HLA-DRB1*11:01	310.4
				HLA-DRB5*01:01	288.8
	PIWVYFPPQYAYLTV	402	416	HLADQA1*05:01/DQB1*03:01	425.9
				HLA-DRB1*01:01	5.3
				HLA-DRB1*04:05	450.6
				HLA-DRB1*11:01	437.7
				HLA-DRB5*01:01	321.4
	IWVYFPPQYAYLTVG	403	417	HLA-DRB1*01:01	5.9
				HLA-DRB1*09:01	39.3
	WVYFPPQYAYLTVGD	404	418	HLADPA1*02:01/DPB1*01:01	121.4
				HLA-DRB1*01:01	8
				HLA-DRB1*15:01	132.8

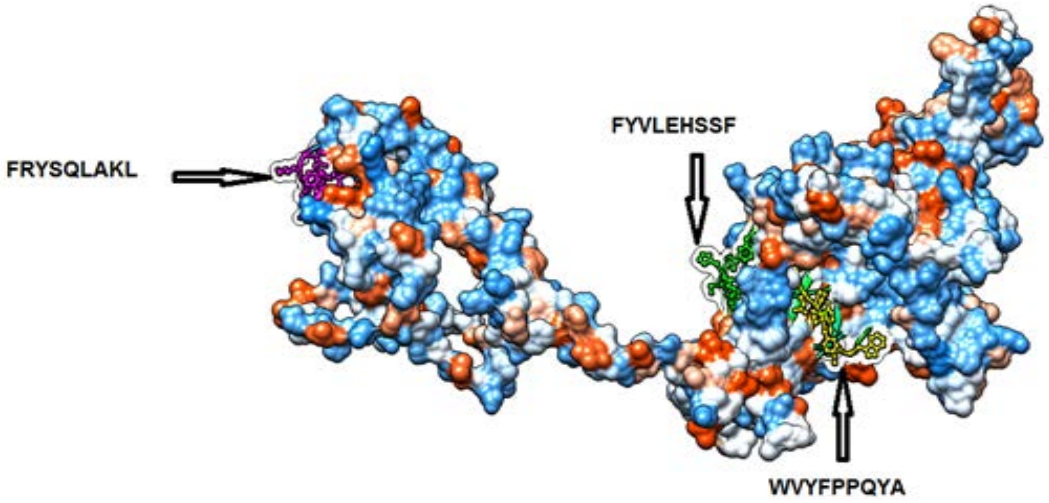

Figure 6. Position of proposed conserved T cell epitopes that interact with MHC-II

Table 5. The population coverage against the whole world for the predicted epitopes. The overall population coverage epitope set for predicted epitopes in MHC-1 was 76.36% and for MHC-11 was 99.44%.

Epitope	Coverage Class I	Total HLA Hits	Epitope	Coverage Class II	Total HLA Hits
FRYSQLAKL	56.26%	6	FRYSQLAKL	99.37%	20
YLDFNALNL	43.86%	2	FYVLEHSSF	94.85%	11
Epitope set	76.36%		**Epitope set**	99.44%	

3.5. Analysis of the Population Coverage

As shown in Table 5 two epitopes, $_{155}$FRYSQLAKL$_{163}$ and $_{316}$YLDFNALNL$_{324}$, interacted with most frequent MHC-I alleles and they demonstrated population coverage against the whole world 56.26% and 43.86% respectively. Two epitopes, $_{155}$FRYSQLAKL$_{163}$ and $_{438}$FYVLEHSSF$_{446}$, demonstrated population coverage against the whole world 99.37% and 94.85% respectively against MHC-II. Interestingly the epitope $_{155}$FRYSQLAKL$_{163}$ was shown to interact with both MHC-I and MHC-II alleles. As shown in Table 6 the overall epitope sets for the predicted epitopes against MHC-I and MHC-II alleles was 99.44%.

Table 6. The population coverage against the whole world for the predicted epitopes against both MHC-1 and MHC-11. The overall population coverage epitope set for predicted epitopes is 99.87%

Epitope	Coverage Class I&II	Total HLA Hits
FRYSQLAKL	99.73%	26
FYVLEHSSF	94.85%	11
YLDFNALNL	43.86%	2
Epitope set	99.87%	

4. Discussion

Recently there have been considerable efforts toward developing a synthetic peptide vaccines which include B and T cell epitopes that could potentially lead to improved vaccination against parvovirus B19 [35,36,37]. Many recombinants B19 parvovirus capsids of various structural protein compositions like VP1 & VP2 were evaluated as vaccine. Other studies used virus-like particles (VLPs) by mix VP1 and VP2 with specific ratio which gives antibody levels similar to those elicited by infection but it caused significant reactogenicity like headache, fever, gastrointestinal related distress and fatigue [37,38].

To our knowledge, there is no peptide prediction has been conducted specifically for B19V with a good immune response and less immunological side effect. In this study we determine a 100% conserved regions which are then investigated to predict the highly potential immunogenic epitopes for both B and T cells using VP1 capsid protein. VP1 has been proposed from different study as a good candidate protein for vaccine against B19V [2,38]. Our results revealed that all the proposed epitopes for B cell were above threshold scores in Bepipred linear epitope, Emini surface accessibility and Kolaskar and Tongaonkar antigenicity using prediction methods in IEDB. One of the promising predicted epitopes was $_{214}$PEVP$_{217}$. This tetra peptide probably activating humeral immune response as it is part of VP1 capsid protein. [39]

Since the immune response of T cell is long lasting response comparing with B cell, where the antigen can easily escape the antibody memory response and considering that $CD8^+$T and $CD4^+$T cell responses play a major role in antiviral immunity [40]. Many peptides were proposed by this study that binds to MHC-I molecules (Table 3). All the proposed epitopes were interacted with MHC-I exceeding the thresholds. Moreover the epitope $_{155}$FRYSQLAKL$_{163}$ binds to six alleles with worldwide population coverage 56.26% to MHC-I alleles. This finding is not consistent with another study which proposed a single HLAB 35-restricted peptide (QPTRVDQKM) to stimulate immunity [41] however this study recommended further mapping down to the epitopes restricted to MHC-I [41].

For MHC-II ($CD4^+$) three peptides were proposed ($_{438}$-FYVLEHSSF-$_{446}$, $_{404}$-WVYFPPQYA-$_{412}$ and $_{155}$-FRYSQLAKL-$_{163}$) that they bound successfully to many HLA alleles of MHC-II (Table 4). These peptides were above proposed thresholds as well as they have higher population coverage. One of the most promising and interested finding of this study was that the epitope $_{155}$-FRYSQLAKL-$_{163}$ was shared in both MHC-I & II as well as it has population coverage of 99.73%.

5. Conclusion

Parvo virus (B19V) has high prevalence among children and due to it is vertical transmission from mother to fetus which lead to fetal loss, developing of a vaccine with less immunological side effect remains a challenging issue. In this study we proposed many peptides that could be a powerful multi epitopes vaccine against B19V especially the peptide $_{155}$-FRYSQLAKL-$_{163}$ which interacted against both MHC-I & II. To determine the efficacy of these proposed epitopes clinical trials is required.

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Competing Interest

The authors declare that they have no competing interest.

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EXTRA SHEET

Core Sequence	Peptides	Start	End	Alleles	IC50
AARIHDFRY	VDSAARIHDFRYSQL	146	160	HLA-DRB5*01:01	381.4
	SPAASSCHNASGKEA	285	299	HLA-DQA1*05:01/DQB1*03:01	288.3
AASSCHNAS	PAASSCHNASGKEAK	286	300	HLA-DQA1*05:01/DQB1*03:01	208.7
	AASSCHNASGKEAKV	287	301	HLA-DQA1*05:01/DQB1*03:01	172.9
				HLA-DPA1*01:03/DPB1*02:01,	214.4
	LASEESAFYVLEHSS	431	445	HLA-DRB1*04:05	271
				HLA-DPA1*02:01/DPB1*01:01	90.9
AFYVLEHSS	ASEESAFYVLEHSSF	432	446	HLA-DPA1*02:01/DPB1*01:01	90.9
	SEESAFYVLEHSSFQ	433	447	HLA-DPA1*02:01/DPB1*01:01	64.4
	ESAFYVLEHSSFQLL	435	449	HLA-DRB4*01:01	424
	SAFYVLEHSSFQLLG	436	450	HLA-DRB4*01:01	336
	AFYVLEHSSFQLLGT	437	451	HLA-DRB4*01:01	394.4
	KEAKVCTISPIMGYS	297	311	HLA-DRB4*01:01	444
AKVCTISPI	EAKVCTISPIMGYST	298	312	HLA-DRB4*01:01	358.7
	AKVCTISPIMGYSTP	299	313	HLA-DRB4*01:01	307.5
	FKTQFAALGGWGLHQ	664	678	HLA-DQA1*05:01/DQB1*03:01	82.9
ALGGWGLHQ	AALGGWGLHQPPPQI	669	683	HLA-DQA1*05:01/DQB1*03:01	173.1
	ALGGWGLHQPPPQIF	670	684	HLA-DQA1*05:01/DQB1*03:01	209.9
	SSCHNASGKEAKVCT	289	303	HLA-DQA1*05:01/DQB1*03:01	159.3
	CHNASGKEAKVCTIS	291	305	HLA-DQA1*05:01/DQB1*03:01	167.8
ASGKEAKVC	HNASGKEAKVCTISP	292	306	HLA-DQA1*05:01/DQB1*03:01	212.7
	NASGKEAKVCTISPI	293	307	HLA-DQA1*05:01/DQB1*03:01	266.7
	ASGKEAKVCTISPIM	294	308	HLA-DQA1*05:01/DQB1*03:01	363.9
	PQSAVDSAARIHDFR	142	156	HLA-DQA1*05:01/DQB1*03:01	45.5
AVDSAARIH	QSAVDSAARIHDFRY	143	157	HLA-DQA1*05:01/DQB1*03:01	78.3
	SAVDSAARIHDFRYS	144	158	HLA-DQA1*05:01/DQB1*03:01	80.1
	AVDSAARIHDFRYSQ	145	159	HLA-DQA1*05:01/DQB1*03:01	154.7
CHNASGKEA	ASSCHNASGKEAKVC	288	302	HLA-DQA1*05:01/DQB1*03:01	156.3
	GKEAKVCTISPIMGY	296	310	HLA-DQA1*01:02/DQB1*06:02	155.8
	KEAKVCTISPIMGYS	297	311	HLA-DQA1*01:02/DQB1*06:02	148.2
CTISPIMGY	EAKVCTISPIMGYST	298	312	HLA-DQA1*01:02/DQB1*06:02	114.9
	AKVCTISPIMGYSTP	299	313	HLA-DQA1*01:02/DQB1*06:02	133
	KVCTISPIMGYSTPW	300	314	HLA-DQA1*01:02/DQB1*06:02	196.5
	VCTISPIMGYSTPWR	301	315	HLA-DQA1*01:02/DQB1*06:02	288.1
	SAARIHDFRYSQLAK	148	162	HLA-DPA1*03:01/DPB1*04:02	127.9
DFRYSQLAK	ARIHDFRYSQLAKLG	150	164	HLA-DPA1*03:01/DPB1*04:02	11.8
	ARIHDFRYSQLAKLG	150	164	HLA-DPA1*03:01/DPB1*04:02	11.8
	HEDHAIQPQNFMPGP	505	519	HLA-DRB4*01:01	465.8
DHAIQPQNF	EDHAIQPQNFMPGPL	506	520	HLA-DRB4*01:01	361.4
	DHAIQPQNFMPGPLV	507	521	HLA-DRB4*01:01	328.3
DPKFRSLTH	DPKFRSLTHEDHAIQ	497	511	HLA-DRB4*01:01	353.1
DQIERPLMV	GTQQYTDQIERPLMV	624	638	HLA-DRB1*07:01	307.3
	TQQYTDQIERPLMVG	625	639	HLA-DRB1*07:01	480.6

	QYTDQIERPLMVGSV	627	641	HLA-DRB1*01:01	88.7
	YTDQIERPLMVGSVW	628	642	HLA-DRB1*01:01	204.1
	TDQIERPLMVGSVWN	629	643	HLA-DRB1*01:01	388.3
	PPQSAVDSAARIHDF	141	155	HLA-DQA1*01:02/DQB1*06:02	478.2
DSAARIHDF	PQSAVDSAARIHDFR	142	156	HLA-DQA1*01:02/DQB1*06:02	394.5
	QSAVDSAARIHDFRY	143	157	HLA-DQA1*01:02/DQB1*06:02	400.3
DTLAPELPI	QGQDTLAPELPIWVY	392	406	HLA-DRB1*01:01	264.4
	GQDTLAPELPIWVYF	393	407	HLA-DRB1*01:01	385.3
	SKKLASEESAFYVLE	428	442	HLA-DQA1*03:01/DQB1*03:02	96.7
	KKLASEESAFYVLEH	429	443	HLA-DQA1*03:01/DQB1*03:02	84
	KLASEESAFYVLEHS	430	444	HLA-DQA1*03:01/DQB1*03:02	93
	LASEESAFYVLEHSS	431	445	HLA-DQA1*03:01/DQB1*03:02	101.6
				HLA-DQA1*04:01/DQB1*04:02	280.1
EESAFYVLE	ASEESAFYVLEHSSF	432	446	HLA-DQA1*03:01/DQB1*03:02	128.9
		432	446	HLA-DQA1*04:01/DQB1*04:02	344.3
	SEESAFYVLEHSSFQ	433	447	HLA-DQA1*03:01/DQB1*03:02	168.9
				HLA-DQA1*04:01/DQB1*04:02	421.1
	EESAFYVLEHSSFQL	434	448	HLA-DQA1*03:01/DQB1*03:02	203.8
				HLA-DQA1*04:01/DQB1*04:02	488.9
	TDQIERPLMVGSVWN	629	643	HLA-DQA1*05:01/DQB1*03:01	478.7
ERPLMVGSV	DQIERPLMVGSVWNR	630	644	HLA-DRB1*01:01	253.2
	QIERPLMVGSVWNRR	631	645	HLA-DRB1*01:01	275.1
	IERPLMVGSVWNRRA	632	646	HLA-DRB1*01:01	308.8
ESAFYVLEH	KKLASEESAFYVLEH	429	443	HLA-DQA1*04:01/DQB1*04:02	266.7
	KLASEESAFYVLEHS	430	444	HLA-DQA1*04:01/DQB1*04:02	274.3
	MLVDHEYKYPYVLGQ	378	392	HLA-DPA1*03:01/DPB1*04:02	361.6
	LVDHEYKYPYVLGQG	379	393	HLA-DPA1*03:01/DPB1*04:02	304.4
	LVDHEYKYPYVLGQG			HLA-DRB1*01:01	480.1
FAALGGWGL	VDHEYKYPYVLGQGQ	380	394	HLA-DPA1*03:01/DPB1*04:02	211.1
	VDHEYKYPYVLGQGQ			HLA-DRB1*01:01	382.7
	DHEYKYPYVLGQGQD	381	395	HLA-DPA1*03:01/DPB1*04:02	274
	DHEYKYPYVLGQGQD			HLA-DRB1*01:01	450.1
	HEYKYPYVLGQGQDT	382	396	HLA-DPA1*03:01/DPB1*04:02	394
				HLA-DQA1*05:01/DQB1*03:01	467.9
				HLA-DRB1*01:01	13.1
	PNLDDSFKTQFAALG	658	672	HLA-DRB1*04:01	177.9
				HLA-DRB1*04:05	175.7
				HLA-DRB1*09:01	52.6
				HLA-DRB5*01:01	154.9
				HLA-DQA1*05:01/DQB1*03:01	442.9
				HLA-DRB1*01:01	10.2
				HLA-DRB1*04:01	103.9
	NLDDSFKTQFAALGG	659	673	HLA-DRB1*04:05	168.1
				HLA-DRB1*09:01	44.2
				HLA-DRB1*11:01	394.3
				HLA-DRB5*01:01	107
				HLA-DQA1*05:01/DQB1*03:01	197.3
				HLA-DRB1*01:01	7.4
FKTQFAALG				HLA-DRB1*04:01	80.6
				HLA-DRB1*04:05	158.9
	LDDSFKTQFAALGGW	660	674	HLA-DRB1*08:02	478.5
				HLA-DRB1*09:01	35.5
				HLA-DRB1*11:01	195.3
				HLA-DRB5*01:01	64.7
				HLA-DQA1*05:01/DQB1*03:01	155.4
				HLA-DRB1*01:01	6.5
				HLA-DRB1*04:01	67.6
				HLA-DRB1*04:04	448.6
	DDSFKTQFAALGGWG	661	675	HLA-DRB1*04:05	195.7
				HLA-DRB1*08:02	390.1
				HLA-DRB1*09:01	28.1
				HLA-DRB1*11:01	122.6
				HLA-DRB5*01:01	53.3

				HLA-DQA1*05:01/DQB1*03:01	140.7
				HLA-DRB1*01:01	5.9
				HLA-DRB1*04:01	72.2
				HLA-DRB1*04:04	340.3
	DSFKTQFAALGGWGL	662	676	HLA-DRB1*04:05	226.7
				HLA-DRB1*09:01	22.5
				HLA-DRB1*11:01	161
				HLA-DRB5*01:01	46.5
				HLA-DQA1*05:01/DQB1*03:01	113.9
				HLA-DRB1*04:01	89
				HLA-DRB1*04:04	314.3
				HLA-DRB1*04:05	297.9
				HLA-DRB1*09:01	28.4
	SFKTQFAALGGWGLH	663	677	HLA-DRB1*11:01	229.3
				HLA-DRB5*01:01	41.9
				HLA-DRB1*04:01	132.5
				HLA-DRB1*04:04	493.2
				HLA-DRB1*11:01	388.2
				HLA-DRB5*01:01	48.3
				HLA-DPA1*02:01/DPB1*05:01	53.6
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*04:04	70.3
				HLA-DRB1*04:05	33.7
				HLA-DPA1*02:01/DPB1*05:01	45.7
				HLA-DQA1*01:02/DQB1*06:02	207.6
	WRYLDFNALNLFFSP	314	328	HLA-DRB1*04:04	73
				HLA-DRB1*04:05	46
				HLA-DRB1*11:01	296.5
				HLA-DPA1*02:01/DPB1*05:01	40.3
				HLA-DQA1*01:02/DQB1*06:02	177
	RYLDFNALNLFFSPL	315	329	HLA-DRB1*04:04	82.5
				HLA-DRB1*04:05	55.6
FNALNLFFS				HLA-DRB1*11:01	203.3
				HLA-DPA1*02:01/DPB1*05:01	43.4
	YLDFNALNLFFSPLE	316	330	HLA-DQA1*01:02/DQB1*06:02	167.7
				HLA-DRB1*01:01	37.8
				HLA-DRB1*11:01	223.8
				HLA-DPA1*02:01/DPB1*05:01	48.7
	LDFNALNLFFSPLEF	317	331	HLA-DQA1*01:02/DQB1*06:02	213.2
				HLA-DRB1*01:01	95.1
				HLA-DRB1*11:01	385.8
	DFNALNLFFSPLEFQ	318	332	HLA-DPA1*02:01/DPB1*05:01	60.6
				HLA-DQA1*01:02/DQB1*06:02	194.8
	FNALNLFFSPLEFQH	319	333	HLA-DPA1*02:01/DPB1*05:01	52.4
				HLA-DQA1*01:02/DQB1*06:02	197.3
				HLA-DRB1*04:01	300.6
	LGGDPKFRSLTHEDH	494	508	HLA-DRB1*04:05	115.2
				HLA-DRB1*11:01	293.4
				HLA-DRB1*04:01	211.4
	GGDPKFRSLTHEDHA	495	509	HLA-DRB1*04:05	97.3
				HLA-DRB1*11:01	177.6
				HLA-DRB5*01:01	494.8
				HLA-DRB1*04:01	144
FRSLTHEDH				HLA-DRB1*04:05	77.7
	GDPKFRSLTHEDHAI	496	510	HLA-DRB1*11:01	93
				HLA-DRB4*01:01	458
				HLA-DRB5*01:01	321.5
				HLA-DRB1*04:01	105.8
				HLA-DRB1*04:05	82
	DPKFRSLTHEDHAIQ	497	511	HLA-DRB1*09:01	479.1
				HLA-DRB1*11:01	53.9
				HLA-DRB5*01:01	238.7
	PKFRSLTHEDHAIQP	498	512	HLA-DRB1*04:01	153.1

				HLA-DRB1*04:05	117.9
				HLA-DRB1*11:01	64.7
				HLA-DRB5*01:01	345.3
				HLA-DRB1*04:01	226.1
	KFRSLTHEDHAIQPQ	499	513	HLA-DRB1*04:05	249.1
				HLA-DRB1*11:01	93.3
				HLA-DRB1*04:01	446.9
	FRSLTHEDHAIQPQN	500	514	HLA-DRB1*11:01	146.1
				HLA-DPA1*03:01/DPB1*04:02	14.7
				HLA-DPA1*01:03/DPB1*02:01	14.1
				HLA-DPA1*02:01/DPB1*01:01	7.6
				HLA-DPA1*03:01/DPB1*04:02	14.7
				HLA-DQA1*05:01/DQB1*03:01	141.5
				HLA-DRB1*01:01	16
				HLA-DRB1*03:01	375.8
				HLA-DRB1*04:01	301.1
	AARIHDFRYSQLAKL	149	163	HLA-DRB1*04:05	137.2
				HLA-DRB1*07:01	9.5
				HLA-DRB1*08:02	263.9
				HLA-DRB1*09:01	26.4
				HLA-DRB1*11:01	110.6
				HLA-DRB1*13:02	460.2
				HLA-DRB3*01:01	257.1
				HLA-DRB5*01:01	20.8
				HLA-DPA1*01:03/DPB1*02:01	13.9
				HLA-DPA1*02:01/DPB1*01:01	7.6
				HLA-DQA1*05:01/DQB1*03:01	117.5
				HLA-DRB1*01:01	12.2
				HLA-DRB1*03:01	435.2
				HLA-DRB1*04:01	210.6
				HLA-DRB1*04:04	385.6
	ARIHDFRYSQLAKLG	150	164	HLA-DRB1*04:05	156.7
				HLA-DRB1*07:01	10.7
				HLA-DRB1*08:02	207.6
				HLA-DRB1*09:01	23.1
				HLA-DRB1*11:01	77.2
				HLA-DRB1*13:02	453.6
				HLA-DRB3*01:01	286.2
FRYSQLAKL				HLA-DRB5*01:01	23.1
				HLA-DPA1*03:01/DPB1*04:02	7.5
				HLA-DPA1*01:03/DPB1*02:01	12.3
				HLA-DPA1*02:01/DPB1*01:01	7
				HLA-DPA1*02:01/DPB1*05:01	414.6
				HLA-DPA1*03:01/DPB1*04:02	7.5
				HLA-DQA1*05:01/DQB1*03:01	122.9
				HLA-DRB1*01:01	8.7
				HLA-DRB1*03:01	338.1
				HLA-DRB1*04:01	175.6
	RIHDFRYSQLAKLGI	151	165	HLA-DRB1*04:04	247.9
				HLA-DRB1*04:05	133.8
				HLA-DRB1*07:01	7.7
				HLA-DRB1*08:02	194.7
				HLA-DRB1*09:01	17.5
				HLA-DRB1*11:01	29.1
				HLA-DRB1*13:02	334.1
				HLA-DRB3*01:01	253.8
				HLA-DRB5*01:01	20.1
				HLA-DPA1*03:01/DPB1*04:02	8
				HLA-DPA1*01:03/DPB1*02:01	14.6
				HLA-DPA1*02:01/DPB1*01:01	8
				HLA-DPA1*02:01/DPB1*05:01	444.5
				HLA-DPA1*03:01/DPB1*04:02	8
	IHDFRYSQLAKLGIN	152	166	HLA-DQA1*05:01/DQB1*03:01	104.7
				HLA-DRB1*01:01	7.7
				HLA-DRB1*03:01	353.3
				HLA-DRB1*04:01	195
				HLA-DRB1*04:04	238.5
				HLA-DRB1*04:05	146.7

				HLA-DRB1*07:01	8.6
				HLA-DRB1*08:02	288.4
				HLA-DRB1*09:01	14.6
				HLA-DRB1*13:02	323.5
				HLA-DRB3*01:01	272.4
				HLA-DRB5*01:01	21.3
				HLA-DPA1*03:01/DPB1*04:02	10.8
				HLA-DPA1*01:03/DPB1*02:01	19
				HLA-DPA1*02:01/DPB1*01:01	12.9
				HLA-DPA1*03:01/DPB1*04:02	10.8
				HLA-DQA1*05:01/DQB1*03:01	120.4
	HDFRYSQLAKLGINP	153	167	HLA-DRB1*01:01	11.2
				HLA-DRB1*04:04	224.3
				HLA-DRB1*04:05	211.1
				HLA-DRB1*07:01	11.8
				HLA-DRB1*08:02	381.5
				HLA-DRB1*09:01	16.9
				HLA-DRB5*01:01	33.2
				HLA-DPA1*03:01/DPB1*04:02	16.2
				HLA-DPA1*01:03/DPB1*02:01	37.2
				HLA-DPA1*02:01/DPB1*01:01	29.4
				HLA-DPA1*03:01/DPB1*04:02	16.2
				HLA-DQA1*05:01/DQB1*03:01	274.7
	DFRYSQLAKLGINPY	154	168	HLA-DRB1*01:01	15.7
				HLA-DRB1*04:04	208.2
				HLA-DRB1*04:05	125.9
				HLA-DRB1*07:01	17.1
				HLA-DRB1*09:01	20
				HLA-DRB5*01:01	51.9
				HLA-DPA1*03:01/DPB1*04:02	122.8
				HLA-DPA1*01:03/DPB1*02:01	211.3
				HLA-DPA1*02:01/DPB1*01:01	142.6
				HLA-DPA1*03:01/DPB1*04:02	122.8
	FRYSQLAKLGINPYT	155	169	HLA-DRB1*01:01	18.1
				HLA-DRB1*04:04	170.5
				HLA-DRB1*07:01	20.9
				HLA-DRB1*09:01	36.4
				HLA-DRB5*01:01	73.6
				HLA-DPA1*01:03/DPB1*02:01	64.1
				HLA-DRB1*01:01	62.2
				HLA-DRB1*04:01	304.9
	ASEESAFYVLEHSSF	432	446	HLA-DRB1*04:05	35.2
				HLA-DRB1*07:01	261.9
				HLA-DRB1*11:01	322.8
				HLA-DRB3*01:01	89.2
				HLA-DPA1*01:03/DPB1*02:01	51.8
				HLA-DRB1*01:01	26.5
	SEESAFYVLEHSSFQ	433	447	HLA-DRB1*04:05	24.5
				HLA-DRB1*11:01	133.2
FYVLEHSSF				HLA-DRB3*01:01	57.4
				HLA-DPA1*01:03/DPB1*02:01	30.7
				HLA-DPA1*02:01/DPB1*01:01	36.9
				HLA-DRB1*01:01	11
	EESAFYVLEHSSFQL	434	448	HLA-DRB1*04:05	19.5
				HLA-DRB1*09:01	243.5
				HLA-DRB1*11:01	63
				HLA-DRB3*01:01	49
				HLA-DRB1*01:01	6.6
				HLA-DRB1*04:05	17.5
	ESAFYVLEHSSFQLL	435	449	HLA-DRB1*09:01	195.5
				HLA-DRB1*11:01	35.3
				HLA-DRB3*01:01	44

				HLA-DRB1*01:01	7.5
	SAFYVLEHSSFQLLG	436	450	HLA-DRB1*04:05	20.4
				HLA-DRB1*09:01	228
				HLA-DRB1*11:01	41.8
				HLA-DRB1*01:01	10.3
	AFYVLEHSSFQLLGT	437	451	HLA-DRB1*04:05	30.2
				HLA-DRB1*11:01	64
	FYVLEHSSFQLLGTG	438	452	HLA-DRB1*01:01	16.3
				HLA-DRB1*11:01	117.1
GGWGLHQPP	LGGWGLHQPPPQIFL	671	685	HLA-DQA1*05:01/DQB1*03:01	385.2
	GGWGLHQPPPQIFLK	672	686	HLA-DQA1*05:01/DQB1*03:01	378.8
GQGQDTLAP	YPYVLGQGQDTLAPE	386	400	HLA-DQA1*05:01/DQB1*03:01	418
	PYVLGQGQDTLAPEL	387	401	HLA-DQA1*05:01/DQB1*03:01	427.5
	TISPIMGYSTPWRYL	303	317	HLA-DPA1*01:03/DPB1*02:01	347.5
	ISPIMGYSTPWRYLD	304	318	HLA-DPA1*01:03/DPB1*02:01	273.1
GYSTPWRYL	SPIMGYSTPWRYLDF	305	319	HLA-DPA1*01:03/DPB1*02:01	197.3
	PIMGYSTPWRYLDFN	306	320	HLA-DPA1*01:03/DPB1*02:01	153.6
	IMGYSTPWRYLDFNA	307	321	HLA-DPA1*01:03/DPB1*02:01	136.6
	SAARIHDFRYSQLAK	148	162	HLA-DRB1*15:01	151.4
	AARIHDFRYSQLAKL	149	163	HLA-DRB1*15:01	91.1
HDFRYSQLA	ARIHDFRYSQLAKLG	150	164	HLA-DRB1*15:01	111
	RIHDFRYSQLAKLGI	151	165	HLA-DRB1*15:01	114.4
	IHDFRYSQLAKLGIN	152	166	HLA-DRB1*15:01	157.1
	HDFRYSQLAKLGINP	153	167	HLA-DRB1*15:01	287.5
HNASGKEAK	SCHNASGKEAKVCTI	290	304	HLA-DQA1*05:01/DQB1*03:01	153.9
HTYFPNKGT	LNMHTYFPNKGTQQY	614	628	HLA-DRB1*11:01	364.8
	NMHTYFPNKGTQQYT	615	629	HLA-DRB1*11:01	393.4
	QYTDQIERPLMVGSV	627	641	HLA-DQA1*01:02/DQB1*06:02	251.2
	YTDQIERPLMVGSVW	628	642	HLA-DQA1*01:02/DQB1*06:02	217.5
IERPLMVGS	TDQIERPLMVGSVWN	629	643	HLA-DQA1*01:02/DQB1*06:02	249.6
	DQIERPLMVGSVWNR	630	644	HLA-DQA1*01:02/DQB1*06:02	324.3
	QIERPLMVGSVWNRR	631	645	HLA-DQA1*01:02/DQB1*06:02	492.4
				HLA-DPA1*01:03/DPB1*02:01	408.7
	VDSAARIHDFRYSQL	146	160	HLA-DPA1*02:01/DPB1*01:01	369.6
				HLA-DRB4*01:01	270.1
				HLA-DPA1*01:03/DPB1*02:01	292.1
	DSAARIHDFRYSQLA	147	161	HLA-DPA1*02:01/DPB1*01:01	162.3
				HLA-DRB1*15:01	265.3
				HLA-DRB4*01:01	214
IHDFRYSQL				HLA-DPA1*01:03/DPB1*02:01	98.5
	SAARIHDFRYSQLAK	148	162	HLA-DPA1*02:01/DPB1*01:01	43.6
				HLA-DRB1*01:01	446.1
				HLA-DRB4*01:01	145.6
	AARIHDFRYSQLAKL	149	163	HLA-DRB4*01:01	99.1
	ARIHDFRYSQLAKLG	150	164	HLA-DRB4*01:01	89.5
	RIHDFRYSQLAKLGI	151	165	HLA-DRB4*01:01	83.5
	IHDFRYSQLAKLGIN	152	166	HLA-DRB4*01:01	91.8
ISLRPGPVS	QNTRISLRPGPVSQP	549	563	HLA-DRB1*08:02	432.1
	NTRISLRPGPVSQPY	550	564	HLA-DRB1*08:02	381.8
	EAKVCTISPIMGYST	298	312	HLA-DQA1*05:01/DQB1*03:01	333.9
	AKVCTISPIMGYSTP	299	313	HLA-DQA1*05:01/DQB1*03:01	311.8
	KVCTISPIMGYSTPW	300	314	HLA-DQA1*05:01/DQB1*03:01	305.9
				HLA-DRB1*01:01	89
	VCTISPIMGYSTPWR	301	315	HLA-DQA1*05:01/DQB1*03:01	243.1
ISPIMGYST				HLA-DRB1*01:01	50.2
				HLA-DRB1*11:01	375.8
	CTISPIMGYSTPWRY	302	316	HLA-DQA1*05:01/DQB1*03:01	245.7
				HLA-DRB1*01:01	115.8
	TISPIMGYSTPWRYL	303	317	HLA-DQA1*05:01/DQB1*03:01	247.1
	TISPIMGYSTPWRYL	303	317	HLA-DRB1*01:01	194.5
	ISPIMGYSTPWRYLD	304	318	HLA-DQA1*05:01/DQB1*03:01	292.7
				HLA-DRB1*01:01	363.8
IWVYFPPQY	LAPELPIWVYFPPQY	397	411	HLA-DQA1*01:01/DQB1*05:01	163.1

				HLA-DQA1*05:01/DQB1*02:01	483.9
				HLA-DRB1*09:01	179.8
				HLA-DRB1*15:01	17.8
				HLA-DPA1*02:01/DPB1*01:01	256.4
				HLA-DQA1*01:01/DQB1*05:01	101.2
	APELPIWVYFPPQYA	398	412	HLA-DQA1*05:01/DQB1*02:01	381.7
				HLA-DRB1*08:02	365.3
				HLA-DRB1*09:01	55.1
				HLA-DRB1*15:01	9.6
				HLA-DQA1*01:01/DQB1*05:01	80.3
				HLA-DQA1*05:01/DQB1*02:01	384.8
	PELPIWVYFPPQYAY	399	413	HLA-DRB1*08:02	276
				HLA-DRB1*09:01	41.9
				HLA-DRB1*15:01	7.6
				HLA-DQA1*01:01/DQB1*05:01	67.9
				HLA-DQA1*05:01/DQB1*02:01	435.7
	ELPIWVYFPPQYAYL	400	414	HLA-DRB1*08:02	241.7
				HLA-DRB1*09:01	21.5
				HLA-DRB1*15:01	6
				HLA-DQA1*01:01/DQB1*05:01	77.5
				HLA-DQA1*05:01/DQB1*02:01	489.9
	LPIWVYFPPQYAYLT	401	415	HLA-DRB1*08:02	254.3
				HLA-DRB1*09:01	23.1
				HLA-DRB1*15:01	6.3
				HLA-DQA1*01:01/DQB1*05:01	96.1
	PIWVYFPPQYAYLTV	402	416	HLA-DRB1*08:02	295.7
				HLA-DRB1*09:01	25.1
				HLA-DRB1*15:01	6.8
	IWVYFPPQYAYLTVG	403	417	HLA-DQA1*01:01/DQB1*05:01	117
				HLA-DRB1*15:01	8.1
	ASGKEAKVCTISPIM	294	308	HLA-DRB1*07:01	403.8
	SGKEAKVCTISPIMG	295	309	HLA-DRB1*07:01	343.3
KVCTISPIM	GKEAKVCTISPIMGY	296	310	HLA-DRB1*07:01	376.5
	KEAKVCTISPIMGYS	297	311	HLA-DRB1*15:01	446.3
	EAKVCTISPIMGYST	298	312	HLA-DRB1*15:01	260.5
	AKVCTISPIMGYSTP	299	313	HLA-DRB1*15:01	270.5
	DFRYSQLAKLGINPY	154	168	HLA-DRB1*15:01	350.1
				HLA-DRB4*01:01	445.9
				HLA-DRB1*04:01	229.2
	FRYSQLAKLGINPYT	155	169	HLA-DRB1*04:05	140.1
				HLA-DRB1*15:01	321.6
				HLA-DRB1*01:01	78.7
				HLA-DRB1*04:01	185.5
	RYSQLAKLGINPYTH	156	170	HLA-DRB1*04:05	358.9
				HLA-DRB1*15:01	309.8
				HLA-DRB4*01:01	306.4
LAKLGINPY				HLA-DRB1*01:01	36.3
	YSQLAKLGINPYTHW	157	171	HLA-DRB1*04:01	162
				HLA-DRB1*04:05	337.2
				HLA-DRB1*15:01	231.6
				HLA-DRB1*01:01	84.7
				HLA-DRB1*04:01	180
	SQLAKLGINPYTHWT	158	172	HLA-DRB1*04:05	447.4
				HLA-DRB1*15:01	220.5
				HLA-DRB4*01:01	432.4
	QLAKLGINPYTHWTV	159	173	HLA-DRB1*01:01	175.3
				HLA-DRB4*01:01	486.9
	LAKLGINPYTHWTVA	160	174	HLA-DRB1*01:01	356.6
				HLA-DRB1*04:01	392.6
	SGDSKKLASEESAFY	425	439	HLA-DRB3*01:01	182.3
				HLA-DRB5*01:01	444.5
LASEESAFY				HLA-DQA1*05:01/DQB1*02:01	460.6
	GDSKKLASEESAFYV	426	440	HLA-DRB1*04:01	226.7
				HLA-DRB1*09:01	471
				HLA-DRB3*01:01	135.5

				HLA-DRB5*01:01	244.7
				HLA-DRB1*01:01	428.7
				HLA-DRB1*03:01	294.3
				HLA-DRB1*04:01	126
	DSKKLASEESAFYVL	427	441	HLA-DRB1*04:05	405.3
				HLA-DRB1*09:01	409.8
				HLA-DRB3*01:01	113.3
				HLA-DRB5*01:01	117.8
				HLA-DRB1*01:01	301.5
				HLA-DRB1*03:01	172.8
				HLA-DRB1*04:01	92.2
	SKKLASEESAFYVLE	428	442	HLA-DRB1*04:05	295.1
				HLA-DRB1*09:01	382.2
				HLA-DRB3*01:01	112.7
				HLA-DRB5*01:01	89.7
				HLA-DRB1*01:01	428.4
				HLA-DRB1*03:01	404
	KKLASEESAFYVLEH	429	443	HLA-DRB1*04:01	137.4
				HLA-DRB1*04:05	403.1
				HLA-DRB3*01:01	232.2
				HLA-DRB5*01:01	148.8
	KLASEESAFYVLEHS	430	444	HLA-DRB1*04:01	241.3
				HLA-DRB5*01:01	310.7
	LASEESAFYVLEHSS	431	445	HLA-DRB1*04:01	387
	WSKIPNLDDSFKTQF	654	668	HLA-DRB1*03:01	450.7
	SKIPNLDDSFKTQFA	655	669	HLA-DRB1*03:01	317.4
	KIPNLDDSFKTQFAA	656	670	HLA-DRB1*03:01	251.8
LDDSFKTQF	IPNLDDSFKTQFAAL	657	671	HLA-DPA1*02:01/DPB1*01:01	470.8
				HLA-DRB1*03:01	172.7
	PNLDDSFKTQFAALG	658	672	HLA-DRB1*03:01	460.4
	STPWRYLDFNALNLF	311	325	HLA-DQA1*05:01/DQB1*02:01	488.6
				HLA-DRB3*01:01	304.3
				HLA-DPA1*02:01/DPB1*05:01	173.6
	TPWRYLDFNALNLFF	312	326	HLA-DQA1*05:01/DQB1*02:01	494.7
				HLA-DRB1*13:02	349.5
				HLA-DRB3*01:01	250.8
				HLA-DPA1*02:01/DPB1*01:01	41.3
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*13:02	303.7
				HLA-DRB3*01:01	288.4
				HLA-DPA1*02:01/DPB1*01:01	50.1
LDFNALNLF	WRYLDFNALNLFFSP	314	328	HLA-DRB1*13:02	315.2
				HLA-DRB3*01:01	309.2
				HLA-DPA1*02:01/DPB1*01:01	50.2
				HLA-DRB1*13:02	390.9
	RYLDFNALNLFFSPL	315	329	HLA-DRB1*15:01	224.1
				HLA-DRB3*01:01	399.4
				HLA-DRB4*01:01	338.7
	YLDFNALNLFFSPLE	316	330	HLA-DPA1*02:01/DPB1*01:01	51.2
				HLA-DRB4*01:01	487
				HLA-DPA1*03:01/DPB1*04:02	136.9
	LDFNALNLFFSPLEF	317	331	HLA-DPA1*03:01/DPB1*04:02	136.9
				HLA-DRB4*01:01	460.6
	GVPDTLGGDPKFRSL	489	503	HLA-DRB1*03:01	453.6
LGGDPKFRS	VPDTLGGDPKFRSLT	490	504	HLA-DRB1*03:01	292.8
	PDTLGGDPKFRSLTH	491	505	HLA-DRB1*03:01	234.9
	DTLGGDPKFRSLTHE	492	506	HLA-DRB1*03:01	392.1
	TQFAALGGWGLHQPP	666	680	HLA-DQA1*01:01/DQB1*05:01	458.3
	QFAALGGWGLHQPPP	667	681	HLA-DQA1*01:01/DQB1*05:01	316.4
LGGWGLHQP	FAALGGWGLHQPPPQ	668	682	HLA-DQA1*01:01/DQB1*05:01	201.2
	AALGGWGLHQPPPQI	669	683	HLA-DQA1*01:01/DQB1*05:01	223.5
	ALGGWGLHQPPPQIF	670	684	HLA-DQA1*01:01/DQB1*05:01	301.9
LHQPPPQIF	LGGWGLHQPPPQIFL	671	685	HLA-DRB1*07:01	418.2
	GWGLHQPPPQIFLKI	673	687	HLA-DRB1*01:01	27.8

				HLA-DRB1*03:01	449.1
	WGLHQPPPQIFLKIL	674	688	HLA-DRB1*01:01	55.9
	GLHQPPPQIFLKILP	675	689	HLA-DRB1*01:01	193.1
	DTLAPELPIWVYFPP	395	409	HLA-DRB1*04:04	416.6
	TLAPELPIWVYFPPQ	396	410	HLA-DRB1*04:04	172.4
	LAPELPIWVYFPPQY	397	411	HLA-DRB1*04:04	93.6
LPIWVYFPP	APELPIWVYFPPQYA	398	412	HLA-DRB1*04:04	47.6
	PELPIWVYFPPQYAY	399	413	HLA-DRB1*04:04	40.6
	ELPIWVYFPPQYAYL	400	414	HLA-DRB1*04:04	33.6
	LPIWVYFPPQYAYLT	401	415	HLA-DRB1*04:04	29.6
	QNTRISLRPGPVSQP	549	563	HLA-DQA1*05:01/DQB1*03:01	289.4
	NTRISLRPGPVSQPY	550	564	HLA-DQA1*05:01/DQB1*03:01	263.1
LRPGPVSQP	TRISLRPGPVSQPYH	551	565	HLA-DQA1*05:01/DQB1*03:01	259.3
	RISLRPGPVSQPYHH	552	566	HLA-DQA1*05:01/DQB1*03:01	267.4
				HLA-DRB1*01:01	274.5
	ISLRPGPVSQPYHHW	553	567	HLA-DQA1*05:01/DQB1*03:01	290.4
	YEKPEELWTAKSRVH	765	779	HLA-DRB1*07:01	121.3
LWTAKSRVH	EKPEELWTAKSRVHP	766	780	HLA-DRB1*07:01	157.3
	KPEELWTAKSRVHPL	767	781	HLA-DQA1*05:01/DQB1*03:01	379.5
				HLA-DRB5*01:01	340.6
				HLA-DRB1*07:01	47.1
	CTISPIMGYSTPWRY	302	316	HLA-DRB1*09:01	166.2
				HLA-DRB5*01:01	430.8
				HLA-DRB1*03:01	306.3
	TISPIMGYSTPWRYL	303	317	HLA-DRB1*07:01	21.5
				HLA-DRB1*09:01	112.1
				HLA-DRB5*01:01	243.5
				HLA-DRB1*03:01	255
	ISPIMGYSTPWRYLD	304	318	HLA-DRB1*07:01	28.8
				HLA-DRB1*09:01	93.5
				HLA-DRB5*01:01	284.8
				HLA-DRB1*03:01	193.4
MGYSTPWRY	SPIMGYSTPWRYLDF	305	319	HLA-DRB1*07:01	31.1
				HLA-DRB1*09:01	77.7
				HLA-DRB5*01:01	280.3
				HLA-DRB1*03:01	403.3
	PIMGYSTPWRYLDFN	306	320	HLA-DRB1*07:01	43.2
				HLA-DRB1*09:01	141.1
				HLA-DRB5*01:01	490.8
	IMGYSTPWRYLDFNA	307	321	HLA-DRB1*07:01	59.9
				HLA-DRB1*09:01	220.9
				HLA-DRB1*07:01	103
	MGYSTPWRYLDFNAL	308	322	HLA-DRB1*09:01	130.8
				HLA-DRB1*15:01	239.2
				HLA-DPA1*02:01/DPB1*05:01	53.6
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*04:04	70.3
				HLA-DRB1*04:05	33.7
				HLA-DPA1*02:01/DPB1*05:01	45.7
				HLA-DQA1*01:02/DQB1*06:02	207.6
	WRYLDFNALNLFFSP	314	328	HLA-DRB1*04:04	73
				HLA-DRB1*04:05	46
				HLA-DRB1*11:01	296.5
NALNLFFSP				HLA-DPA1*02:01/DPB1*05:01	40.3
				HLA-DQA1*01:02/DQB1*06:02	177
	RYLDFNALNLFFSPL	315	329	HLA-DRB1*04:04	82.5
				HLA-DRB1*04:05	55.6
				HLA-DRB1*11:01	203.3
				HLA-DPA1*02:01/DPB1*05:01	43.4
	YLDFNALNLFFSPLE	316	330	HLA-DQA1*01:02/DQB1*06:02	167.7
				HLA-DRB1*01:01	37.8
				HLA-DRB1*11:01	223.8
	LDFNALNLFFSPLEF	317	331	HLA-DPA1*02:01/DPB1*05:01	48.7

				HLA-DQA1*01:02/DQB1*06:02	213.2
				HLA-DRB1*01:01	95.1
				HLA-DRB1*11:01	385.8
				HLA-DPA1*02:01/DPB1*05:01	60.6
	DFNALNLFFSPLEFQ	318	332	HLA-DQA1*01:02/DQB1*06:02	194.8
				HLA-DRB1*04:04	60.4
				HLA-DPA1*02:01/DPB1*05:01	52.4
	FNALNLFFSPLEFQH	319	333	HLA-DQA1*01:02/DQB1*06:02	197.3
				HLA-DRB1*04:04	47.5
	GKEAKVCTISPIMGY	296	310	HLA-DQA1*01:02/DQB1*06:02	155.8
	KEAKVCTISPIMGYS	297	311	HLA-DQA1*01:02/DQB1*06:02	148.2
	EAKVCTISPIMGYST	298	312	HLA-DQA1*01:02/DQB1*06:02	114.9
	AKVCTISPIMGYSTP	299	313	HLA-DQA1*01:02/DQB1*06:02	133
	KVCTISPIMGYSTPW	300	314	HLA-DQA1*01:02/DQB1*06:02	196.5
PIMGYSTPW				HLA-DRB1*15:01	106.1
	VCTISPIMGYSTPWR	301	315	HLA-DQA1*01:02/DQB1*06:02	288.1
	CTISPIMGYSTPWRY	302	316	HLA-DRB1*04:04	119
	TISPIMGYSTPWRYL	303	317	HLA-DRB1*04:04	107.6
	SPIMGYSTPWRYLDF	305	319	HLA-DRB1*04:04	118.2
	PIMGYSTPWRYLDFN	306	320	HLA-DRB1*04:04	196.6
PIWVYFPPQ	PIWVYFPPQYAYLTV	402	416	HLA-DRB1*04:04	46.2
	DQIERPLMVGSVWNR	630	644	HLA-DRB1*04:04	472.4
	QIERPLMVGSVWNRR	631	645	HLA-DRB1*04:04	249.4
PLMVGSVWN	IERPLMVGSVWNRRA	632	646	HLA-DRB1*04:04	185.7
	ERPLMVGSVWNRRAL	633	647	HLA-DRB1*04:04	155.8
	RPLMVGSVWNRRALH	634	648	HLA-DRB1*04:04	134.4
	PLMVGSVWNRRALHY	635	649	HLA-DRB1*04:04	132.9
PWRYLDFNA	GYSTPWRYLDFNALN	309	323	HLA-DRB1*15:01	408
				HLA-DRB1*01:01	414.2
	GTSQNTRISLRPGPV	546	560	HLA-DRB1*07:01	152.5
				HLA-DRB1*13:02	455.1
				HLA-DRB1*01:01	209.5
	TSQNTRISLRPGPVS	547	561	HLA-DRB1*07:01	195.4
				HLA-DRB1*13:02	409.4
				HLA-DRB1*01:01	114.2
				HLA-DRB1*07:01	315
RISLRPGPV	SQNTRISLRPGPVSQ	548	562	HLA-DRB1*09:01	349.4
				HLA-DRB1*13:02	369
				HLA-DRB1*01:01	127.7
	QNTRISLRPGPVSQP	549	563	HLA-DRB1*09:01	334.3
				HLA-DRB1*13:02	374.8
				HLA-DRB1*01:01	174
	NTRISLRPGPVSQPY	550	564	HLA-DRB1*09:01	454.8
	TRISLRPGPVSQPYH	551	565	HLA-DRB1*01:01	266.5
	GYSTPWRYLDFNALN	309	323	HLA-DRB1*04:01	73
	YSTPWRYLDFNALNL	310	324	HLA-DRB1*04:01	39.6
				HLA-DRB1*04:05	55.5
	STPWRYLDFNALNLF	311	325	HLA-DRB1*04:01	32.3
				HLA-DRB1*04:05	49
				HLA-DRB1*04:01	27.3
RYLDFNALN	TPWRYLDFNALNLFF	312	326	HLA-DRB1*04:05	51
				HLA-DRB1*15:01	89.3
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*04:01	31.4
				HLA-DRB1*15:01	115.9
	WRYLDFNALNLFFSP	314	328	HLA-DRB1*04:01	44.5
				HLA-DRB1*15:01	165.1
	RYLDFNALNLFFSPL	315	329	HLA-DRB1*04:01	49.2
	HDFRYSQLAKLGINP	153	167	HLA-DRB1*04:01	232
RYSQLAKLG	DFRYSQLAKLGINPY	154	168	HLA-DRB1*04:01	173.9
	SKKLASEESAFYVLE	428	442	HLA-DPA1*01:03/DPB1*02:01	464.9
SEESAFYVL				HLA-DPA1*02:01/DPB1*01:01	373.7
	KKLASEESAFYVLEH	429	443	HLA-DPA1*01:03/DPB1*02:01	444.3
				HLA-DPA1*02:01/DPB1*01:01	268

				HLA-DPA1*01:03/DPB1*02:01	364.6
	KLASEESAFYVLEHS	430	444	HLA-DPA1*02:01/DPB1*01:01	204.4
				HLA-DRB1*01:01	474.1
	LASEESAFYVLEHSS	431	445	HLA-DQA1*01:02/DQB1*06:02	403.8
	IPNLDDSFKTQFAAL	657	671	HLA-DPA1*01:03/DPB1*02:01	217.8
	PNLDDSFKTQFAALG	658	672	HLA-DPA1*01:03/DPB1*02:01	223.4
				HLA-DPA1*02:01/DPB1*01:01	256.8
SFKTQFAAL	NLDDSFKTQFAALGG	659	673	HLA-DPA1*01:03/DPB1*02:01	269.8
				HLA-DPA1*02:01/DPB1*01:01	256.5
	LDDSFKTQFAALGGW	660	674	HLA-DPA1*01:03/DPB1*02:01	288.3
				HLA-DPA1*02:01/DPB1*01:01	277.9
	DDSFKTQFAALGGWG	661	675	HLA-DPA1*01:03/DPB1*02:01	458.7
				HLA-DPA1*02:01/DPB1*01:01	496.7
SPIMGYSTP	SPIMGYSTPWRYLDF	305	319	HLA-DRB4*01:01	486.2
SQLAKLGIN	FRYSQLAKLGINPYT	155	169	HLA-DQA1*05:01/DQB1*03:01	239.3
	RYSQLAKLGINPYTH	156	170	HLA-DQA1*05:01/DQB1*03:01	402.1
TAKSRVHPL	KPEELWTAKSRVHPL	767	781	HLA-DRB1*07:01	55.6
TISPIMGYS	KVCTISPIMGYSTPW	300	314	HLA-DRB1*08:02	466.6
	VCTISPIMGYSTPWR	301	315	HLA-DRB1*08:02	342.6
TLAPELPIW	QDTLAPELPIWVYFP	394	408	HLA-DRB1*01:01	487.1
	RLGVPDTLGGDPKFR	487	501	HLA-DQA1*05:01/DQB1*03:01	182.6
	LGVPDTLGGDPKFRS	488	502	HLA-DQA1*05:01/DQB1*03:01	157.9
	GVPDTLGGDPKFRSL	489	503	HLA-DQA1*05:01/DQB1*03:01	149.5
TLGGDPKFR	VPDTLGGDPKFRSLT	490	504	HLA-DQA1*05:01/DQB1*03:01	133.1
	PDTLGGDPKFRSLTH	491	505	HLA-DQA1*05:01/DQB1*03:01	157.5
	DTLGGDPKFRSLTHE	492	506	HLA-DQA1*05:01/DQB1*03:01	201.7
	TLGGDPKFRSLTHED	493	507	HLA-DQA1*05:01/DQB1*03:01	222
	LDDSFKTQFAALGGW	660	674	HLA-DQA1*01:02/DQB1*06:02	400.7
	DDSFKTQFAALGGWG	661	675	HLA-DQA1*01:02/DQB1*06:02	246.1
TQFAALGGW	DSFKTQFAALGGWGL	662	676	HLA-DQA1*01:02/DQB1*06:02	243.6
	SFKTQFAALGGWGLH	663	677	HLA-DQA1*01:02/DQB1*06:02	305.5
	FKTQFAALGGWGLHQ	664	678	HLA-DQA1*01:02/DQB1*06:02	369.2
	TSQNTRISLRPGPVS	547	561	HLA-DRB1*11:01	413.3
TRISLRPGP	SQNTRISLRPGPVSQ	548	562	HLA-DRB1*11:01	250.5
	QNTRISLRPGPVSQP	549	563	HLA-DRB1*11:01	316.3
	NTRISLRPGPVSQPY	550	564	HLA-DRB1*11:01	421.9
	SGKEAKVCTISPIMG	295	309	HLA-DRB1*01:01	325.9
				HLA-DRB1*04:04	479
	GKEAKVCTISPIMGY	296	310	HLA-DRB1*01:01	138.8
				HLA-DRB1*04:04	386.6
VCTISPIMG	KEAKVCTISPIMGYS	297	311	HLA-DRB1*01:01	78
				HLA-DRB1*04:04	288.6
	EAKVCTISPIMGYST	298	312	HLA-DRB1*01:01	44.5
				HLA-DRB1*04:04	234.4
	AKVCTISPIMGYSTP	299	313	HLA-DRB1*01:01	76.9
				HLA-DRB1*04:04	201.7
	KVCTISPIMGYSTPW	300	314	HLA-DRB1*04:04	196
	EYKYPYVLGQGQDTL	383	397	HLA-DQA1*05:01/DQB1*02:01	278.4
	YKYPYVLGQGQDTLA	384	398	HLA-DQA1*05:01/DQB1*02:01	282.4
VLGQGQDTL	KYPYVLGQGQDTLAP	385	399	HLA-DQA1*05:01/DQB1*02:01	383.7
				HLA-DQA1*05:01/DQB1*03:01	450.2
	PYVLGQGQDTLAPEL	387	401	HLA-DRB4*01:01	285.5
	YVLGQGQDTLAPELP	388	402	HLA-DRB4*01:01	372.1
	AALGGWGLHQPPPQI	669	683	HLA-DRB1*01:01	141.9
				HLA-DRB1*09:01	382.1
	ALGGWGLHQPPPQIF	670	684	HLA-DRB1*01:01	49
				HLA-DRB1*09:01	250.2
WGLHQPPPQ	LGGWGLHQPPPQIFL	671	685	HLA-DRB1*01:01	20.9
				HLA-DRB1*09:01	179.6
	GGWGLHQPPPQIFLK	672	686	HLA-DRB1*01:01	32
				HLA-DRB1*09:01	207.4
	GWGLHQPPPQIFLKI	673	687	HLA-DRB1*09:01	320.6
WRYLDFNAL	MGYSTPWRYLDFNAL	308	322	HLA-DPA1*03:01/DPB1*04:02	348.4
				HLA-DPA1*01:03/DPB1*02:01	54.1

				HLA-DPA1*02:01/DPB1*01:01	145.8
				HLA-DPA1*03:01/DPB1*04:02	348.4
				HLA-DRB1*01:01	74.9
				HLA-DRB1*04:04	387.1
				HLA-DRB1*04:05	174.9
				HLA-DRB1*11:01	439.8
				HLA-DPA1*03:01/DPB1*04:02	231
				HLA-DPA1*01:03/DPB1*02:01	60.8
				HLA-DPA1*02:01/DPB1*01:01	136.4
				HLA-DPA1*03:01/DPB1*04:02	231
	GYSTPWRYLDFNALN	309	323	HLA-DRB1*01:01	44.7
				HLA-DRB1*04:04	226.7
				HLA-DRB1*04:05	77.8
				HLA-DRB1*09:01	381.9
				HLA-DRB1*11:01	359.4
				HLA-DPA1*03:01/DPB1*04:02	68.6
				HLA-DPA1*01:03/DPB1*02:01	51.3
				HLA-DPA1*02:01/DPB1*01:01	71.4
				HLA-DPA1*03:01/DPB1*04:02	68.6
	YSTPWRYLDFNALNL	310	324	HLA-DRB1*01:01	16.2
				HLA-DRB1*04:04	155.4
				HLA-DRB1*09:01	170.8
				HLA-DRB1*11:01	246.2
				HLA-DRB4*01:01	473.1
				HLA-DPA1*03:01/DPB1*04:02	50.3
				HLA-DPA1*01:03/DPB1*02:01	54.3
				HLA-DPA1*02:01/DPB1*01:01	43.7
				HLA-DPA1*03:01/DPB1*04:02	50.3
	STPWRYLDFNALNLF	311	325	HLA-DRB1*01:01	10.7
				HLA-DRB1*04:04	127.3
				HLA-DRB1*09:01	149.3
				HLA-DRB1*11:01	190.1
				HLA-DRB4*01:01	266.2
				HLA-DPA1*01:03/DPB1*02:01	61.5
				HLA-DPA1*02:01/DPB1*01:01	39.5
	TPWRYLDFNALNLFF	312	326	HLA-DRB1*04:04	110.7
				HLA-DRB1*09:01	189
				HLA-DRB1*11:01	235.7
				HLA-DRB4*01:01	224.4
				HLA-DPA1*01:03/DPB1*02:01	85.2
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*09:01	236
				HLA-DRB1*11:01	277.9
				HLA-DRB4*01:01	199.8
				HLA-DPA1*01:03/DPB1*02:01	90
	WRYLDFNALNLFFSP	314	328	HLA-DRB1*09:01	410.9
				HLA-DRB4*01:01	192.6
	HYESQLWSKIPNLDD	648	662	HLA-DRB1*04:04	80.6
				HLA-DRB1*04:05	78.8
	YESQLWSKIPNLDDS	649	663	HLA-DRB1*04:04	84.6
				HLA-DRB1*04:05	61.3
	ESQLWSKIPNLDDSF	650	664	HLA-DRB1*04:04	98.2
				HLA-DRB1*04:05	56.2
				HLA-DRB1*01:01	301.2
WSKIPNLDD	SQLWSKIPNLDDSFK	651	665	HLA-DRB1*04:04	84.9
				HLA-DRB1*04:05	50.1
	QLWSKIPNLDDSFKT	652	666	HLA-DRB1*04:04	111.4
				HLA-DRB1*04:05	68
	LWSKIPNLDDSFKTQ	653	667	HLA-DRB1*04:04	208.5
				HLA-DRB1*04:05	115.7
	WSKIPNLDDSFKTQF	654	668	HLA-DRB1*04:04	247.5
				HLA-DRB1*04:05	183.2
WTAKSRVHP	KPEELWTAKSRVHPL	767	781	HLA-DRB1*11:01	230.3
WVYFPPQYA	APELPIWVYFPPQYA	398	412	HLA-DPA1*01:03/DPB1*02:01	311.4
				HLA-DRB1*01:01	10.5

				HLA-DRB1*04:05	385.1
				HLA-DRB1*07:01	393.1
				HLA-DPA1*01:03/DPB1*02:01	176.2
				HLA-DPA1*02:01/DPB1*01:01	170.8
	PELPIWVYFPPQYAY	399	413	HLA-DRB1*01:01	6.6
				HLA-DRB1*04:05	340.2
				HLA-DRB1*07:01	390.6
				HLA-DPA1*02:01/DPB1*01:01	94.6
				HLA-DRB1*01:01	4.9
	ELPIWVYFPPQYAYL	400	414	HLA-DRB1*04:05	301
				HLA-DRB1*07:01	287.6
				HLA-DRB1*11:01	437.9
				HLA-DRB5*01:01	471.8
				HLA-DPA1*02:01/DPB1*01:01	55.4
				HLA-DQA1*05:01/DQB1*03:01	423.9
				HLA-DRB1*01:01	4.5
	LPIWVYFPPQYAYLT	401	415	HLA-DRB1*04:05	328.6
				HLA-DRB1*07:01	380.3
				HLA-DRB1*11:01	310.4
				HLA-DRB5*01:01	288.8
				HLA-DQA1*05:01/DQB1*03:01	425.9
				HLA-DRB1*01:01	5.3
	PIWVYFPPQYAYLTV	402	416	HLA-DRB1*04:05	450.6
				HLA-DRB1*11:01	437.7
				HLA-DRB5*01:01	321.4
	IWVYFPPQYAYLTVG	403	417	HLA-DRB1*01:01	5.9
				HLA-DRB1*09:01	39.3
				HLA-DPA1*02:01/DPB1*01:01	121.4
	WVYFPPQYAYLTVGD	404	418	HLA-DRB1*01:01	8
				HLA-DRB1*15:01	132.8
	GLNMHTYFPNKGTQQ	613	627	HLA-DRB1*01:01	321.7
				HLA-DRB1*04:01	220.1
	LNMHTYFPNKGTQQY	614	628	HLA-DRB1*01:01	106.1
				HLA-DRB1*04:01	201.3
	NMHTYFPNKGTQQYT	615	629	HLA-DRB1*01:01	46.8
YFPNKGTQQ				HLA-DRB1*04:01	178.5
				HLA-DRB1*01:01	47.2
	MHTYFPNKGTQQYTD	616	630	HLA-DRB1*04:01	179.3
				HLA-DRB1*11:01	422.3
	HTYFPNKGTQQYTDQ	617	631	HLA-DRB1*01:01	137.3
				HLA-DRB1*04:01	405.9
	TYFPNKGTQQYTDQI	618	632	HLA-DRB1*01:01	310.1
	ELPIWVYFPPQYAYL	400	414	HLA-DPA1*01:03/DPB1*02:01	43.9
	LPIWVYFPPQYAYLT	401	415	HLA-DPA1*01:03/DPB1*02:01	44.8
	PIWVYFPPQYAYLTV	402	416	HLA-DPA1*01:03/DPB1*02:01	46
				HLA-DPA1*02:01/DPB1*01:01	57.7
	IWVYFPPQYAYLTVG	403	417	HLA-DPA1*01:03/DPB1*02:01	60.4
YFPPQYAYL				HLA-DPA1*02:01/DPB1*01:01	71.5
	WVYFPPQYAYLTVGD	404	418	HLA-DPA1*01:03/DPB1*02:01	113.1
				HLA-DRB1*09:01	127
	VYFPPQYAYLTVGDV	405	419	HLA-DPA1*01:03/DPB1*02:01	186.6
				HLA-DPA1*02:01/DPB1*01:01	219.4
	YFPPQYAYLTVGDVN	406	420	HLA-DPA1*01:03/DPB1*02:01	498.2
				HLA-DPA1*02:01/DPB1*01:01	457.7
YKYPYVLGQ	MLVDHEYKYPYVLGQ	378	392	HLA-DPA1*01:03/DPB1*02:01	300.7
	VDHEYKYPYVLGQGQ	380	394	HLA-DRB5*01:01	444
	YSTPWRYLDFNALNL	310	324	HLA-DRB1*07:01	37.6
				HLA-DRB1*15:01	198.5
				HLA-DPA1*02:01/DPB1*05:01	336.8
YLDFNALNL	STPWRYLDFNALNLF	311	325	HLA-DQA1*01:01/DQB1*05:01	498.2
				HLA-DRB1*07:01	38.3
				HLA-DRB1*15:01	121.2
	TPWRYLDFNALNLFF	312	326	HLA-DPA1*03:01/DPB1*04:02	42.5

				HLA-DPA1*03:01/DPB1*04:02	42.5
				HLA-DQA1*01:01/DQB1*05:01	464.4
				HLA-DRB1*01:01	12.1
				HLA-DRB1*07:01	46.1
				HLA-DRB5*01:01	469.5
				HLA-DPA1*03:01/DPB1*04:02	35.9
				HLA-DPA1*03:01/DPB1*04:02	35.9
	PWRYLDFNALNLFFS	313	327	HLA-DRB1*01:01	11.9
				HLA-DRB1*07:01	71.7
				HLA-DRB5*01:01	475
				HLA-DPA1*03:01/DPB1*04:02	40.8
	WRYLDFNALNLFFSP	314	328	HLA-DPA1*03:01/DPB1*04:02	40.8
				HLA-DRB1*01:01	16.5
				HLA-DRB1*07:01	107.4
				HLA-DPA1*03:01/DPB1*04:02	63.8
	RYLDFNALNLFFSPL	315	329	HLA-DPA1*03:01/DPB1*04:02	63.8
				HLA-DRB1*01:01	25.3
				HLA-DRB1*07:01	163
				HLA-DPA1*03:01/DPB1*04:02	77.1
	YLDFNALNLFFSPLE	316	330	HLA-DPA1*03:01/DPB1*04:02	77.1
				HLA-DRB1*04:01	329.1
				HLA-DRB1*07:01	189
	KGTQQYTDQIERPLM	623	637	HLA-DRB1*01:01	403.6
	GTQQYTDQIERPLMV	624	638	HLA-DRB1*01:01	121.8
YTDQIERPL	TQQYTDQIERPLMVG	625	639	HLA-DRB1*01:01	69.1
				HLA-DRB1*04:01	384.7
	QQYTDQIERPLMVGS	626	640	HLA-DRB1*01:01	138.7
				HLA-DRB1*04:01	473.8
	HEYKYPYVLGQGQDT	382	396	HLA-DRB1*01:01	33.9
	EYKYPYVLGQGQDTL	383	397	HLA-DRB1*01:01	12.2
	YKYPYVLGQGQDTLA	384	398	HLA-DRB1*01:01	7.8
YVLGQGQDT				HLA-DRB1*04:04	479.7
	KYPYVLGQGQDTLAP	385	399	HLA-DRB1*01:01	8
	YPYVLGQGQDTLAPE	386	400	HLA-DRB1*01:01	11.6
	PYVLGQGQDTLAPEL	387	401	HLA-DRB1*01:01	21.8
	YVLGQGQDTLAPELP	388	402	HLA-DRB1*01:01	29.9