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Study on Protein Peptide Interaction (peptide-MHC allele) in Vaccine Development

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Abstract:

Vaccines induce protective immunity, an enhanced adaptive immune response to re-infection. It is generally accepted that only peptides that bind to major histocompatibility complexes (MHC) with an affinity above a threshold typically a value of 500 nM function as T-cell epitopes and that peptide–MHC affinity roughly correlates with T-cell response.In an era of failing antibiotics, vaccines, with their low cost and low frequency dosing, have generated renewed interest as prophylactic therapies. In present study the finding methods with reference to affinity of peptide to a particular MHC allele (HLA-A*0201) was given.

Keywords: Immunity, Vaccine, Peptide, Protein interaction, MHC molecules.

Introduction:

Vaccines induce protective immunity is an example of enhanced adaptive immune response to re-infection. In an era of failing antibiotics, vaccines, with their low cost and low frequency dosing, have generated renewed interest as prophylactic therapies. Historically, vaccines have been attenuated, or empirically weakened, whole pathogenic agents, such as viruses or bacteria. However, interest is now focusing on more rationally designed vaccines. These can be genetically modified pathogens, whole protein antigens or isolated poly-epitopes. Although the importance of non-peptide epitopes, such as lipids and carbohydrates, has become increasingly well recognized, it is the accurate prediction of proteinacious B-cell and T-cell epitopes (around which modern epitope-based vaccines are constructed) that remains the pivotal challenge for informatics with immunology. While B-cell epitope prediction remains unsophisticated, or is dependent on an often-indefinable knowledge of three-dimensional protein structure, a wide variety of advanced methods for T-cell epitopes prediction have arisen.

It is generally accepted that only peptides that bind to major histocompatibility complexes (MHC) with an affinity above a threshold typically a value of 500 nM function as T-cell epitopes and that peptide–MHC affinity roughly correlates with T-cell response. Most current methods for the prediction of T-cell epitopes depend on predicting peptides binding affinity to MHCs.

The binding of T-cell antigenic peptides to MHC molecules is a prerequisite for their immunogenicity. The ability to identify binding peptides based on the protein sequence is of great importance to the rational design of peptide vaccines. As the requirements for peptide binding cannot be fully explained by the peptide sequence per se, structural considerations should be taken into account and are expected to improve predictive algorithms. The first step in such an algorithm requires accurate and fast modeling of the peptide structure in the MHC-binding groove.

Objective:

To find the affinity of peptide to a particular MHC allele (HLA-A*0201).

Materials and Methods:

Data set:

Retrieve the five HLA-A*0201-peptide complexes from MPID-T database whose PDB-ID and MPID-ID are given below in the Table 1.0.

Table 1.0: Selected MHC-peptide complex for analysis:

S.NO.	PDB-ID	MHC-ID	Peptide Sequence
1	1DUZ	MHCA0040	LLFGYPVYV
2	1EEZ	MHCA0071	ILSALVGIL
3	1EEY	MHCA0001	ILSALVGIV
4	1HHG	MHCA0008	TLTSCNTSV
5	1JHT	MHCA0058	ALGIGILTV

Methodology:

Algorithm:

(1) Downloaded the MHC class I-peptide complex for the allele A0201 having length 9- mer from the MPID-T database.

(2) Submitted the query (PDB ID) of the complex for finding the contact residue between MHC and peptide to the LPC\CSU software.

(3) Tabulation of the contact residues and running the software for finding the affinity.

(4) Use of contact potential table (Betancourt Table).

(5) Generation of position specific scoring (PSSM)

(6) Finding energy score of peptide.

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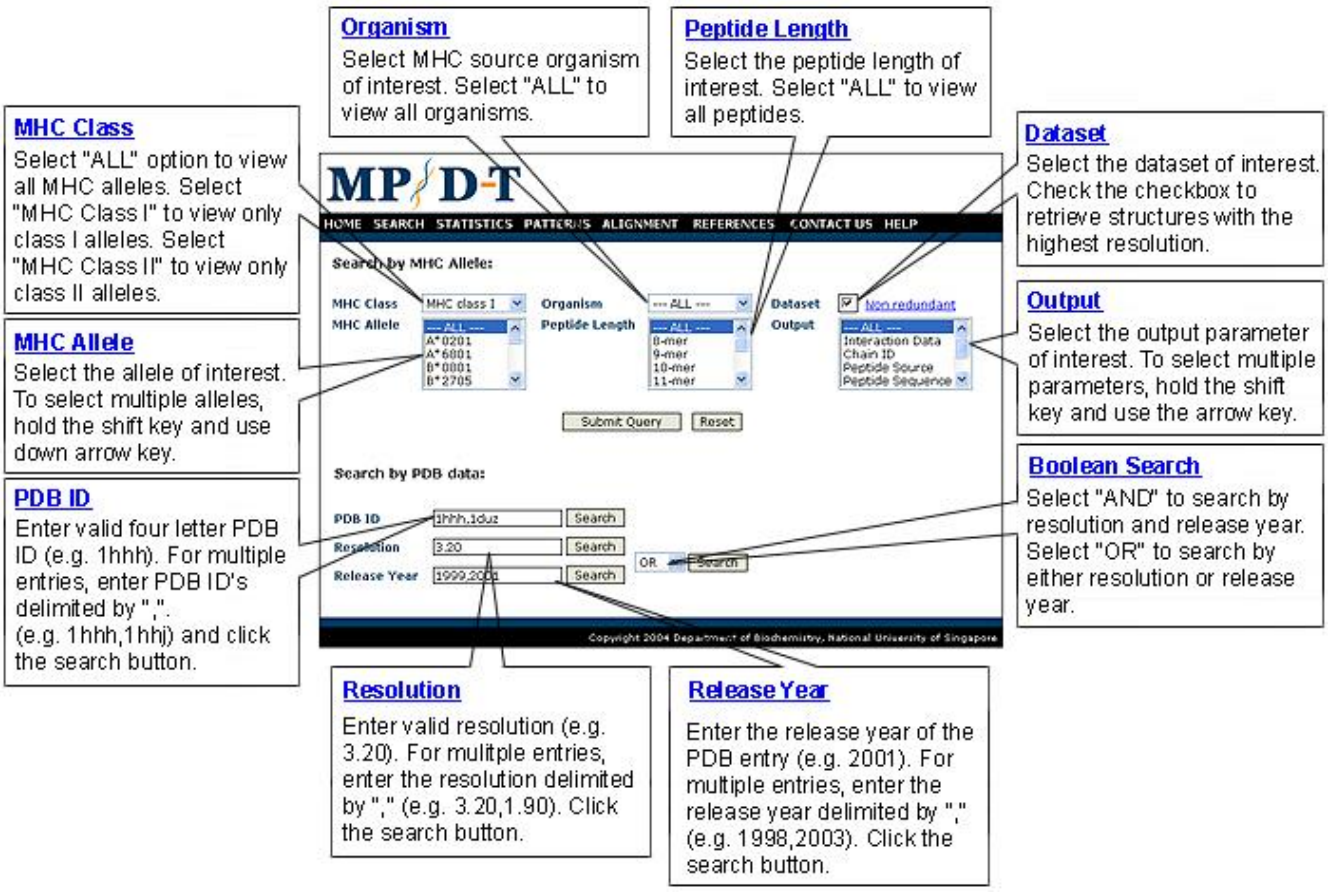
MPID-T Database:

Search by MHC Allele:

This search function allows you to access MPID-T by MHC Class, MHC Allele, Organism, Peptide Length and Dataset of your interest. To get the results of all the MHC class I and/or class II structures, choose the *MHC Class* (i.e. MHC class I, MHC class II or ALL) in the option, select "ALL" in the *MHC Allele* option, select "ALL" in the *Organism* option, select "ALL" in the *Peptide Length* option, and check/uncheck the *Non redundant* checkbox for the data set you are interested (i.e. redundant or non-redundant).



Search by PDB Data:

This search function allows you to access MPID-T by PDB ID, Resolution, Release year and combined querying based on resolution and release year.

 To query by PDB ID, enter the valid four letter PDB code (e.g. 1hhj) and click the search button. To enter multiple PDB code, use "," as delimiter as shown in the text area (e.g. 1hhh, 1hhj).

 To query by Resolution, enter the resolution with two decimals (e.g. 3.20, 3.00) and click the search button. To enter multiple resolution, use "," as delimiter (e.g. 3.00, 3.20).

 To query by PDB release year, enter the release year (e.g. 2001) and click the search button. To enter multiple PDB release year use "," as delimiter (e.g. 2001, 2000).
 To do a combined query on Resolution and Release year, choose the "AND" option for combined querying and "OR" option to query either by resolution or release year. Click the search button.

Definition of Interaction Parameters:

 Total Hydrogen Bonds –
Total number of hydrogen bonds between the MHC molecule and its corresponding bound peptide.

 Interface Area –
The interface area for class I pMHC complexes was define as the change in their solvent accessible surface area when going from a monomeric MHC molecule to a dimeric pMHC complex state. Similarly, the interface area for class II pMHC complexes was defined as the change in their solvent accessible surface area when going from a dimeric MHC molecule to a trimeric pMHC complex state.

 Gap Volume –
The gap volume gives a measure of the complementarity of the interacting surfaces. The volume of the gaps between the two interacting subunits is calculated using a program SURFNET (Laskowski, 1991). Each pair of subunit atoms are considered in turn, placing a sphere (maximum radius 5.0 angstroms) halfway between the surfaces of the two atoms, such that its surface touches the surfaces of the atoms in the pair. Checks are made to test if any other atoms intercepts this sphere and each time an intercept is detected the size of the sphere is reduced accordingly. If at any time the size of the sphere falls below a minimium (minimium radius 1.0 angstroms) the sphere is discarded. If the sphere remains after all checks, its sizr is recorded. The sizes of all the allowable gap-spheres are then used to calculate the gap volume between the two subunits.

 Gap Index –
One essential feature in receptor-ligand binding is the electrostatic and geometric complementarity observed between associating molecules. Gap index is used as a means to evaluate the complementarity of interacting surfaces. The gap index is calculated using the formula Gap Index=Gap Volume/Change in solvent accessible surface area.

Results:

Table 1: Contacts of peptide residues 1 - 9 (chain C) in PDB entry 1DUZ using CSU/LPC

LEGEND:

Dist	-	nearest distance (Å) between atoms of two residues
Surf	-	contact surface area (Å2) between two residues
HB	-	hydrophilic-hydrophilic contact (hydrogen bond)
Arom	-	aromatic-aromatic contact
Phob	-	hydrophobic-hydrophobic contact
DC	-	hydrophobic-hydrophilic contact (destabilizing contact)
+/-	-	indicates presence/absence of a specific contacts
*	-	indicates residues forming contacts by their side chain (Including CA atoms)

Residues in contact with LEU 1 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
5A MET*	4.0	6.0	-	-	-	+
7A TYR*	2.8	27.6	+	-	-	-
59A TYR*	3.8	12.3	-	-	+	-
63A GLU*	3.3	30.3	-	-	-	+
66A LYS*	3.5	12.6	-	-	-	+
159A TYR*	2.7	30.7	+	-	-	-
163A THR*	3.8	17.9	-	-	+	+
167A TRP*	3.7	63.1	-	-	+	+
171A TYR*	2.8	29.3	+	-	-	-
2C LEU*	1.3	56.8	+	-	-	+

Residues in contact with LEU 2 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
7A TYR*	3.6	33.9	-	-	+	-
9A PHE*	3.7	18.4	-	-	+	-
45A MET*	3.6	24.5	-	-	+	-
63A GLU*	2.9	24.0	+	-	-	+
66A LYS*	3.0	27.7	+	-	+	+
67A VAL*	3.6	29.6	-	-	+	+
99A TYR*	3.4	16.8	-	-	-	+
159A TYR*	3.7	6.2	-	-	-	-

1C	LEU*	1.3	81.5	-	-	-	+
3C	PHE*	1.3	66.9	-	-	-	+
4C	GLY	3.7	0.9	+	-	-	-

Residues in contact with PHE 3 (chain C).

				Specific contacts			
Residue		**Dist**	**Surf**	**HB**	**Arom**	**Phob**	**DC**
70A	HIS*	3.2	23.9	-	+	-	-
97A	ARG*	4.0	12.3	-	-	-	-
99A	TYR*	2.9	27.2	+	-	+	+
155A	GLN*	3.9	33.7	-	-	+	-
156A	LEU*	3.8	28.0	-	-	+	-
159A	TYR*	3.5	41.2	-	+	+	-
2C	LEU*	1.3	74.1	-	-	-	+
4C	GLY*	1.3	61.7	+	-	-	+
5C	TYR*	3.3	57.9	-	+	+	-
7C	VAL*	3.9	13.2	-	-	+	-

Residues in contact with GLY 4 (chain C).

				Specific contacts			
Residue		**Dist**	**Surf**	**HB**	**Arom**	**Phob**	**DC**
2C	LEU	3.7	1.8	+	-	-	-
3C	PHE*	1.3	79.5	-	-	-	+
5C	TYR*	1.3	74.5	+	-	-	+

Residues in contact with TYR 5 (chain C).

				Specific contacts			
Residue		**Dist**	**Surf**	**HB**	**Arom**	**Phob**	**DC**
155A	GLN*	3.8	33.7	-	-	+	+
3C	PHE*	3.3	50.3	+	+	+	+
4C	GLY*	1.3	88.1	-	-	-	+
6C	PRO*	1.3	76.9	-	-	+	+
7C	VAL*	3.7	1.6	+	-	-	+

Residues in contact with PRO 6 (chain C).

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Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
5C TYR*	1.3	94.7	-	-	+	+
7C VAL*	1.3	65.2	+	-	-	+

Residues in contact with VAL 7 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
73A THR*	3.4	24.7	+	-	-	+
97A ARG*	3.8	25.9	+	-	-	+
116A TYR*	3.9	15.9	+	-	-	+
147A TRP*	3.5	38.1	-	-	+	+
3C PHE*	3.9	13.0	-	-	+	-
5C TYR*	3.7	7.6	+	-	+	+
6C PRO*	1.3	81.6	-	-	-	+
8C TYR*	1.3	62.6	+	-	-	+

Residues in contact with TYR 8 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
73A THR*	3.9	28.1	+	-	+	+
76A VAL*	3.6	45.5	-	-	+	+
77A ASP*	3.6	5.2	-	-	-	+
146A LYS*	3.8	10.1	-	-	+	+
147A TRP*	2.7	25.6	+	-	-	+
7C VAL*	1.3	77.3	-	-	-	+
9C VAL*	1.3	68.8	+	-	-	+

Residues in contact with VAL 9 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
77A ASP*	3.0	44.1	+	-	+	+
80A THR*	3.5	24.0	+	-	+	+
81A LEU*	3.9	25.8	-	-	+	-
84A TYR*	2.7	20.0	+	-	+	-
116A TYR*	3.9	24.2	+	-	+	-
143A THR*	2.7	40.7	+	-	-	+
146A LYS*	2.7	26.1	+	-	-	-
147A TRP*	4.0	12.1	-	-	+	-
8C TYR*	1.3	78.6	-	-	-	+

Table 2. Contacts of peptide residues 1 - 9 (chain C) in PDB entry 1EEY :

Residues in contact with ILE 1 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
5A MET*	4.0	5.9	-	-	-	+
7A TYR*	3.0	20.6	+	-	-	-
59A TYR*	3.5	21.8	-	-	+	-
63A GLU*	3.3	17.3	-	-	-	+
66A LYS*	3.8	13.9	-	-	-	+
159A TYR*	2.8	28.2	+	-	-	-
163A THR*	3.6	18.8	-	-	+	-
167A TRP*	3.4	55.8	-	-	+	+
171A TYR*	2.8	42.5	+	-	-	+
2C LEU*	1.3	57.3	+	-	-	+

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Residues in contact with LEU 2 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
7A TYR*	3.4	24.8	+	-	+	-
9A PHE*	3.5	26.5	-	-	+	-
45A MET*	3.3	30.5	-	-	+	-
63A GLU*	2.8	20.9	+	-	-	+
66A LYS*	2.9	27.3	+	-	+	+
67A VAL*	3.6	31.2	-	-	+	+
70A HIS*	4.0	4.5	-	-	+	+
99A TYR*	3.4	17.0	-	-	-	+
159A TYR*	3.7	5.7	-	-	-	-
1C ILE*	1.3	78.7	-	-	-	+
3C SER*	1.3	66.5	+	-	-	+
4C ALA	3.8	0.3	+	-	-	-

Residues in contact with SER 3 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
66A LYS*	4.0	6.5	-	-	-	+
70A HIS*	3.4	18.4	-	-	-	-
99A TYR*	2.9	30.1	+	-	-	-
159A TYR*	3.5	34.7	-	-	-	+
2C LEU*	1.3	74.9	-	-	-	+
4C ALA*	1.3	67.6	+	-	-	+
5C LEU	3.6	16.6	+	-	-	-

Residues in contact with ALA 4 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
2C LEU	3.8	1.4	+	-	-	-
3C SER*	1.3	81.1	+	-	-	+
5C LEU*	1.3	74.2	+	-	+	+

Residues in contact with LEU 5 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
155A GLN*	3.7	31.3	+	-	-	+
3C SER*	3.6	15.3	+	-	-	-
4C ALA*	1.3	87.1	-	-	+	+
6C VAL*	1.3	68.4	+	-	-	+

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Residues in contact with VAL 6 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
70A HIS*	3.3	52.3	-	-	+	+
73A THR*	2.9	43.1	+	-	+	+
97A ARG*	3.8	24.7	-	-	-	+
5C LEU*	1.3	81.6	-	-	-	+
7C GLY*	1.3	59.5	+	-	-	+
8C ILE*	3.8	1.2	+	-	-	+

Residues in contact with GLY 7 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
73A THR*	4.0	6.1	-	-	-	+
97A ARG*	4.3	7.0	+	-	-	+
147A TRP*	3.8	21.7	-	-	-	-
6C VAL*	1.3	74.8	-	-	-	+
8C ILE*	1.3	68.0	+	-	-	+

Residues in contact with ILE 8 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
76A VAL*	3.7	39.0	-	-	+	-
77A ASP*	3.3	11.2	-	-	-	+
147A TRP*	2.7	27.4	+	-	-	-
7C GLY*	1.3	74.0	-	-	-	-
9C VAL*	1.3	66.9	-	-	-	+

Residues in contact with VAL 9 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
77A ASP*	2.8	36.3	+	-	+	+
80A THR*	3.6	17.0	+	-	+	+
81A LEU*	4.0	23.1	-	-	+	-
84A TYR*	2.9	18.2	+	-	+	-
116A TYR*	3.6	36.8	-	-	+	+
43A THR*	2.5	42.4	+	-	+	+
146A LYS*	3.1	29.3	+	-	-	-
147A TRP*	3.9	17.0	-	-	+	+
8C ILE*	1.3	82.7	-	-	-	+

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(3) Contacts of residues 1 - 9 (chain C) in PDB entry 1EEZ

Residues in contact with ILE 1 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
7A	TYR*	3.0	22.5	+	-	-	-
59A	TYR*	3.4	22.9	-	-	+	-
63A	GLU*	3.4	17.3	-	-	-	+
159A	TYR*	2.7	28.9	+	-	-	-
163A	THR*	3.6	17.7	-	-	+	+
167A	TRP*	3.2	53.9	-	-	+	+
171A	TYR*	2.9	42.3	+	-	-	+
2C	LEU*	1.3	57.6	+	-	-	+

Residues in contact with LEU 2 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
7A	TYR*	3.4	31.6	+	-	+	-
9A	PHE*	3.8	16.2	-	-	+	-
45A	MET*	3.5	25.6	-	-	+	-
63A	GLU*	2.8	27.0	+	-	-	+
66A	LYS*	3.2	22.3	+	-	+	+
67A	VAL*	3.6	32.3	-	-	+	+
99A	TYR*	3.6	14.1	-	-	-	+
159A	TYR*	3.5	6.0	-	-	-	-
1C	ILE*	1.3	81.8	-	-	-	+
3C	SER*	1.3	70.4	+	-	-	+
4C	ALA*	3.5	1.2	+	-	-	+

Residues in contact with SER 3 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
70A	HIS*	3.2	22.9	-	-	-	-
99A	TYR*	2.8	32.1	+	-	-	-
159A	TYR*	3.4	33.3	-	-	-	+
2C	LEU*	1.3	75.1	-	-	-	+
4C	ALA*	1.3	60.4	+	-	-	+
5C	LEU*	3.0	36.6	+	-	-	+

Residues in contact with ALA 4 (chain C).

				Specific contacts			

Residue	Dist	Surf	HB	Arom	Phob	DC
65A ARG*	6.1	0.2	-	-	-	+
66A LYS*	3.9	26.2	-	-	+	+
159A TYR*	4.8	2.4	-	-	-	-
2C LEU	3.5	2.8	+	-	-	-
3C SER*	1.3	73.5	+	-	-	+
5C LEU*	1.3	62.1	+	-	+	+

Residues in contact with LEU 5 (chain C).

		Specific contacts				
Residue	Dist	Surf	HB	Arom	Phob	DC
155A GLN*	2.9	57.9	-	-	+	+
156A LEU*	3.9	24.6	-	-	+	+
3C SER*	3.0	30.5	+	-	-	+
4C ALA*	1.3	82.7	-	-	+	+
6C VAL*	1.3	62.3	+	-	-	+
7C GLY	3.7	3.6	+	-	-	+

Residues in contact with VAL 6 (chain C).

		Specific contacts				
Residue	Dist	Surf	HB	Arom	Phob	DC
70A HIS*	3.4	63.0	-	-	+	+
73A THR*	3.1	27.5	+	-	+	+
74A HIS*	5.1	0.2	-	-	+	-
5C LEU*	1.3	74.3	-	-	-	+
7C GLY*	1.3	67.8	-	-	-	+

Residues in contact with GLY 7 (chain C).

		Specific contacts				
Residue	Dist	Surf	HB	Arom	Phob	DC
73A THR*	3.5	8.7	-	-	-	+
97A ARG*	4.0	9.7	+	-	-	-
5C LEU*	3.7	4.6	+	-	-	+
6C VAL*	1.3	79.7	-	-	-	+
8C ILE*	1.3	62.0	+	-	-	-

Residues in contact with ILE 8 (chain C).

		Specific contacts				

Residue		Dist	Surf	HB	Arom	Phob	DC
73A	THR*	3.3	43.7	-	-	+	+
76A	VAL*	3.7	34.8	-	-	+	-
77A	ASP*	3.0	17.3	-	-	-	+
147A	TRP*	3.3	12.8	+	-	-	-
7C	GLY*	1.3	74.7	-	-	-	-
9C	LEU*	1.3	88.4	+	-	+	+

Residues in contact with LEU 9 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
77A	ASP*	3.0	32.3	+	-	+	+
80A	THR*	3.9	22.6	+	-	+	+
81A	LEU*	3.6	45.1	-	-	+	-
116A	TYR*	3.8	21.1	-	-	+	+
123A	TYR*	4.0	9.4	-	-	+	+
143A	THR*	3.7	26.5	-	-	+	+
146A	LYS*	2.8	45.5	+	-	-	+
147A	TRP*	3.7	32.3	+	-	+	+
8C	ILE*	1.3	89.4	-	-	+	+

(4) Contacts of residues 1 - 9 (chain C) in PDB entry 1HHG.

Residues in contact with THR 1 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
7A	TYR*	2.6	21.8	+	-	-	-
63A	GLU*	2.7	26.3	+	-	-	-
66A	LYS*	3.5	5.7	+	-	-	+
159A	TYR*	2.7	27.7	+	-	+	-
163A	THR*	3.6	18.2	-	-	+	-
167A	TRP*	3.6	53.4	-	-	+	+
171A	TYR*	2.6	34.2	+	-	-	-
2C	LEU*	1.3	58.2	+	-	-	+

Residues in contact with LEU 2 (chain C).

				Specific contacts			

Residue	Dist	Surf	HB	Arom	Phob	DC
7A TYR*	3.5	26.7	-	-	+	-
9A PHE*	3.7	17.5	-	-	+	-
45A MET*	3.6	18.4	-	-	+	-
63A GLU*	2.8	30.9	+	-	-	+
66A LYS*	2.8	28.9	+	-	+	+
67A VAL*	3.4	34.8	-	-	+	+
70A HIS*	3.8	3.6	-	-	-	+
99A TYR*	3.1	21.5	-	-	-	+
159A TYR*	3.9	2.9	-	-	-	-
1C THR*	1.3	79.8	-	-	-	+
3C THR*	1.3	67.4	+	-	-	+

Residues in contact with THR 3 (chain C).

			Specific contacts			
Residue	Dist	Surf	HB	Arom	Phob	DC
66A LYS*	3.9	4.1	-	-	-	+
70A HIS*	2.9	30.2	-	-	+	+
99A TYR*	3.1	33.3	+	-	+	+
159A TYR*	3.5	38.2	-	-	+	+
2C LEU*	1.3	79.4	-	-	-	+
4C SER*	1.3	61.0	+	-	-	+
5C CYS*	3.6	21.5	-	-	+	+

Residues in contact with SER 4 (chain C).

			Specific contacts			
Residue	Dist	Surf	HB	Arom	Phob	DC
66A LYS*	3.7	25.4	-	-	-	+
155A GLN*	4.0	9.4	+	-	-	-
2C LEU	4.0	0.2	+	-	-	-
3C THR*	1.3	73.5	+	-	-	+
5C CYS*	1.3	60.1	+	-	-	+

Residues in contact with CYS 5 (chain C).

			Specific contacts			
Residue	Dist	Surf	HB	Arom	Phob	DC
70A HIS*	3.9	16.9	+	-	+	-

155A	GLN*	4.0	18.8	-	-	-	+
3C	THR*	3.6	25.5	+	-	+	+
4C	SER*	1.3	76.9	-	-	-	+
6C	ASN*	1.3	59.6	+	-	-	+
7C	THR*	3.6	28.9	-	-	-	-

Residues in contact with ASN 6 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
73A	THR*	3.5	21.5	+	-	-	+
5C	CYS*	1.3	72.7	-	-	-	+
7C	THR*	1.3	67.9	+	-	-	+
8C	SER*	3.4	4.3	+	-	-	-

Residues in contact with THR 7 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
73A	THR*	3.4	11.0	-	-	-	+
97A	ARG*	3.7	17.3	+	-	-	-
147A	TRP*	3.8	21.8	-	-	+	+
152A	VAL*	3.8	35.6	-	-	+	+
5C	CYS*	3.6	22.9	-	-	-	-
6C	ASN*	1.3	80.3	+	-	-	+
8C	SER*	1.3	62.4	+	-	-	+

Residues in contact with SER 8 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
73A	THR*	3.9	9.2	-	-	-	-
76A	VAL*	3.3	30.1	-	-	-	+
77A	ASP*	3.0	25.4	+	-	-	-
147A	TRP*	2.9	26.0	+	-	-	-
6C	ASN	3.4	4.3	+	-	-	-
7C	THR*	1.3	75.9	-	-	-	+
9C	VAL*	1.3	64.7	+	-	-	+

Residues in contact with VAL 9 (chain C).

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				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
77A	ASP*	2.9	42.7	+	-	+	+
80A	THR*	3.4	24.0	+	-	+	+
81A	LEU*	4.0	12.3	-	-	+	-
84A	TYR*	2.9	14.0	+	-	-	-
116A	TYR*	4.0	22.0	-	-	+	-
123A	TYR*	4.0	14.8	-	-	+	+
143A	THR*	3.1	40.4	+	-	+	+
146A	LYS*	2.6	43.0	+	-	-	+
147A	TRP*	3.9	12.3	-	-	+	-
8C	SER*	1.3	76.9	+	-	-	+

(5) Contacts of residues 1 - 9 (chain C) in PDB entry 1JHT.

Residues in contact with ALA 1 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
5A	MET*	3.5	12.3	-	-	-	+
7A	TYR*	3.0	21.3	+	-	-	-
63A	GLU*	3.4	20.0	-	-	-	+
66A	LYS*	4.0	6.3	-	-	-	+
159A	TYR*	2.6	31.9	+	-	-	-
167A	TRP*	3.2	46.0	-	-	+	+
171A	TYR*	2.8	36.4	+	-	-	+
2C	LEU*	1.3	57.5	+	-	-	+

Residues in contact with LEU 2 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
7A	TYR*	3.5	30.9	+	-	+	-
9A	PHE*	3.7	17.0	-	-	+	-
45A	MET*	3.5	25.4	-	-	+	-
63A	GLU*	2.8	24.0	+	-	-	+
66A	LYS*	2.9	29.4	+	-	+	+
67A	VAL*	3.4	35.4	-	-	+	+
99A	TYR*	3.5	15.9	-	-	-	+
159A	TYR*	3.8	6.1	-	-	-	-
1C	ALA*	1.3	77.3	-	-	-	+
3C	GLY*	1.3	64.5	+	-	-	+

Residues in contact with GLY 3 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
66A	LYS*	3.9	4.0	-	-	-	+
70A	HIS*	3.2	19.9	-	-	-	-
99A	TYR*	2.9	17.4	+	-	-	-
159A	TYR*	3.6	30.8	-	-	-	-
2C	LEU*	1.3	76.3	-	-	-	+
4C	ILE*	1.3	68.4	+	-	-	+
6C	ILE*	4.0	6.7	-	-	-	-

Residues in contact with ILE 4 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
66A	LYS*	3.6	25.8	-	-	+	-
155A	GLN*	2.9	54.2	+	-	+	+
3C	GLY*	1.3	79.9	-	-	-	+
5C	GLY*	1.3	68.5	+	-	-	+
6C	ILE*	3.1	16.7	-	-	-	+

Residues in contact with GLY 5 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
152A	VAL*	4.0	17.0	-	-	-	+
155A	GLN*	4.1	10.8	+	-	-	+
156A	LEU*	4.2	4.0	-	-	-	+
4C	ILE*	1.3	89.7	-	-	-	+
6C	ILE*	1.3	62.6	+	-	-	+
7C	LEU*	3.3	19.0	+	-	-	+

Residues in contact with ILE 6 (chain C).

				Specific contacts			
Residue		Dist	Surf	HB	Arom	Phob	DC
70A	HIS*	4.0	30.1	-	-	+	+
73A	THR*	3.6	22.0	+	-	+	-
74A	HIS*	5.1	0.9	-	-	+	-
97A	ARG*	3.3	37.2	-	-	-	
3C	GLY*	4.0	6.1	-	-	-	-
4C	ILE*	3.1	32.1	-	-	-	+
5C	GLY*	1.3	75.9	-	-	-	+
7C	LEU*	1.3	64.7	+	-	-	+

Residues in contact with LEU 7 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
73A THR*	3.6	7.2	-	-	-	+
147A TRP*	3.3	30.5	-	-	+	+
150A ALA*	4.0	19.5	-	-	+	+
152A VAL*	3.6	26.3	-	-	+	+
5C GLY*	3.3	18.7	+	-	-	+
6C ILE*	1.3	85.9	-	-	-	+
8C THR*	1.3	66.6	+	-	+	+

Residues in contact with THR 8 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
73A THR*	3.5	13.4	+	-	-	+
76A VAL*	3.5	29.5	-	-	+	+
77A ASP*	2.6	24.9	+	-	-	-
147A TRP*	2.9	17.0	+	-	-	-
7C LEU*	1.3	76.8	-	-	+	+
9C VAL*	1.3	69.9	+	-	-	+

Residues in contact with VAL 9 (chain C).

Residue	Dist	Surf	Specific contacts HB	Arom	Phob	DC
77A ASP*	3.0	21.6	+	-	-	+
80A THR*	3.9	25.2	+	-	+	+
81A LEU*	3.9	21.5	-	-	+	-
84A TYR*	2.7	18.7	+	-	+	-
116A TYR*	3.7	31.6	-	-	+	+
143A THR*	2.6	47.6	+	-	+	+
146A LYS*	2.7	26.5	+	-	-	-
147A TRP*	3.7	20.2	-	-	+	-
8C THR*	1.3	81.2	+	-	-	+

Discussion:

For a given a solved structure of a peptide-MHC complex, the contacting MHC residues for each peptide position are determined. The interaction of an amino acid at a certain position with all its contacting residues can be scored using statistical amino-acid pair wise potentials. Thus, for each position we obtain 20 scores for the 20 Amino-acids, which express their fitness for binding in the groove when placed at that position. Consequently, for a peptide of length L we can

compute a 20xL matrix that contains scores for each of the 20 amino-acids at each of the 20 amino-acids at each of the L peptide positions.

This matrix is essentially similar to the weight matrices extracted from binding data, but the weight for each amino-acid at each of the peptide's positions are based on the interaction preferences between amino-acids. As in the other matrix-based algorithms we assume position independence, and the peptide score is simply the sum of scores over all the peptide's positions. Thus, although the algorithm uses structural considerations, the computation is as simple and fast as that of the sequence based algorithms, and it can be easily applied to search all overlapping peptide of a given sequence as well as whole proteomes.

Conclusion:

Computational binding predictions provide useful data complementary to wet lab experiment. Predictions are useful for peptide selection for binding studies, planning experiments and better understanding of immune system.

The combination of accurate binding prediction with new experimental methods for identification of T-cell epitopes will allow tracking of antigen specific CTL response in clinical studies. The ability of the bioinformatics methods to reliably predict MHC binding peptides and thereby potential T- cell epitopes clearly has major implications of clinical immunology, particularly in the area of Vaccine design.

The accurate prediction of T-cell epitopes is crucial to the development of computational vaccinology or computer aided vaccine design (28, 29). The ability to predict MHC binding reliably will help us to analyze microbial immunomes, identifying the most antigenic epitopes and favored putative vaccines. By using efficient and accurate software, we hope to foster collaboration within computer aided vaccine design. Such cooperation is vital if the field is to impact upon the discovery of novel vaccines in a way similar to that of other informatics techniques on the design, discovery and exploitation of new pharmaceuticals.

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