

## REVIEW

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## SYFPEITHI: database for MHC ligands and peptide motifs

**Abstract** The first version of the major histocompatibility complex (MHC) databank SYFPEITHI: database for MHC ligands and peptide motifs, is now available to the general public. It contains a collection of MHC class I and class II ligands and peptide motifs of humans and other species, such as apes, cattle, chicken, and mouse, for example, and is continuously updated. All motifs currently available are accessible as individual entries. Searches for MHC alleles, MHC motifs, natural ligands, T-cell epitopes, source proteins/organisms and references are possible. Hyperlinks to the EMBL and PubMed databases are included. In addition, ligand predictions are available for a number of MHC allelic products. The database content is restricted to published data only.

**Key words** MHC · Peptide motif · T-cell epitope

### Introduction

The function of MHC molecules is the transfer of information about the current stock of proteins within a cell to the cell surface, thus enabling the immune system to react if necessary, for example by inducing cytotoxic T lymphocytes to kill virus-infected cells or by activating B cells by a helper T lymphocyte. In this context, the peptide specificity of MHC class I and class II mole-

cules is important for the selection of relevant peptides.

The first collection of MHC ligands and peptide motifs was published as the First Listing in the anniversary issue of Immunogenetics in 1995 (Rammensee et al. 1995) and already contained at this time a few hundred entries, mainly consisting of human ligands and T-cell epitopes. By 1997, an enormous amount of information on the peptides associated with MHC molecules had been accumulated and an update of the first collection was published (Rammensee et al. 1997). This collection contained not only MHC peptide motifs, MHC ligands, and T-cell epitopes but also the amino acid sequences of MHC molecules, to enable the elucidation of the structural basis of MHC motifs by analyzing the nature of the pockets involved in the binding process. Since then, even more MHC motifs have become available. In order to meet the needs of colleagues involved with MHC-associated peptides and to provide a handy source of MHC ligands and epitopes and related entries, the database SYFPEITHI was designed and published via the World-Wide-Web (WWW). The name SYFPEITHI was chosen to acknowledge the first MHC-eluted peptide that was directly sequenced (Falk et al. 1991). Data related to peptides eluted from MHC molecules have been compiled in the database; at present, it comprises approximately 2000 entries reported for human, mouse, rat, ape, cattle, and chicken MHC alleles. All entries are linked to the respective sequences of the EMBL database and the abstracts published in PubMed. The possibility of epitope predictions for a limited number of MHC motifs has been opened, and in the near future the molecular mass of the peptides will complement the collection.

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### Materials and methods

All data are stored centrally in a relational client-server database system (RDBMS). The main table of the RDBMS contains examples of ligands and T-cell epitopes, as well as additional informa-

# Find Your Motif



**1. Select MHC type**

all
<b>Bota-A11</b>
Bota-A20
Chicken B-F12
Chicken B-F15
Chicken B-F19
Chicken B-F4
H2-Db
H2-Dd
H2-Kb
H2-Kd
H2-Kk
H2-Kkm1
H2-Ld
H2-M3
HLA-A*0101
HLA-A*0201

Hold down ctrl key when clicking to select multiple items

**2. Paste a sequence (optional)**

 (Use "?" or "\*" as wildcards)

**3. Define further search conditions (optional)**

AND	Source of Peptide	<input type="text"/>
AND	mass	<input type="text"/>
AND	Reference	<input type="text"/>

**4. Choose aminoacids at anchor positions (optional)**

AND	Histidine (H)	position 2
AND	Leucine (L)	position 9
AND	[no selection]	position 1
AND	[no selection]	position 1

**5.  Include mass to output (optional)**

**6. Start query**

Do Query	Reset	Home
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**Fig. 1** 'Find Your Motif' section of the SYFPEITHI database

tion on the specific role (anchor and auxiliary anchor amino acids) and position of each individual amino acid (aa). When data are browsed, the information is transformed to present a formatted version in which anchor aa are given in bold letters and auxiliary anchors are underlined. The main table is linked in a many-to-one relationship to the list of sources, and in a many-to-many relationship with the table of references. Each record in the table of source proteins refers to the specific EMBL ID, whereas each entry in the table of references is linked to the accession number (AN) of the reference in the NLM-PubMed database.

**Table 1** Motif pattern for the prediction of HLA-B\*1510 ligands

AA	1	2	3	4	5	6	7	8	9
A	0	0	1	0	0	0	0	1	0
C	0	0	0	0	0	0	0	0	0
D	0	0	0	1	0	0	0	0	0
E	1	0	1	1	0	0	0	1	0
F	0	0	0	0	0	0	0	0	<b>6</b>
G	1	0	0	1	1	0	0	0	0
H	0	<b>10</b>	0	0	0	0	0	0	0
I	2	0	0	0	0	1	0	0	0
K	0	0	0	1	0	1	0	0	0
L	0	0	0	0	0	0	0	0	<b>10</b>
M	0	0	0	0	0	1	0	0	<b>6</b>
N	0	0	0	0	1	0	0	0	0
P	0	0	0	2	1	1	1	0	0
Q	0	0	0	1	0	0	0	0	0
R	0	0	0	0	0	1	2	2	0
S	0	0	1	0	0	0	0	0	0
T	1	0	0	0	0	0	0	1	0
V	0	0	0	1	0	1	2	2	0
W	0	0	0	0	0	0	0	0	0
X	0	0	0	0	0	0	0	0	0
Y	1	0	0	0	0	0	0	0	0

Database retrieval can be performed on any HTML-browser supporting JavaScript. The main page of the database (<http://www.uni-tuebingen.de/uni/kxi/>) offers three sections: "Find Your Motif", "Epitope prediction" and "Information". After a preselection of one or multiple MHC-types, the "Find Your Motif" section (Fig. 1) allows the user to search for a complete or truncated sequence of up to nine aa, a given peptide source, or a reference. The search can be narrowed down even further by choosing a specific aa on a given position as anchor or auxiliary anchor. All search criteria may also be combined to obtain a complex analysis. When a search is performed, an SQL-query is generated and the results are presented on a dynamically composed HTML page. The page of results lists the MHC type, motifs, peptide sources, and references. From each peptide source and each reference, a hyperlink to the EMBL or PubMed database is generated, respectively.

The algorithm used for epitope prediction is written in Object-Pascal. In brief, a two-dimensional data array is built up, where the letters of the aa represent the row index and the pocket numbers represent the column index (Table 1). The scores in the array-cells of the matrix shown in Table 1 can be addressed directly by a pair of indices. Starting at the first aa, the sequence is then divided into octa-, nona- or decamers and for each oligomer the sum of the scores of the aa contained is calculated. The process is then repeated until the end of the sequence is reached. Amino acids that frequently occur in anchor positions are given the value 10, the value 8 is given to amino acids present in a significant number of ligands, and 6 for rarely occurring residues; amino acids of auxiliary anchor positions are given the value 6, less frequent residues of the same set have a coefficient of 4; preferred amino acids have coefficients of 1–4 according to the strength of signals in pool sequencing or the occurrence in individual sequences. Amino acids that are regarded as unfavorable for binding have a coefficient of –1 to –3. These values are taken into account in the algorithm.

## Results and discussion

The main contents of the first SYFPEITHI release are shown in Table 3. Since the First Listing, a nearly five-

**Table 2** Peptide motif and natural ligands of HLA-DRB1\*0301

	Position									Source protein	Reference														
	1	2	3	4	5	6	7	8	9																
<b>Anchors</b>	<b>L</b>	<b>D</b>	<b>K</b>	<b>Y</b>							Malcherek et al. 1993; Geluk et al. 1992, 1994														
	<b>I</b>		<b>R</b>	<b>L</b>																					
	<b>F</b>		<b>E</b>	<b>F</b>																					
	<b>M</b>		<b>Q</b>																						
	<b>V</b>		<b>N</b>																						
<b>Examples for ligands</b>																									
	I	S	N	Q	L	T	L	D	S	N	T	K	Y	F	H	K	L	N	Apolipoprotein B-100 (2877–2894)	Malcherek et al. 1993					
	I	S	N	Q	L	T	L	D	S	N	T	K	Y	F	H	K	L	N	Apolipoprotein B-100 (2877–2893)	Malcherek et al. 1993					
	I	S	N	Q	L	T	L	D	S	N	T	K	Y	F	H	K			Apolipoprotein B-100 (2877–2892)	Malcherek et al. 1993					
	V	D	T	F	L	E	D	V	K	N	L	Y	H	S	E	A			$\alpha$ 1-Antitrypsin (149–164)	Malcherek et al. 1993					
	K	P	R	A	I	V	V	D	P	V	H	G	F	M	Y				LDL receptor (518–532)	Malcherek et al. 1993					
	K	Q	T	I	S	P	D	Y	R	N	M								IG2a (384–395)	Malcherek et al. 1993					
	Y	P	D	F	I	M	D	P	K	E	K	D	K	V					Unknown	Malcherek et al. 1993					
	N	I	Q	L	I	N	D	Q	E	V	A	R	F	D					Unknown	Malcherek et al. 1993					
	L	L	S	F	V	R	D	L	N	O	Y	R	A	D					Transferrin receptor (618–632)	Malcherek et al. 1993					
L	P	K	P	P	K	P	V	S	K	M	R	M	A	T	P	L			Invariant chain (97–111)	Riberdy et al. 1992; Chiciz et al. 1993; Sette et al. 1992					
L	P	K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q	A	L	P			
L	P	K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q	A	L	P	M		
P	K	P	P	K	P	V	S	K	M	R	M	A	T	P	L					Invariant chain (98–113)	Riberdy et al. 1992; Chiciz et al. 1993; Sette et al. 1992				
P	K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q	A						
K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q			Invariant chain (98–117)	Riberdy et al. 1992; Chiciz et al. 1993; Sette et al. 1992				
K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q			Invariant chain (99–116)	Riberdy et al. 1992; Chiciz et al. 1993; Sette et al. 1992				
K	P	P	K	P	V	S	K	M	R	M	A	T	P	L	L	M	Q	A	L	P	M				
V	D	D	T	Q	F	V	R	F	D	S	D	A	A	S	Q					HLA-A30 (52–67)	Chicz et al. 1993				
A	T	K	Y	G	N	M	T	E	D	H	V	M	H	L	L	Q	N	A		Invariant chain (131–149)	Chicz et al. 1993				
V	F	L	L	L	L	A	D	K	V	P	E	T	S	L	S					ACh receptor (289–304)	Chicz et al. 1993				
L	N	K	I	L	L	D	E	Q	A	Q	W	K							ICAM-2 (64–76)	Chicz et al. 1993					
G	P	P	K	L	D	I	R	K	E	E	Q	I	M	I	D	I	F	H		IFN $\gamma$ receptor (128–147)	Chicz et al. 1993				
G	P	P	K	L	D	I	R	K	E	E	Q	I	M	I	D	I	F	H	P		IFN $\gamma$ receptor (128–148)	Chicz et al. 1993			
G	F	K	A	I	R	P	D	K	K	S	N	P	I	I	R	T	V			Cyt-B5 (155–172)	Chicz et al. 1993				
Y	A	N	I	L	L	D	R	R	V	P	Q	T	D	M	T	F				Apolipoprotein B-100 (1207–1224)	Chicz et al. 1993				
N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N	K	N	S	L	K		Apolipoprotein B-100 (1276–1295)	Chicz et al. 1993			
I	P	D	N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N	K	N		Apolipoprotein B-100 (1273–1292)	Chicz et al. 1993			
I	P	D	N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N	K		Apolipoprotein B-100 (1273–1291)	Chicz et al. 1993				
I	P	D	N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N			Apolipoprotein B-100 (1273–1290)	Malcherek et al. 1993; Chiciz et al. 1993				
I	P	D	N	L	F	L	K	S	D	G	R	I	K	Y	T	L				Apolipoprotein B-100 (1273–1289)	Chicz et al. 1993				
N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N	K					Apolipoprotein B-100 (1276–1291)	Chicz et al. 1993				
N	L	F	L	K	S	D	G	R	I	K	Y	T	L	N						Apolipoprotein B-100 (1276–1290)	Chicz et al. 1993				
V	T	T	L	N	S	D	L	K	Y	N	A	L	D	L	T	N				Apolipoprotein B-100 (1294–1310)	Chicz et al. 1993				
V	G	S	D	W	R	F	L	R	G	Y	H	Q	Y	A						HLA-A2 (103–117)	Chicz et al. 1993				
<b>T-cell epitopes</b>																									
G	D	V	V	A	V	V	D	I	K	E	K	G	K	D	K	W	I	E	L	K					
K	T	I	A	Y	D	E	E	A	R																
M	G	R	S	I	K	V	Q	L	Q																
S	D	K	N	P	L	F	L	D	E	Q	L	I													
																				Lol pol. P1 (171–190)	Geluk et al. 1994				
																				HSP65 (cattle) (3–13)	Hawes et al. 1995				
																				M. tuberculosis 30/31 kD protein	Geluk et al. 1997				
																				(56–65)					
																				M. tuberculosis HSP70 (257–269)	Geluk et al. 1997				

fold increase in MHC motifs has been registered; the database SYFPEITHI now includes approximately 200 peptide motifs and 2000 peptide sequences. Each entry contains the peptide sequence, its MHC specificity, source protein, anchor positions, and publication references with links to the respective sequences in the EMBL databank and to the NLM-literature database PubMed. We refrained from including sequences other than those confirmed to ensure that only natural ligands and T-cell epitopes that are relevant for the respective MHC molecule are listed. A different database, MHCPEP (<http://wehih.wehi.edu.au/mhcpep/>), offered at the WEHI in Australia (Brusić et al. 1998) includes as many as 13 000 entries, in which submissions of preliminary data are included. MHCPEP also contains peptides that have been reported to bind to MHC in the absence of any functional data. Such peptides have been omitted from the SYFPEITHI database.

Table 4 depicts the MHC ligands of HLA-B\*1510 with the anchoring amino acids printed in bold letters as an example of a database entry. If available, auxiliary anchors are underlined, and preferred residues are also given. The typical length of a class I ligand comprises 9 amino acids. Below the anchor positions a list of ligands and T-cell epitopes specific for the respective molecule follows. This includes the respective protein sources and references, which are directly linked to other databases available on-line. Every single MHC allele has its individual peptide specificity that is defined primarily by the position and specificity of the pockets that accommodate the side chains of the anchoring amino acids and in the second place by interactions of non-anchoring amino acid residues of the peptides.

Class II ligands consist of 12 to 25 amino acids, nine of which occupy the binding groove; between two and four are anchored in the pockets. As in the case of class

**Table 3** MHC molecules currently included in the database

Class I			Class II
<b>Human:</b>			<b>Human:</b>
HLA-A1	HLA-B*2709	<b>Macacca fascicularis:</b>	HLA-DQ1
HLA-A*0201	HLA-B35	Mafa-A2	HLA-DQ6 or -DQ2
HLA-A*0202	HLA-B*3501	<b>Macacca mulatta:</b>	HLA-DQA1*0201/DQB1*0202
HLA-A*0203	HLA-B*3503	Mamu-A*01	HLA-DQA1*0301/DQB1*0302 (DQ8)
HLA-A*0204	HLA-B37	Mamu-A*08	HLA-DQA1*0301/DQB1*0303 (DQ9)
HLA-A*0205	HLA-B*3701	Mamu-B*12	HLA-DQA1*0501/DQB1*0201 (DQ2)
HLA-A*0206	HLA-B*3801	<b>Pan paniscus:</b>	HLA-DQA1*0501/DQB1*0301 (DQ7)
HLA-A*0207	HLA-B39	Papa-Q*06	HLA-DQB1*0201
HLA-A*0209	HLA-B*39011	<b>Pan troglodytes:</b>	HLA-DQA1*0301/DQB1*0301 (DQ3.1)
HLA-A*0214	HLA-B*3902	Patr-A*04	HLA-DQA1*0301/DQB1*0401 (DQ4)
HLA-A3	HLA-B*40011	Patr-A*11	HLA-DQB1*0603
HLA-A*0301	HLA-B*40012 (B60)	Patr-B*01	HLA-DR2
HLA-A*1101	HLA-B*4002	Patr-B*13	HLA-DR2 (DRB5*0101 or DRB1*1501)
HLA-A24	HLA-B*4006 (B61)	Patr-B*16	HLA-DRB1*0101
HLA-A*2402	HLA-B42	<b>Saguinus oedipus:</b>	HLA-DRB1*0102
HLA-A25	HLA-B44	Saoe-G*01	HLA-DR17 or DRw52
HLA-A26	HLA-B*4402	Saoe-G*06 or Saoe-G*04	HLA-DR3
HLA-A*2601	HLA-B*4403	Saoe-G*08	HLA-DRB1*0301 (DR17)
HLA-A*2602	HLA-B*4405	Saoe-G, unassigned	HLA-DRB1*0401 (DR4Dw4)
HLA-A*2603	HLA-B45	<b>Mouse:</b>	HLA-DRB1*0402 (DR4Dw10)
HLA-A29	HLA-B*4501	H2-D <sup>b</sup>	HLA-DRB1*0403 (DR3Dw13)
HLA-A*2902	HLA-B*4601	H2-D <sup>d</sup>	HLA-DRB1*0404 (DR4Dw14)
HLA-A*3001	HLA-B*4801	H2-K <sup>b</sup>	HLA-DRB1*0405 (DR4Dw15)
HLA-A*3002	HLA-B51	H2-K <sup>d</sup>	HLA-DRB1*0406
HLA-A*3003	HLA-B*5101	H2-K <sup>k</sup>	HLA-DRB1*0407
HLA-A*3004	HLA-B*5102	H2-K <sup>km1</sup>	HLA-DR7
HLA-A*3101	HLA-B*5103	H2-L <sup>d</sup>	HLA-DRB1*0701
HLA-A32	HLA-B52	H2-M3	HLA-DR8
HLA-A*3301	HLA-B*5201	H2-M3f	HLA-DRB1*0801
HLA-A*3302	HLA-B*5301	Qa-1a	HLA-DRB1*0802
HLA-A*6601	HLA-B*5401	Qa-1b	HLA-DRB1*08032
HLA-A*6801	HLA-B*5501	Qa-2	HLA-DRB1*0901
HLA-A*6802	HLA-B*5502	<b>Rat:</b>	HLA-DRB1*1001
HLA-A*6901	HLA-B*5601	RT1.A <sup>a</sup>	HLA-DR11
HLA-A*7401	HLA-B57	RT1.A <sup>a</sup> (Tap2A-associated)	HLA-DR11 or Dw52
HLA-B7	HLA-B*5701	RT1.A <sup>a</sup> (Tap2B-associated)	HLA-DRB1*1101
HLA-B*0702	HLA-B*5702	RT1.A <sup>u</sup>	HLA-DRB1*1102
HLA-B*0703	HLA-B58	RT1.A1 <sup>c</sup>	HLA-DRB1*1104
HLA-B*0705	HLA-B*5801	RT1.A <sup>l</sup>	HLA-DRB1*1201
HLA-B8	HLA-B*5802	<b>Cattle:</b>	HLA-DRB1*1301
HLA-B*0801	HLA-B*6701	Bota-A11	HLA-DRB1*1302
HLA-B*0802	HLA-B*7301	Bota-A20	HLA-DRB1*1401
HLA-B13	HLA-B*7801	<b>Chicken:</b>	HLA-DRB1*1405
HLA-B14	HLA-Cw*0301	Chicken B-F12	HLA-DRB1*1501 (DR2b)
HLA-B15	HLA-Cw*0304	Chicken B-F15	HLA-DRB1*1502
HLA-B*1501 (B62)	HLA-Cw*0401	Chicken B-F19	HLA-DRB1*1601
HLA-B*1502	HLA-Cw*0601	Chicken B-F4	HLA-DRB1, unassigned
HLA-B*1503	HLA-Cw*0602	<b>Pig:</b>	HLA-DRB3*0101
HLA-B*1508	HLA-Cw*0702	D/d	HLA-DRB3*0202 (DR52Dw25)
HLA-B*1509	HLA-Cw*1601		HLA-DRB3*0301 (DR52Dw26)
HLA-B*1510	HLA-E		HLA-DRB4
HLA-B*1513	HLA-G		HLA-DRB4*0101
HLA-B*1516			HLA-DRB5*0101 (DR2a)
HLA-B*1517			HLA-DRB5*0202
HLA-B17			HLA-DRB, unassigned
HLA-B18			HLA-DRw11
HLA-B*1801			HLA-DRw52
HLA-B22			HLA-DRw52 or HLA-DQ2
HLA-B27			<b>Macacca mulatta:</b>
HLA-B*2702			Mamu-DRB1*0406
HLA-B*2703			Mamu-DRB*W201
HLA-B*2704			<b>Mouse:</b>
HLA-B*2705			H2-A <sup>b</sup> , H2-A <sup>d</sup> , H2-A <sup>g7</sup> , H2-A <sup>k</sup> , H2-A <sup>s</sup> ,
HLA-B*2706			H2-A <sup>u</sup> , H2-E <sup>b</sup> , H2-E <sup>d</sup>
HLA-B*2707			<b>Rat:</b>
			RT1.B <sup>l</sup>

**Table 4** Peptide motif and natural ligands of HLA-B\*1510 (Seeger and co-workers, in press)

	Position									Source	Accession No. EMBL database		
	1	2	3	4	5	6	7	8	9				
<b>Anchor residues</b>	<b>H</b>									<b>L</b>			
<b>Preferred residues</b>	I	E	P	A	V	V	V	V	F				
	Y	A	D	G	I	R	R	M					
	T	S	E	P	M	P	E						
	G	G	N	K	T								
	E	K	R	A									
		Q											
		V											
Examples for ligands	G	H	D	P	R	A	Q	G	T	L	HLA-DP $\alpha$ chain (220–229)	X00457	
	D	H	C	V	A	H	K	L			Cytochrome C reductase (66–73)	M36647	
	I	H	E	D	S	T	N	R	R	R	Heat shock protein 90 b (440–450)	M16660	
	E	H	A	H	N	M	R	V	M		Elongation factor 2 (489–497)	M19997	
	G	H	L	E	N	N	P	A	L		60 S acidic rib. protein PQ (67–75)	M17885	
	H	H	S	G	A	K	V	V	L		Chaperonin cont. TCP-1 $\eta$ (282–290)	AF026292	
	I	H	D	P	G	R	G	A	P	L	60 S ribosomal protein L8 (49–58)	Z28407	
	T	H	T	Q	P	G	V	Q	L		Septin 2 homologue (70–78)	D50918	
	T	H	Y	V	A	P	R	R	L		Transcription activator SNF2L4 (899–907)	U29175	
	Y	H	G	H	G	V	S	A	F		Human EST	T96718	
	Y	Q	E	K	G	V	R	V	L		Actin-related protein Arp2 (402–410)	AF006082	
	I	H	E	P	E	P	H	I	L		Cyclin-dep. kin. reg. subunit 1 (59–67)	X54941	
	A	H	S	T	I	M	P	R	L		DNA repl. lic. factor MCM4 (694–702)	X74794	
	E	H	A	G	V	I	S	V	L		HBV X interacting protein (40–48)	AF029890	

I ligands, the nonanchoring amino acids play a secondary, but still significant role. A number of examples of ligands specific for HLA-DRB1\*0301 are given in Table 2.

Information on the allelic specificity of the motifs, including preferred and disfavored residues beyond the anchor, enable the prediction of MHC ligands and T-cell epitopes. The second section of the database is dedicated to "Epitope prediction". The main objective of performing theoretical predictions is simply to save time. Instead of synthesizing and testing dozens or even hundreds of peptides, a preselection of a small set of peptides is made. The sequence of the protein or its gene, the restriction element, and its respective motif have to be available.

Motif-based predictions result in a list of peptides that have a high probability of being presented by MHC class I molecules. The prediction method used in the database is based on the principle of a building-up pattern (see Material and methods). The pattern used for the prediction of HLA-B\*1510 nonamers is shown in Table 1. The values of all possible nonamers of a given sequence are added together and the optimal T-cell epitope is expected within the ten high-scoring peptides of each protein. Scores for all source proteins of nonamer peptides and predicted epitopes specific for HLA-B\*1510 are given in Table 5. The correct and therefore naturally presented T-cell epitope from any source protein is assumed to appear among the top 2% of peptides in the high score list in more than 90% of predictions. However, theoretical approaches cannot always guarantee success. About 10% of the predictions are still unable to identify the respective epitope because not all details of the motifs are entirely known.

Epitope predictions are only available at present for a small number of MHC alleles, since all predictions undergo several rounds of thorough cross-checking and a certain number of natural ligands and/or T-cell epitopes have to be available to ensure an accurate and reliable prediction (Table 6). The occurrence of unusual anchor amino acids can be compensated by refining the motif, but still a small percentage of epitopes do not act in accordance with any rules of the respective motif. In these cases, the theoretical approach will fail and experimental epitope mapping is unavoidable. SYFPEITHI is the only freely available MHC database in the internet apart from an HLA peptide binding prediction offered by the NIH ([http://www-bimas.dcrn.nih.gov/cgi-bin/molbio/hla\\_bind/](http://www-bimas.dcrn.nih.gov/cgi-bin/molbio/hla_bind/)). The NIH prediction relies upon binding data (Parker et al. 1994) and estimates the half-time of dissociation of a given MHC-peptide complex. EpiMer (<http://www.brown.edu/Research/TB-HIVLab/Epimatrix/epimerlink.html>; Meister et al. 1995; Roberts et al. 1996) is a commercial site.

Other programs for the prediction of T-cell epitopes are distributed on disk (e.g., Motifs, D'Amaro et al. 1995; Davenport et al. 1995; Devereux et al. 1984; Fleckenstein et al. 1997; Hammer et al. 1994). Prediction patterns for class II are not yet included in our database due to the highly degenerate anchor positions in most MHC class II motifs. These degenerate anchor positions render the prediction of MHC class II ligands rather difficult. If all possible anchor residues of an MHC class II peptide motif are included within a search pattern, a very high number of possible natural MHC II ligands will be predicted. Only few of the class II peptide motifs encompass anchor residues specific

**Table 5** Motif prediction of HLA-B\*1510 self peptides and epitopes

<b>Actin-related protein 2 (ARP2; human)</b>		
AA pos.	Score	Sequence
378	19	YQEKGVRL
227	15	IEQEQKLAL
29	14	EHIFPALVG
60	14	EASELRSML
164	14	THICPVYEG
<b>Septin 2 homologue (SEP2; human)</b>		
AA pos.	Score	Sequence
70	25	THTQPGVQL
156	22	GHSLKSLDL
371	22	LHQDEKKKL
129	17	EELKIRRVL
84	15	DLOESNVRL
<b>60 S acidic ribosomal protein RQ (RLA0; human)</b>		
AA pos.	Score	Sequence
67	25	GHLENNPAL
80	19	PHIRGNVGF
241	18	IINGYKRVL
46	15	SLRGKAVVL
196	15	GSIYNPEVL
<b>Elongation factor 2 (EF2; human)</b>		
AA pos.	Score	Sequence
489	24	EHAHNMRVM
356	18	IHLPSVTA
147	17	IAERIKPVL
491	17	AHNMRVMKF
843	16	GLKEGIPAL
<b>Transcription activator SNF2L4 (SN24; human)</b>		
AA pos.	Score	Sequence
899	27	THYVAPRRL
1009	24	RHMQAKGVL
620	23	IHVESGKIL
889	23	HHCKLTQVL
968	23	LHKVLRPFL
252	18	PHGMGGPNM
522	18	IEKERMRL
<b>Cyclin-dependent kinase regulatory subunit (CKS1; human)</b>		
AA pos.	Score	Sequence
59	26	IHEPEPHIL
16	14	EFEYRHVML
64	14	PHILLFRRP
29	13	AKLVPKTHL
38	13	MSESEWRNL
<b>DNA replication license factor (MCM4; human)</b>		
AA pos.	Score	Sequence
694	25	AHSTIMPRL
331	21	CHTTHSMAL
255	20	EHQIQVRPF
440	16	LFSEKRVEL
741	16	AEAHAKVRL

enough to make motif-based predictions worthwhile, such as HLA-DRB1\*0301, for example. In addition, anchor residues are often not used by class II ligands and epitopes. Inclusion of possibilities to predict class II ligands is in preparation.

Table 5 Continued

<b>HIV1 GAG</b>		
AA pos.	Score	Sequence
192	22	GHQAAMQML
69	15	TGSEELRSL
143	15	HQAISPRTL
354	15	GPGHKARVL
42	14	RFAVNPGLL
<b>Influenza A PR8/34 nucleoprotein</b>		
AA pos.	Score	Sequence
333	21	CHSAAFEDL
323	18	AHKSQLVWM
100	15	VNGKWMREL
336	15	AAFEDLRLV
48	14	KLSDYEGRL

**Table 6** MHC motifs included in the database for epitope predictions

Human	Mouse
HLA-A*0201	H2-D <sup>b</sup>
HLA-A*0202	H2-K <sup>b</sup>
HLA-A*0203	H2-K <sup>d</sup>
HLA-A1	H2-K <sup>k</sup>
HLA-A26	H2-L <sup>d</sup>
HLA-B*0702	
HLA-B*1510	
HLA-B*2705	
HLA-B8	

### Availability

SYFPEITHI is freely available online at the Interfakultäres Institut für Zellbiologie, Abteilung Immunologie, Tübingen (WWW site address: <http://www.uni-tuebingen.de/uni/kxi>).

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