

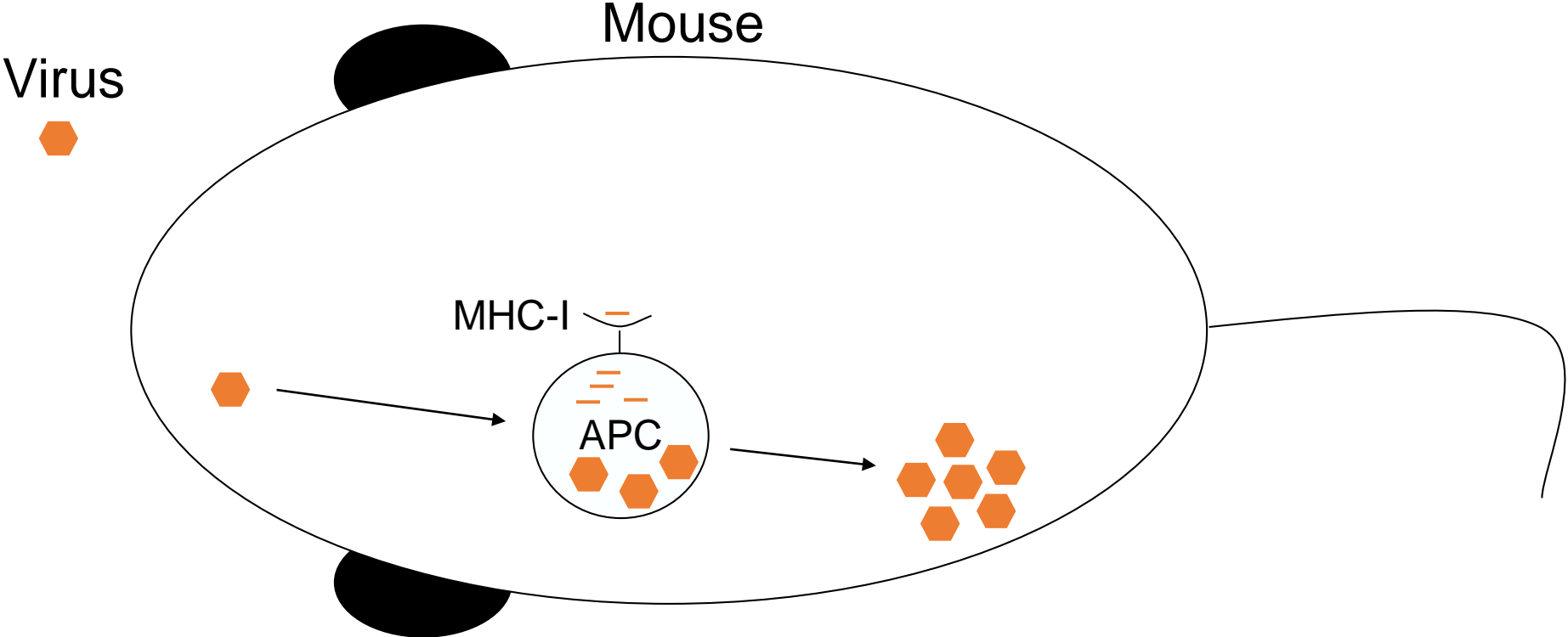


T Cell processing & immunogenicity predictions

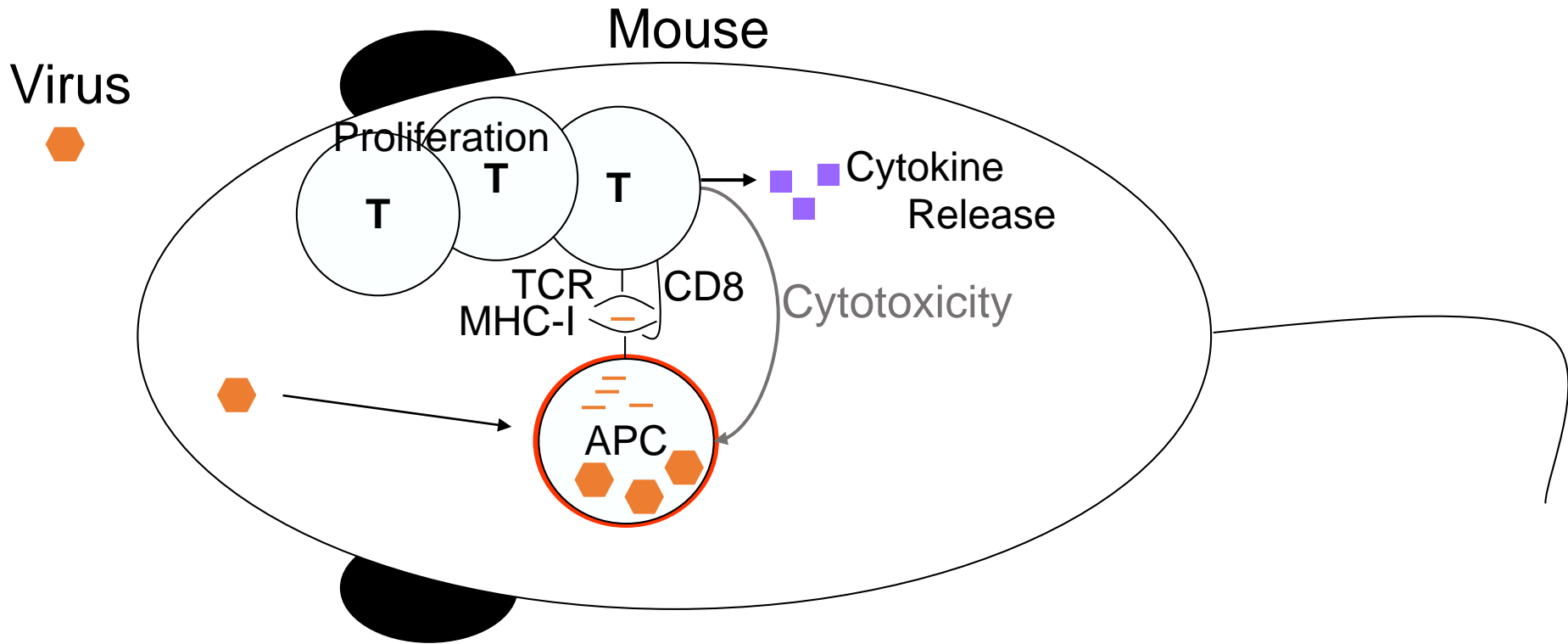
tools.iedb.org

Presented by: Bjoern Peters, PI

CD8+ T cell epitopes in viral infection



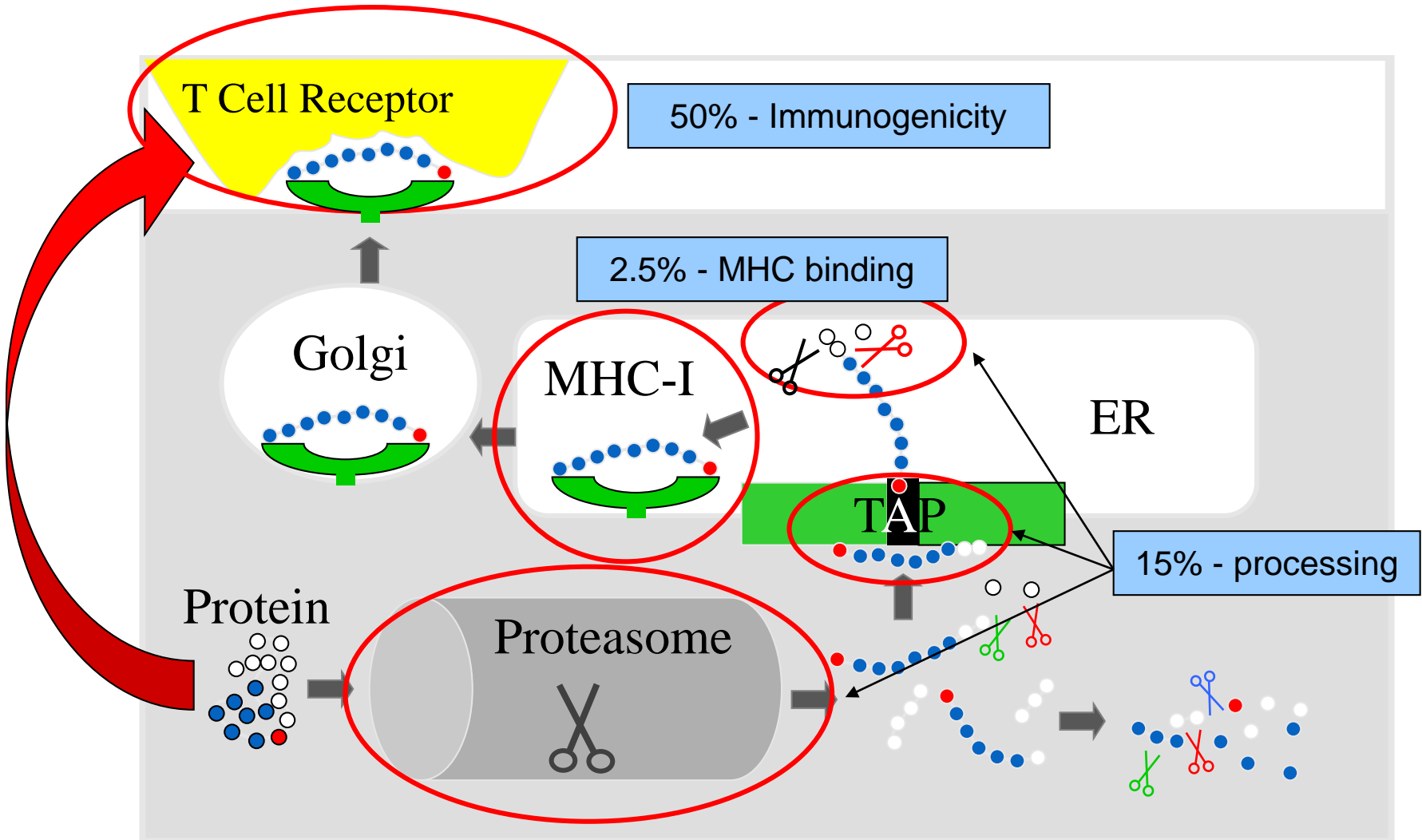
CD8+ T cell epitopes in viral infection



T cell epitope mapping

ORF 1	M G Q I V T M F E A L P H I I D E V I N I V I I V L I V I T G I K A V Y N ...
ORF 2	M G L K G P D I Y K G V Y Q F K S V E F D M S H L N L T M P N A C S A N N ...
ORF 3	M H N F C N L T S A F N K K T F D H T L M S I V S S L H L S I D G N S N Y ...
ORF 4	M S A Q S Q C R T F R G R V L D M F R T A F G G K Y M R S G W G W T G S D ...
ORF 5	M H C T Y A G P F G M S R I L L S Q E K T K F F T R R L A G T F T W T L S ...
ORF 6	M K C F G N T A V A K C N V N H D A E F C D M L R L I D Y N K A A L S K F ...
ORF 7	M L M R N H L L D L M G V P Y C N Y S K F W Y L E H A K T G E T S V P K C ...

MHC I - Antigen processing and presentation pathway

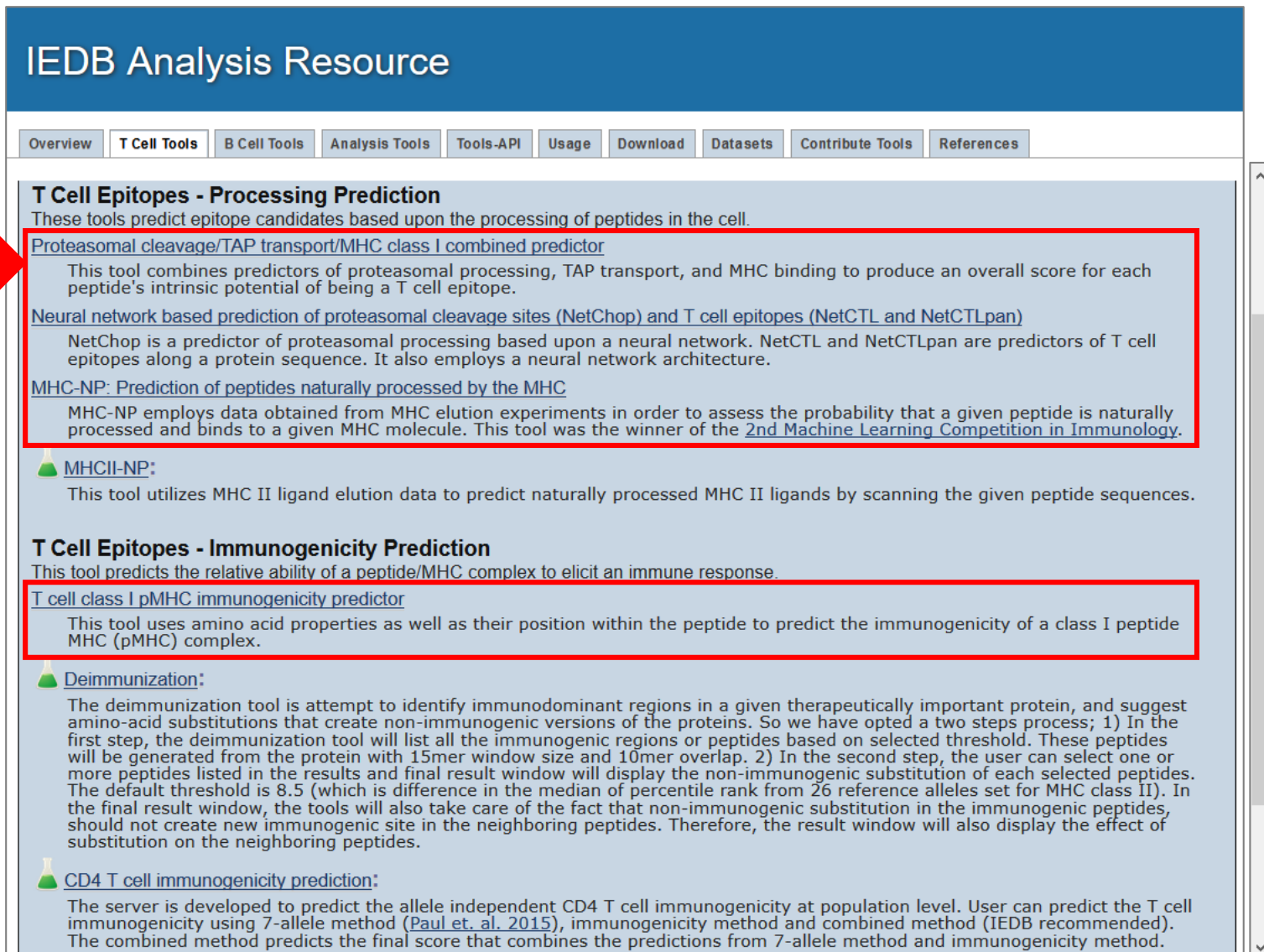


Peters et al, *J Mol Biol* 2002, *Bioinformatics* 2003, *J Immunol.* 2003; CMLS 2005;

Assarson, *J Immunol* 2007

Class I Processing + immunogenicity tools available in the IEDB

<http://tools.iedb.org/main/tcell/>



IEDB Analysis Resource

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Class I 'combined predictor'

<http://tools.iedb.org/processing/>

Home Help Example Reference Download Contact

MHC-I Processing Predictions

Prediction Method Version 2013-02-22 [\[Older versions\]](#)

Specify Sequence(s)

Enter protein sequence(s) in FASTA format
[\(Browse for sequences in NCBI\)](#)

Or select file containing sequence(s) No file selected.

Choose sequence format auto detect format

Choose a Prediction Method

Prediction Method IEDB recommended [Help on prediction method selections](#)

Specify what to make binding predictions for

MHC source species human

Show only frequently occurring alleles: [?](#)

Select MHC allele(s) Allele Length [Upload allele file](#) [?](#)

Proteasomal cleavage prediction

Specify proteasome type immuno

TAP transport predictions

Maximum precursor extension 1

Alpha factor 0.2


Specify Output

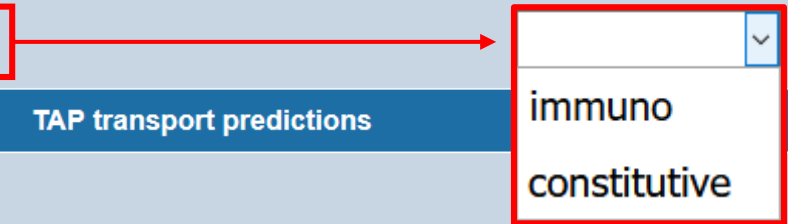
Output format XHTML table

- Combines predictions for:
 - proteasomal cleavage
 - TAP transport
- Trained on specific in vitro datasets

Proteasomal cleavage

<http://tools.iedb.org/processing/>

Proteasomal cleavage prediction	
Specify proteasome type	<input type="text" value="immuno"/> 
TAP transport predictions	
Maximum precursor extension	<input type="text" value="1"/>
Alpha factor	<input type="text" value="0.2"/>



- Proteasomes create the C-terminal end of peptides
- Prediction looks for sequence motive up and downstream of potential cleavage site
- Cleavage sequence motif determined based on in vitro protein digests by proteasomes

TAP Transport

<http://tools.iedb.org/processing/>

Proteasomal cleavage prediction	
Specify proteasome type	<input type="text" value="immuno"/>
TAP transport predictions	
Maximum precursor extension	<input type="text" value="1"/>
Alpha factor	<input type="text" value="0.2"/>

- TAP transport efficiency of peptides is sequence dependent; motif derived based on in vitro assays
- Overall TAP transport efficiency of a presented MHC ligand can be result of a collection of precursors
- Unless paper specifically read and details about the precursor length distribution are known, **keep parameters unchanged**

Class I 'combined predictor' - example

<http://tools.iedb.org/processing/>

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```
>LCMV Armstrong, Protein GP
MGQIVTMFEALPHIIDEVINIVIIVLIVITGIRKAVYNFATCGIFALISFLLLAGRSCGM
YGLKGPDIYKGVYQFKSVEFDMSHLNLTPNACSNNSHHYISMGTSGLELFTTNSII
SHNFCNLTSAPNKKTPDHTLMSIVSSLHLSIRGNSNYKAVSCDFNNGITIQYNLTFSDA
QSAQSQCRTRFRGRVLDMPRTAFGGKYMRSWGWTGSDGKTTWCSQTSYQYLIIQNRWE
NHCTYAGPFGMSRIILLSQEKTRKFFTRRLAGTFTWTLSDSSGVENPGGYCLTKWMLAAE
LKCFGNTAVAKCNVNHDAEFCMDLRLIDYNKAALSFKFEDVESALHLFKTTVNSLISDQ
LLMRNHLRDLMGVPPYCNYSKFWYLEHARTGETSVPKCWLVTNGSYLNETHPSDQIEQEA
DNMITEMLRKDYIKRQGSTFLALMDLDMFSTSAYLVSIFLHLVKIPTHRIKGGSCPKP
HRLNTRGICSCGAFKVPGVKTVWKR
```

Or select file containing sequence(s) No file selected.

Choose sequence format: auto detect format

Choose a Prediction Method

Prediction Method: IEDB recommended [Help on prediction method selections](#)

Specify what to make binding predictions for

MHC source species: mouse

Select MHC allele(s):
Allele: H-2-Kb Length: 10 [Upload allele file](#) ?

Proteasomal cleavage prediction

Specify proteasome type: immuno

TAP transport predictions

Maximum precursor extension: 1

Alpha factor: 0.2

Specify Output

Output format: XHTML table



Class I 'combined predictor' - example

MHC-I Processing Prediction Results

<http://tools.iedb.org/processing/>

Input Sequences

#	Name	Sequence
1	LCMV Armstrong, Protein GP	MGQIVTMFEALPHIIDEVINIVIIVLIVITGIKAVYNFATCGIFALISFLLLAGRS CGMYGLKGPDIYKGVYQFKSVEFDMSHLNLTMPNACSANNHHYISMGTSGLELTF TNDSEIISHNFCNLTSAFNKKTFDHTLMSIVSSLHLSIRGNSNYKAVSCDFNNGITI QYNLTFSDAQSAQSQCRFRGRVLDMFRTAFGGKYMRSGWGTGSDGKTTWCSQTS YQYLIIQNRTWENHCTYAGPFGMSRILLSQEKTKEFTRRLAGTFTWTLSDSSGVEN PGGYCLTKWMI LAAELKCFGNTAVARCNVNHDAEFCDMLRLIDYNKAALSKFKEDV ESALHLFKTTVNSLISDQLLMRNHLRDLMGVPYCNYSKFWYLEHAKTGETSVPKCW LVTNGSYLNETHFSDOIEQEADNMITEMLRKDYIKRQGSTPLALMDLLMFSTAYL VSI FLHLVKIPTHRRHIGGSCPKPHRLTNKGICSCGAFKVPGVKTVWKRR
2	LCMV Armstrong, Protein NP	MSLSKEVKS FQWTQALRRELQSFTSDVKA AVIKDATNLLNGLDFSEVSNVQIRMRK EKRDDKDLQRLRSLNQTVHSLVDLKSTSKKNVLKVGRLSAEELMSLAADLEKLRKAK IMRSERPQASGVYMGNLTTQQLDQRSQILQIVGMRKPQQGASGVVRVWDVKDSLL NNQFGTMPSLTMACMAKQSTPLNDVVQALTDLGLLYTVKYPNLNDLERLKDHPV LGVITEQQSSINISGYNFSLGA AVKAGAALLDGGNMLESILIKPSNSEDLLKAVLG ARRKLNMFVSDQVDRNPYENILYKVLCSGEGWPYIACRTSIVGRAWENTIDLTS EKPAVNSPRPAPGAAGPPQVGLSYSQTMLLKDLGGIDPNAPTWIDIEGRFNDPVE IAIFQPQNGQFIHFYRE PVDQKQFKQDSKYSHGMDLADLFNAQPGLTSSVIGALPQ GMVLS CQGSDDIRKLLDSQNRKDIKLIDVEMTREASREYEDKVVWDKYGWLCKMHTG IVRDKKKEITPHCALMDCIIFESASKARLPDLKTVHNILPHDLIFRGPNVVTL

Prediction method: recommended | High Score = high efficiency

[Download result](#) 

Citations

Allele	#	Start	End	Peptide Length	Peptide	Proteasome Score	TAP Score	MHC Score	Processing Score	Total Score	MHC IC50[nM]
H-2-Kb	2	203	212	10	LLYTVKYPNL	1.79	0.50	-2.01	2.28	0.27	103.5
H-2-Kb	1	116	125	10	SIISHNFCNL	1.51	0.46	-1.90	1.97	0.08	78.6
H-2-Kb	2	7	16	10	VKS FQWTQAL	1.42	0.39	-2.01	1.81	-0.21	102.9
H-2-Kb	2	235	244	10	INISGYNFSL	1.53	0.41	-2.18	1.95	-0.23	149.7
H-2-Kb	1	35	44	10	VYNFATCGIF	1.42	1.27	-3.12	2.68	-0.44	1327
H-2-Kb	1	75	84	10	KSVEFDMSHL	1.50	0.47	-2.45	1.96	-0.49	283.6
H-2-Kb	1	369	378	10	YCNYSKFWYL	1.45	0.31	-2.32	1.76	-0.56	206.8
H-2-Kb	1	449	458	10	VSI FLHLVKI	1.33	0.33	-2.25	1.66	-0.59	178.2

Class I 'combined predictor' - example

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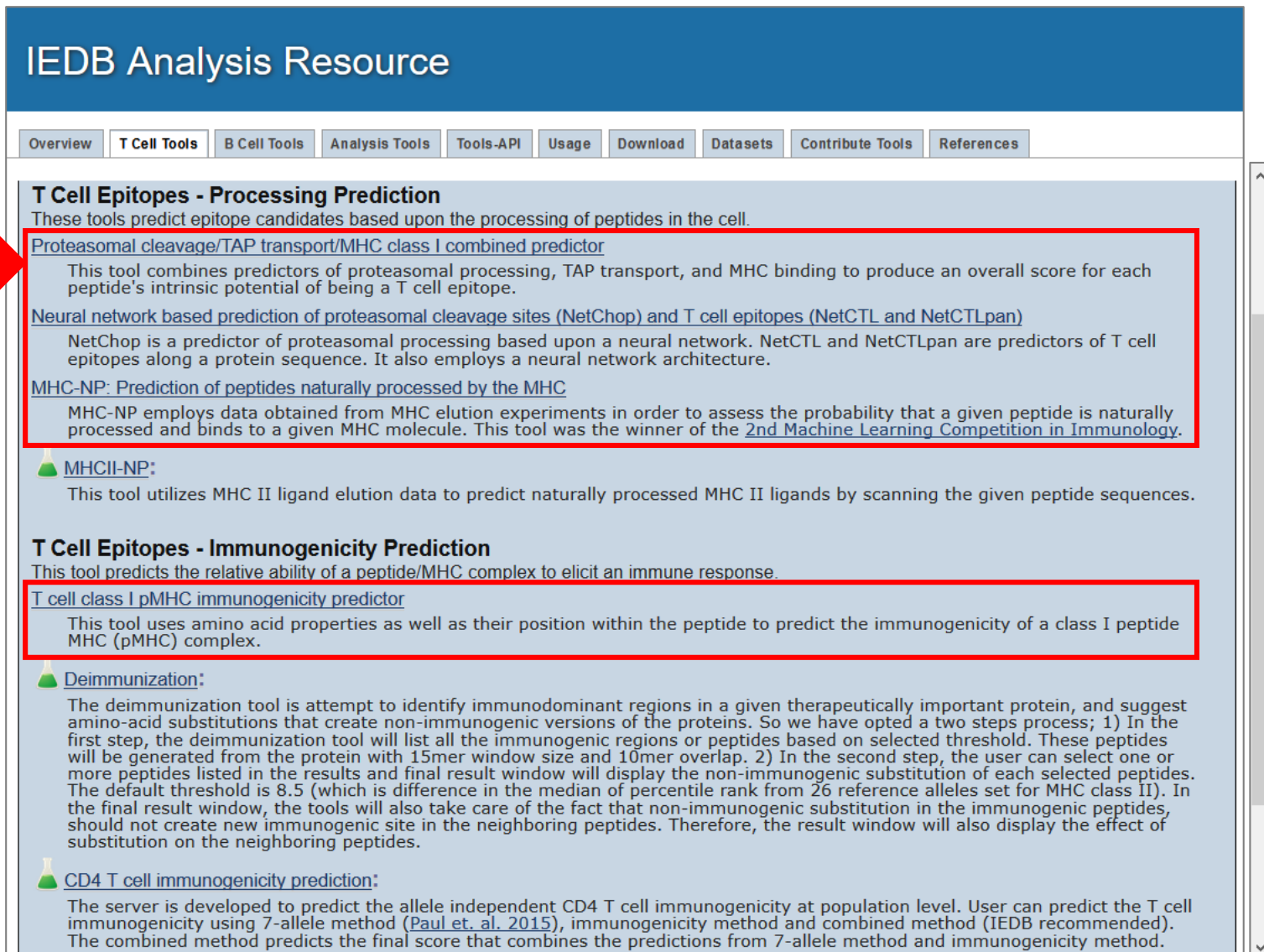
- Higher scores = higher efficiency for MHC-I presentation
- MHC binding score = $-\log_{10}(\text{IC}_{50})$ (sign change)
- Combined scores are additive
 - Processing = proteasome + TAP
 - Total = proteasome + TAP + MHC
- Different variance in scores reflects different selectivity

Caveats / performance of processing predictions

- Processing predictions beat MHC binding predictions when predicting **eluted peptides**
- No clear evidence that processing predictions are better at predicting **epitopes**
- Eluted peptides may over represent 'best possible' ligands, and the difference in processing may not be relevant in practice
- Co-evolution of MHC molecules to bind peptides with motifs that are generated by proteasome and TAP means that most high affinity MHC binders are also efficiently processed
- Recommendation: Use MHC binding predictions alone by default
 - If resources require limiting the number of peptides considered, use total score of processing predictions as additional filter

Class I Processing + immunogenicity tools available in the IEDB

<http://tools.iedb.org/main/tcell/>



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Neural Network based predictors

<http://tools.iedb.org/netchop/>

IEDB Analysis Resource

Home Help Example Reference Download Contact

Proteasomal Cleavage Prediction

NetChop/NetCTL/NetCTLpan

Specify Sequence(s)

Prediction Method: NetChop

Enter protein sequence(s) in FASTA format

Or select file containing sequence(s): Browse... No file selected.

Method Specific Options

Method: C term 3.0

Threshold: 0.5

Submit Reset

- **NetChop:** proteasomal cleavage
- **NetCTL:** combines NetChop, TAP transport, NetMHC
- **NetCTLpan:** combines NetChop, TAP transport, NetMHCpan

Key difference is the use of NetChop

NetChop -example

<http://tools.iedb.org/netchop/>

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Specify Sequence(s)

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Enter protein sequence(s) in FASTA format

```
>BHB191648|gi:90572034|gb:CY010133|UniProtKB:Q1WPY8|Gene  
Symbol:M2|Protein Name:Matrix protein 2|Organism:Influenza A Virus  
A/Canterbury/100/2000|Segment:7|Subtype:H1N1|Host:Human  
MSLLTEVETPIRNEWGCRCDSSDPLVVAASIIGIVHLILWIIDRLFYSKIYRIFKHGLKRGPSSTEGVPE  
SMREEYREEQQNAVDADDGHFVSIIELE  
>BHB191653|gi:90572040|gb:CY010136|UniProtKB:Q1WPY3|Gene  
Symbol:NS1|Protein Name:Nonstructural protein 1|Organism:Influenza A  
Virus A/Canterbury/100/2000|Segment:8|Subtype:H1N1|Host:Human  
MDSHTVSSFQVDCFLWHVRKQVADQDLGDAPFLDRLRRDQKSLKRGSTLGLNIETATCVGKQIVERILK  
EESDEAFKMTMASALASRYLTDMTIEEMSRDWFMLMPKQKRVAGPLCVRMDQAIMDKNIILKANFSVIFDR
```

Or select file containing sequence(s) No file selected.

Method Specific Options

Method: C term 3.0

Threshold: 0.5

C term 3.0

C term 3.0

20S 3.0

- Predicts C-terminal cleavage based on two approaches
 - **C-term 3.0:** C-terminal residues found for MHC ligands
 - **20S 3.0:** Cleavage sites based on in vitro protein digests
- C-term 3.0 is not truly a proteasome predictor but performs better
- NetCTL and NetCTLPan use C-term 3.0 by default

NetChop -example

<http://tools.iedb.org/netchop/>

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Proteasomal Cleavage Prediction

NetChop/NetCTL/NetCTLpan

Threshold: Change Table View Save This Page Save All Pages

Browse by sequence:

NetChop Prediction

— Threshold = 0.5 ■ Positive prediction ■ Negative prediction

Score

Position

View each sequence dropdown:

- BHB191648|
- BHB191653|
- BHB191652|

NetChop -example

<http://tools.iedb.org/netchop/>

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NetChop Result

The positive predictions are displayed in green. Click on header to sort column.

[Chart View](#) [Save This Page](#) [Save All Pages](#)

Browse by sequence:

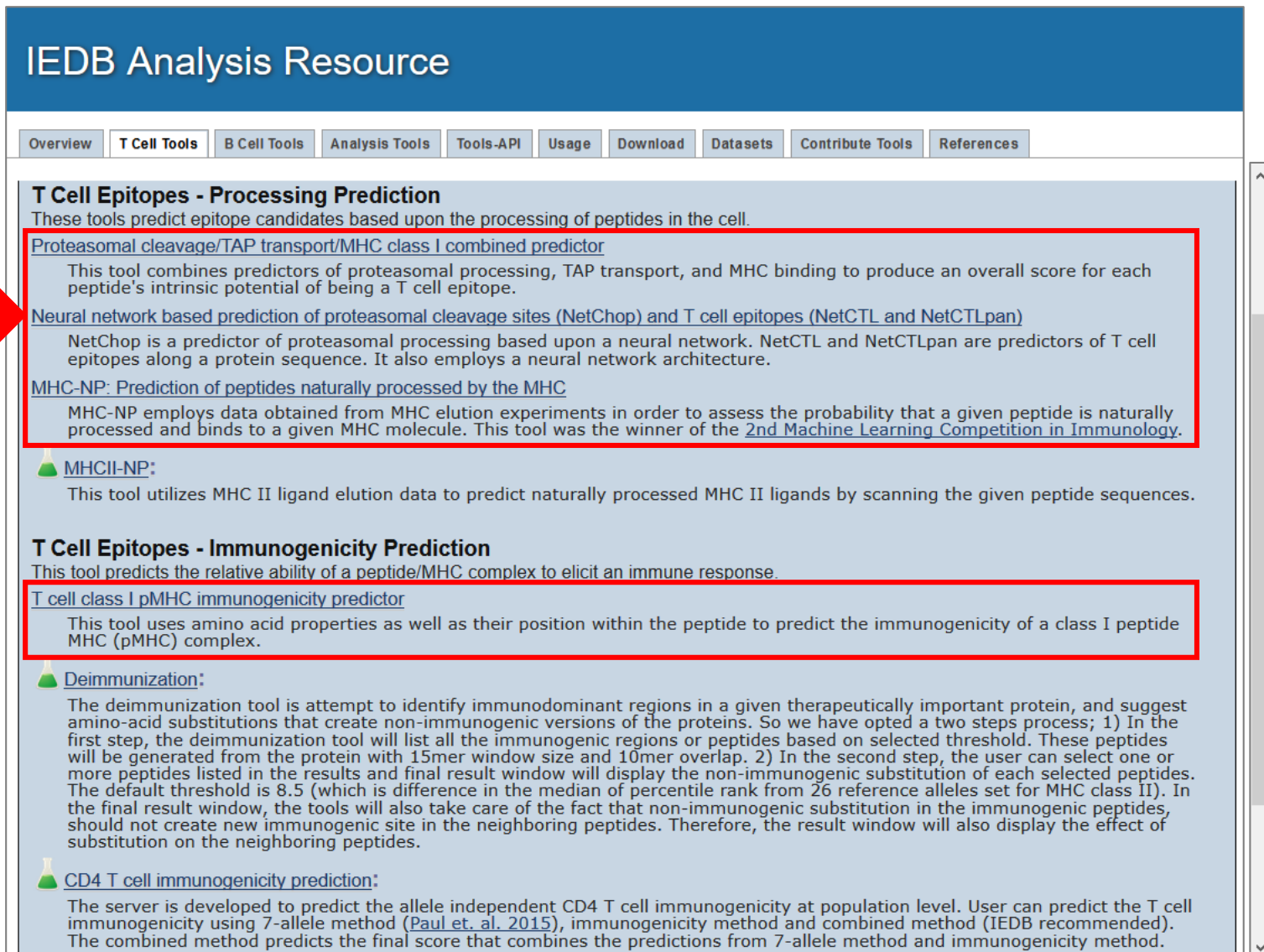
#	Amino acid	Prediction score
1	M	0.618935
2	S	0.046833
3	L	0.923545
4	L	0.756254
5	T	0.037353
6	E	0.025171
7	V	0.523328
8	E	0.023849
9	T	0.039626
10	P	0.058487
11	I	0.853657
12	R	0.239428
13	N	0.034104
14	E	0.036200
15	W	0.974923
16	G	0.090532
17	C	0.132901
18	R	0.517519
19	C	0.345002

References

- Peters et al, JMB 2002 (proteasome)
- Peters et al, J Immunol 2003 (TAP)
- Tenzer et al, CMLS, 2005 (combined)
- Nielsen, Immunogenetics, 2005 (NetChop)
- Larsen, BMC Bioinformatics, 2007 (NetCTL)
- Stranzl, Immunogenetics, 2010 (NetCTLPan)

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MHC-NP: Prediction of peptides naturally processed by the MHC

<http://tools.iedb.org/mhcnp/>

IEDB Analysis Resource

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MHC-NP: Prediction of Peptides Naturally Processed by the MHC

Developed by: Sébastien Giguère, Alexandre Drouin, Alexandre Lacoste, Mario Marchand, Jacques Corbeil and François Lavolette

Specify Sequence(s)

Enter protein sequence(s) in FASTA format
([Browse for sequences in NCB](#))

Or select file containing sequence(s) No file selected.

Choose a Prediction Method

Prediction Method [Help on prediction method selections](#)

MHC-NP
netMHCpan 4.0 EL
e binding predictions for

MHC source species

human

Select MHC allele(s)

Allele Length
 [Upload allele file](#) ?

Specify Output

Sort peptides by

Percentile Rank

Output format

XHTML table

Pan-predictions
trained on both
binding + eluted
ligand data now
available!

J Immunol. 2017 Nov 1;199(9):3360-3368. doi: 10.4049/jimmunol.1700893. Epub 2017 Oct 4.

NetMHCpan-4.0: Improved Peptide-MHC Class I Interaction Predictions Integrating Eluted Ligand and Peptide Binding Affinity Data.

Jurtz V¹, Paul S², Andreatta M³, Marcatili P¹, Peters B², Nielsen M^{4,3}.

PMID: 28978689 PMCID: PMC5679736 DOI: 10.4049/jimmunol.1700893

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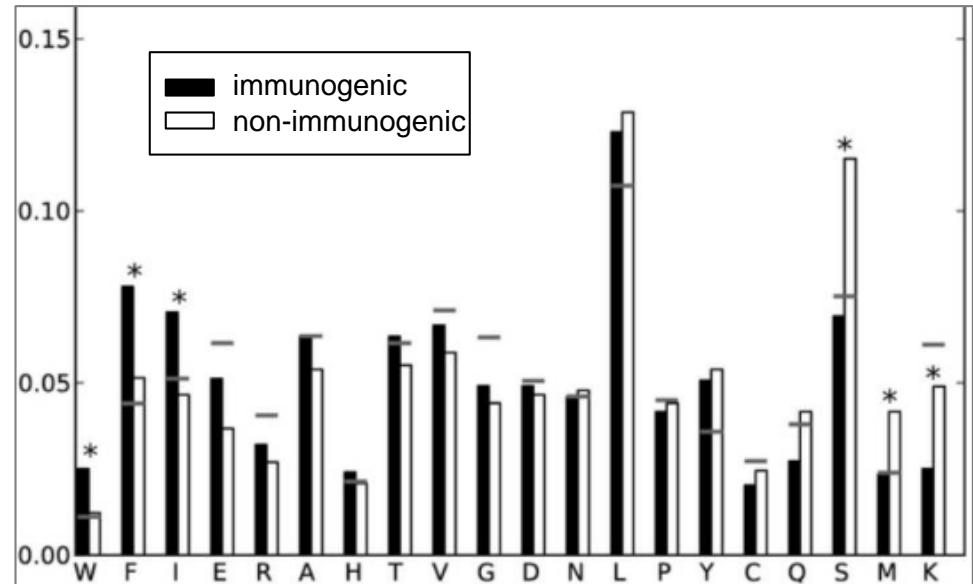
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Class I immunogenicity prediction

- Approach: Assemble two datasets of peptides with similar MHC binding affinity, that are (i) recognized or (ii) not recognized by T cells
- Enrichment of W,F,I and depletion of S,M,K in immunogenic peptides
- Use enrichments to calculate propensity scores



PLoS Comput Biol. 2013 Oct;9(10):e1003266. doi: 10.1371/journal.pcbi.1003266. Epub 2013 Oct 24.

Properties of MHC class I presented peptides that enhance immunogenicity.

Calis JJ¹, Maybeno M, Greenbaum JA, Weiskopf D, De Silva AD, Sette A, Keşmir C, Peters B.

PMID: 24204222 PMCID: PMC3808449 DOI: 10.1371/journal.pcbi.1003266

Class I immunogenicity prediction -example

<http://tools.iedb.org/immunogenicity/>

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Class I Immunogenicity

Specify sequence(s) *

Enter peptide sequence(s)
[\(Browse for sequences in NCBI\)](#)

```
FIAGLIAIV
LITGRLQSL
RLNEVAKNL
KAVYNFATC
FQPQNGQFI
```

Or select file containing sequence(s)

No file selected.

Choose which positions to mask

Specify which positions to mask

Default (1st, 2nd, and C-terminus amino acids)
 Custom (Comma separated numbers)
Peptide lengths must be equal when using custom masking.

*The tool was only validated for 9-mer peptides. However, predictions can be made for peptides of any length.

Mask positions that are MHC anchors

Class I immunogenicity prediction -example

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Class I Immunogenicity

Masking: **default**
Masked variables: [1, 2, 'cterm']

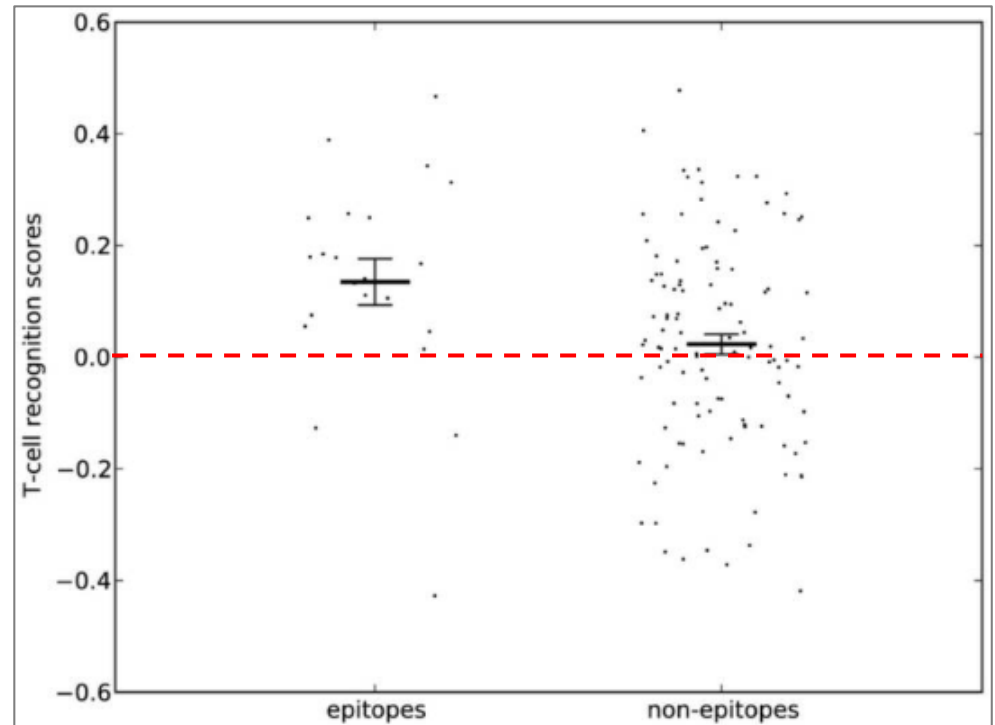
Peptide	Length	Score
FIAGLIAIV	9	0.27206
KAVYNFATC	9	0.16928
RLNEVAKNL	9	-0.0101
LITGRLQSL	9	-0.10776
FQPQNGQFI	9	-0.12392

[Download result](#) 

- Scores are sums of propensity scores at all unmasked predictions
- High scores = peptide is more likely to be immunogenic

Class I immunogenicity prediction caveats / performance

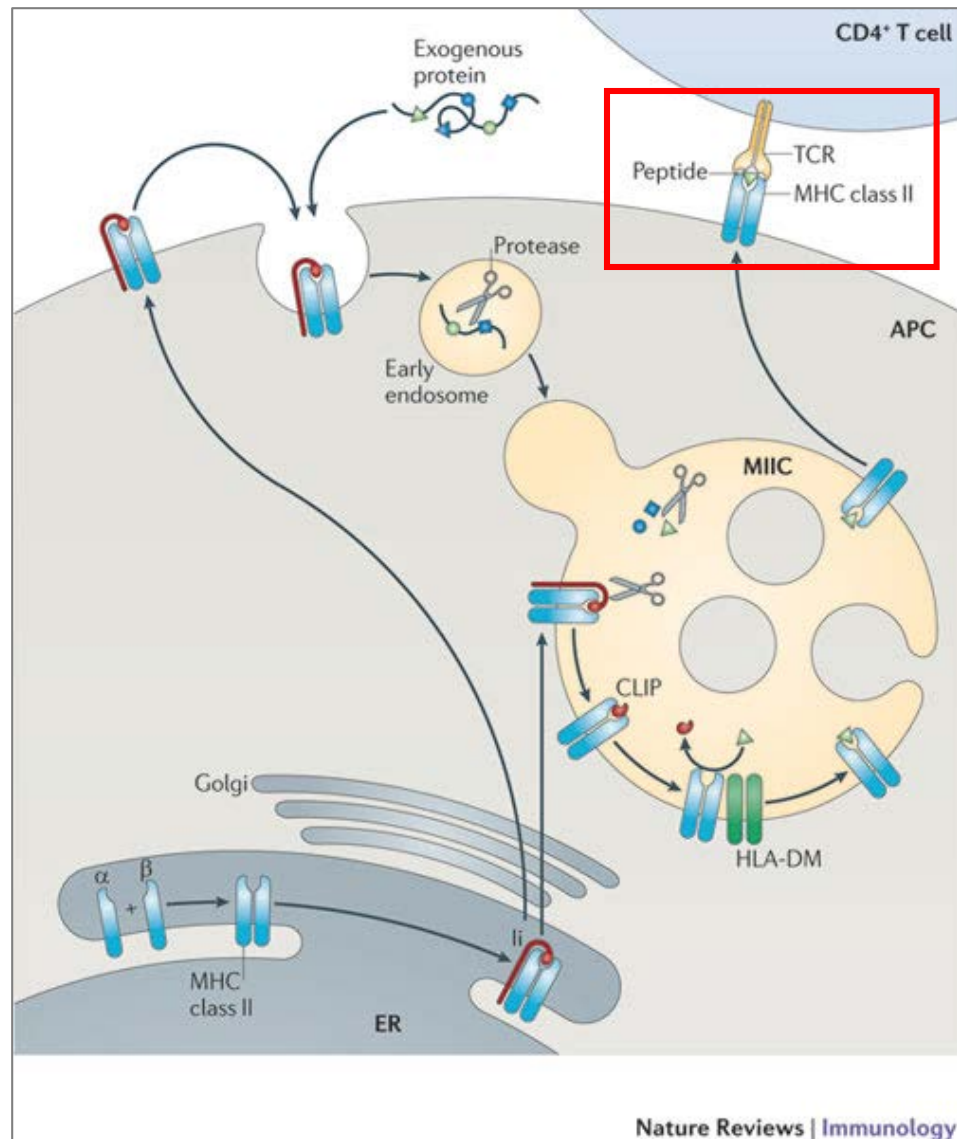
- Experimentally, many MHC binding peptides can be immunogenic (~50%)
- Cross validation gave AUC values ~ 0.65 . Test on independent blind set gave AUC = 0.69
- Recommendation: Use as filter (cutoff 0) if high specificity is desired. Suggested cutoff is 0



Class I Summary

- Processing predictions are better at identifying naturally processed ligands, but have not been shown to be superior in identifying epitopes compared to MHC binding predictions
- Specific processing and immunogenicity predictions are good additional filters if the only goal is to select high likelihood T cell epitopes
- NetMHCPan 4.0 EL scores, which are trained on both MHC binding and ligand elution data are a straightforward replacement of MHC binding predictions, and show some enhanced performance
→ Use these, and consider pairing with immunogenicity scores, when predicting epitope candidates

CD4 T cell epitopes (MHC class II)



Class II Processing + immunogenicity tools available in the IEDB

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IEDB Analysis Resource

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MHCII-NP

- Predicting the naturally processed peptides for MHC class II
- Based on
 - Cleavage motif analysis at C and N terminal of peptides
 - Ligand elution data derived from IEDB
- Ligand predictions is improved markedly when combining the binding and cleavage motifs
- T cell epitope prediction is not significantly improved

MHCII-NP -example

<http://tools.iedb.org/mhciinp/>

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MHC II NP - Prediction of naturally processed MHC II ligands

Sequences

Enter sequences in FASTA or plain format

```
>sp|P15848|ARSB_HUMAN Arylsulfatase B OS=Homo sapiens OX=9606
GN=ARSB PE=1 SV=1
MGPRGAASLPRGPGPRRLLLPVVLPLLLLLLAPPGSGAGASRPPHLVFL LADDLGWNDV
GFHGSRI RTPHLDALAAGGVLLDNYTQPLCTPSRSQLLTG RYQIRTGLQHQI IWPCQPS
CVPLDEKLLPQLLKEAGYTHMVGKWHLGMYRKECLPTRRGFDTYFGYLLGSEDIYSHER
CTLIDALNVTRCALDFRDGEEVATGYKNMYSTNIFTKRAIALITNHPPEKPLFLYLALQS
VHEPLQVP E EYLKPYDFIQDKNRHHYAGMVSLMDEAVGNVTAALKSSGLWNNTVFI FSTD
NGGQTLAGGNWPLRGRKWSLWEGGVRGVGFVASPLLKQKGVKNRELIHISDWLPTLVKL
ARGHTNGTKPLDGFVWVKTI SEGSPSPRIELLNIDPNFVDSSPCPRNSMAPAKDDSSLP
EYSAFNTSVHAAIRHGNWKL LTGYPGCGYWFPPPSQYNVSEI P SSDPPTKTLWLFDIDRD
PEERHDL SREYPHIVTKLLSRLQFYHKHSVPVYFPAQDPRCDPKATGVWGPWM
```

Or upload sequences as a text file No file selected.



MHCII-NP -example

<http://tools.iedb.org/mhciinp/>

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MHC II NP results

Top 5 peptides per protein:

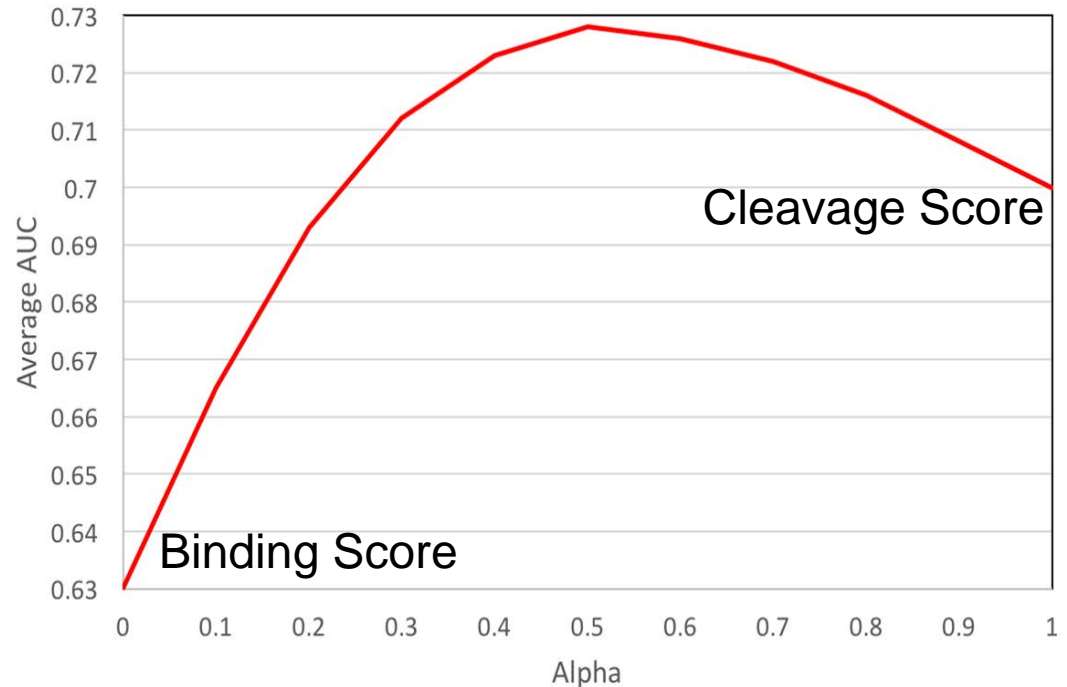
	Seq name	Peptide start	Peptide end	Peptide length	Peptide	N motif	C motif	Cleavage probability score	Cleavage probability percentile rank
1	SP P15848 ARSB_HUMAN ARYLSULFATASE_B OS=HOMO S...	510	524	15	VPVYFPAQDPRCDPK	SVP	PKA	1.75814	0.00
2	SP P15848 ARSB_HUMAN ARYLSULFATASE_B OS=HOMO S...	2	16	15	GPRGAASLPRGPGPR	MGP	PRR	1.73735	0.02
3	SP P15848 ARSB_HUMAN ARYLSULFATASE_B OS=HOMO S...	247	261	15	VPEEYLKPYDFIQDK	QVP	DKN	1.48840	0.04
4	SP P15848 ARSB_HUMAN ARYLSULFATASE_B OS=HOMO S...	384	398	15	SPSPRIELLHNIDPN	GSP	PNF	1.40420	0.05
5	SP P15848 ARSB_HUMAN ARYLSULFATASE_B OS=HOMO S...	12	26	15	GPGPRLLLLPWVLP	RGP	PLL	1.33714	0.07

[Complete results](#)

MHCII-NP scores

- **Cleavage Score:** Derived from the cleavage motif analysis in ligand elution data
- **Binding Score:** Derived from HLA binding affinity using 7-allele method (Paul et. al. 2015).

$$\text{Combined score} = \alpha \times \text{cleavage probability score} + (1 - \alpha) \times \text{binding score}$$



Barra et al. *Genome Medicine* (2018) 10:84
<https://doi.org/10.1186/s13073-018-0594-6>

Genome Medicine

RESEARCH

Open Access



Footprints of antigen processing boost MHC class II natural ligand predictions

Carolina Barra^{1*}, Bruno Alvarez^{1†}, Sinu Paul², Alessandro Sette², Bjoern Peters², Massimo Andreatta¹, Soren Buus³ and Morten Nielsen^{1,4*}

Front Immunol. 2018 Aug 6;9:1795. doi: 10.3389/fimmu.2018.01795. eCollection 2018.

Determination of a Predictive Cleavage Motif for Eluted Major Histocompatibility Complex Class II Ligands.

Paul S¹, Karosiene E¹, Dhanda SK¹, Jurtz V², Edwards L¹, Nielsen M^{2,3}, Sette A^{1,4}, Peters B^{1,4}.

PMID: 30127785 PMCID: PMC6087742 DOI: 10.3389/fimmu.2018.01795

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MHC-II restricted immunogenicity prediction

- Extracted datasets of proteins from the IEDB for which overlapping peptides were tested for immunogenicity
- Utilized these datasets to train a Neural Network to learn 'motifs' associated with immunogenicity independent of specific MHC alleles expressed
- Resulting score can be combined with '7 allele method' quantifying MHC binding across alleles to predict overall immunogenicity


Class II immunogenicity prediction

- Based on Neural network model trained on
 - In house dataset for different antigens tested on different population cohorts
 - Tetramer dataset- derived from IEDB
- Validated on 57 independent studies from different groups across the world
- Implemented three approaches
 - 7-allele method (*Paul et. al. 2015*)
 - Immunogenicity predictions
 - Hybrid approach

Class II immunogenicity prediction -example

<http://tools.iedb.org/CD4episcore/>

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CD4 T cell immunogenicity prediction

Specify Sequence(s)

Enter epitope sequence(s) in PLAIN or FASTA format

```
>sp|P01588|EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1
MGVHECPAWLWLLLSLLSLPLGLPVLGAPPRLICDSRVLERYLLEAKEAENITGCAEHC
SLNENITVPDTKVNFYAWKRMEVGGQAVEVWQGLLALLSEAVLRGQALLVNSSQPWEPLQL
HVDKAVSGLRSLTTLRLALGAQKEAISPDAASAAPLRTITADTFRKLFVYSNFLRGKL
KLYTGACRTGDR
```

Or upload epitope sequence(s) from a file No file selected.

Choose a prediction method

Prediction method:

Specify Output

Sort Peptides by:

Select maximum percentile rank threshold:

Enter the Job Name (Optional)

Email address (optional)

Class II immunogenicity prediction -example

<http://tools.iedb.org/CD4episcore/>

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CD4 Immunogenicity prediction results

Number of proteins: 1

Number of 15mer (overlapping 10mer): 37

Threshold : 50.0%

Method : combined

[Download result](#)

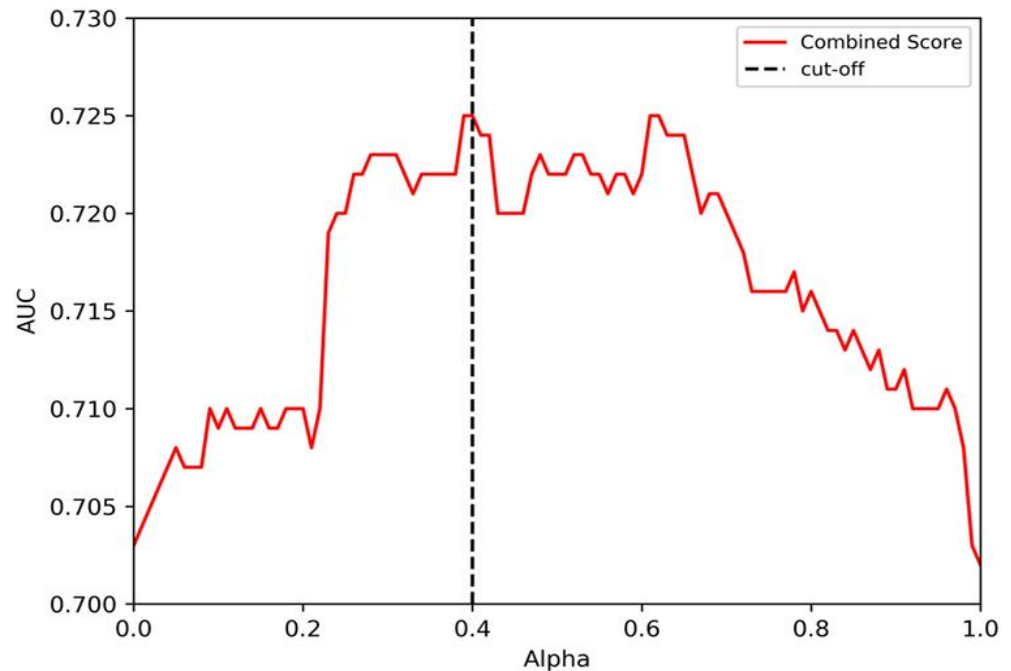
[Citations](#)

Protein Number	Protein Description	Peptide	Start	End	Combined Score	Immunogenicity Score	Peptide core	Median Percentile Rank (7-allele)	HLA-DRB1:03:01	HLA-DRB1:07:01	HLA-DRB1:15:01	HLA-DRB3:01:01	HLA-DRB3:02:02	HLA-DRB4:01:01	HLA-DRB5:01:01
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	WLLLSLLSLPLGLPV	11	25	42.16452	95.0613	LLSLLSLPL	6.9	25.0	3.2	3.6	73.0	33.0	6.9	6.5
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	TKVNFYAWKRMEVGQ	71	85	47.39488	67.4872	TKVNFYAWK	34.0	52.0	22.0	15.0	71.0	30.0	65.0	34.0
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	EPLQLHVDKAVSGLR	116	130	32.55636	43.8909	LHVDKAVSG	25.0	5.4	59.0	40.0	22.0	7.0	38.0	25.0
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	VSGLRSLTLLRALG	126	140	44.95964	86.8991	LTLLRALG	17.0	12.0	17.0	9.3	70.0	20.0	20.0	1.3
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	SLTLLRALGAQKEA	131	145	42.78744	69.4686	LLRALGAQK	25.0	47.0	46.0	21.0	89.0	25.0	14.0	1.6
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	PLRTITADTRFKLFR	156	170	46.18064	85.4516	LRTITADTF	20.0	6.1	47.0	40.0	8.0	20.0	20.0	20.0
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	TADTRFKLFRVYSNF	161	175	46.66984	44.6746	FRKLFVYS	48.0	63.0	58.0	23.0	48.0	33.0	53.0	24.0
1	sp P01588 EPO_HUMAN Erythropoietin OS=Homo sapiens GN=EPO PE=1 SV=1	RKLFVYSNFLRGKL	166	180	13.8966	22.4415	FRVYSNFLR	8.2	53.0	8.2	0.12	27.0	4.8	26.0	1.5

Class II immunogenicity prediction scores

- Immunogenicity Score: Derived from the neural network model trained on Immunogenicity data
- HLA Score: Derived from HLA binding affinity using 7-allele method (Paul et. al. 2015).

$$\text{Combined score} = \alpha \times \text{Imm score} + (1 - \alpha) \times \text{HLA score.}$$



[Front Immunol.](#) 2018 Jun 14;9:1369. doi: 10.3389/fimmu.2018.01369. eCollection 2018.

Predicting HLA CD4 Immunogenicity in Human Populations.

[Dhanda SK](#)¹, [Karosiene E](#)¹, [Edwards L](#)¹, [Grifoni A](#)¹, [Paul S](#)¹, [Andreatta M](#)², [Weiskopf D](#)¹, [Sidney J](#)¹, [Nielsen M](#)^{2,3}, [Peters B](#)^{1,4}, [Sette A](#)^{1,4}.

PMID: 29963059 PMCID: [PMC6010533](#) DOI: [10.3389/fimmu.2018.01369](#)

Class II Summary

- Similar to MHC class I, enhancement of epitope prediction efficacy is minor compared to using MHC binding predictions alone
- Prediction of naturally eluted ligands is greatly improved with processing predictions
- As of now, recommendation is to stick to allele specific MHC binding predictions (NetMHCPanII), or the 7-allele method for broad populations

→ Both class I and II epitope predictions are constantly being re-evaluated, and these recommendations are subject to change