

Analysis Tools

tools.iedb.org

Presented by: Alessandro Sette, IEDB Principal Investigator

http://tools.iedb.org/main/analysis-tools/

IEDB Analysis Resource

Overview T Cell Tools B Cell Tools Analysis Tools Tools-API Usage Download Datasets Contribute Tools References

Analysis Tools

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Population Coverage

This tool calculates the fraction of individuals predicted to respond to a given set of epitopes with known MHC restrictions. This calculation is made on the basis of HLA genotypic frequencies assuming non-linkage disequilibrium between HLA loci.

Epitope Conservancy Analysis

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Computational Methods for Mapping Mimotopes to Protein Antigens

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PepX (Peptide Expression Annotation)

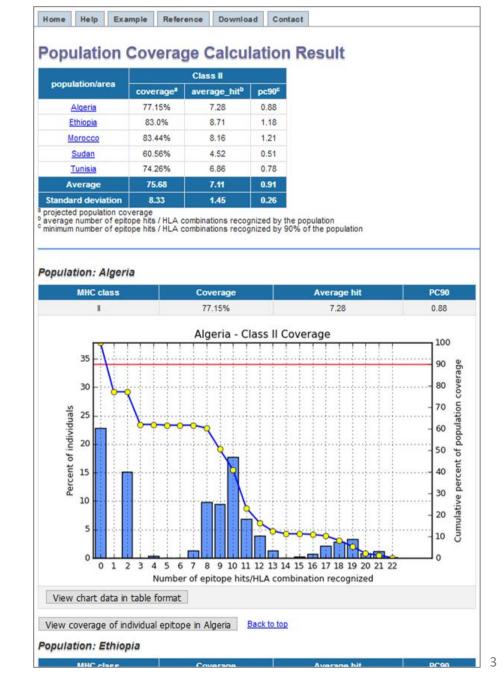
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Population Coverage

http://tools.iedb.org/population/

- Calculates the fraction of individuals projected to bind and/or respond to a given set of epitopes with defined reactivity
- Based on
 - Epitope known HLA binding/restrictions
 - HLA genotypic frequencies
- HLA genotypic frequencies vary in different ethnicities
 - http://allelefrequencies.net
 - Focused more on worldwide migration patterns/based on ancestral studies



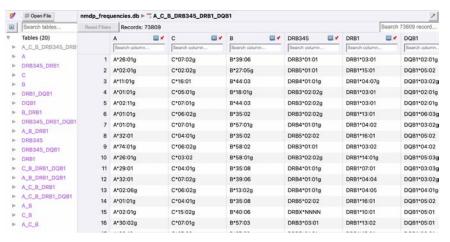
Updated Population Coverage Tool

New Data Source (In Progress)

 National Marrow Donor Program (NMDP) Database



High Resolution HLA Alleles and Haplotypes in the US Population



Gragert, L., Madbouly, A., Freeman, J., & Maiers, M. (2013). Six-locus high resolution HLA haplotype frequencies derived from mixed-resolution DNA typing for the entire US donor registry. Human Immunology, 74(10), 1313–1320. http://dx.doi.org/10.1016/j.humimm.2013.06.025.

Race Code	Detailed Race/Ethnic Description							
AAFA	African American							
AFB	African	AFA						
AINDI	South Asian Indian	API						
AISC	American Indian - South or Central Am.	NAM						
ALANAM	Alaska Native or Aleut	NAM						
AMIND	North American Indian	NAM						
CARB	Caribbean Black	AFA						
CARHIS	Caribbean Hispanic	HIS						
CARIBI	Caribbean Indian	NAM						
EURCAU	European Caucasian	CAU						
FILII	Filipino	API						
HAWI	Hawaiian or other Pacific Islander	API						
JAPI	Japanese	API						
KORI	Korean	API						
MENAFC	Middle Eastern or N. Coast of Africa	CAU						
MSWHIS	Mexican or Chicano	HIS						
NCHI	Chinese	API						
SCAHIS	Hispanic – South or Central American	HIS						
SCAMB	Black - South or Central American	AFA						
SCSEAI	Southeast Asian	API						
VIET	Vietnamese	API						

- Newer data
 (includes DRB345)
- Uniform, high resolution HLA typing
- Better reflection of HLA allele diversity/linkage patterns
- Populations all screened within

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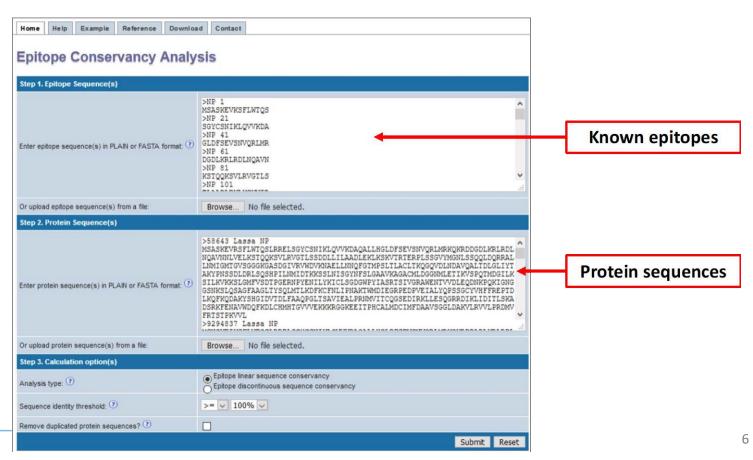


Epitope Conservancy Analysis

http://tools.iedb.org/conservancy/

- Calculates the degrees of conservancy of one or more epitopes,
 within a given set of protein sequences
- Adjustable sequence identity threshold

"Degree of conservation" = the fraction of protein sequences containing the epitope at a given identity level



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Epitope Cluster Analysis Tool

http://tools.iedb.org/cluster/

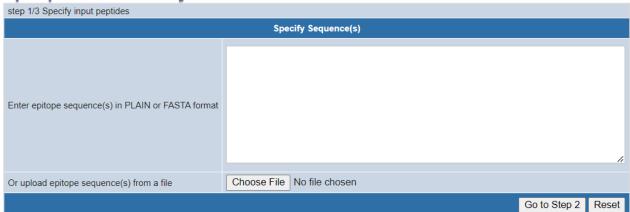
- Analyzes how many epitopes in a set have significant sequence homology
- Groups epitopes into clusters based on having sequence identity greater than a specified threshold
- Three different clustering approaches are implemented
- Enables diverse applications such as generating epitope pools, and understanding cross-reactivity

8

Epitope Cluster Analysis Tool

Clustering Tool Updated! This is an updated version of the IEDB clustering tool that is more robust and has new functionality described in more detail here.

Epitope Cluster Analysis

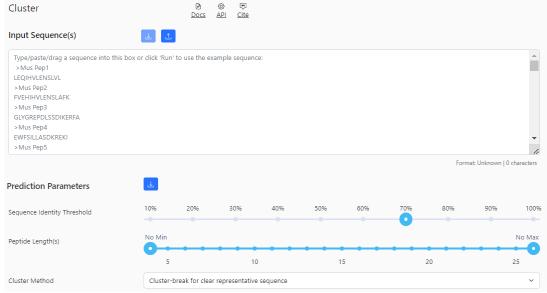


http://tools.iedb.org/cluster/

https://nextgentools.iedb.org/clustering

Learn more about the new Cluster Tool **tomorrow**!

Thursday, November 2, 9am PT Next Generation Tool Pipelines - Cluster & PepMatch



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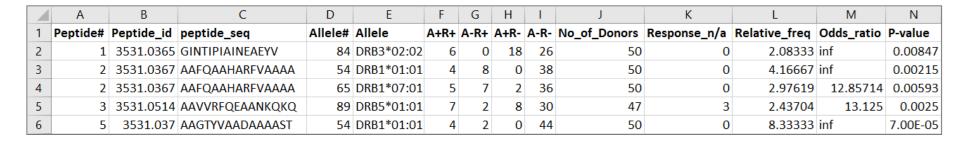
This tool identifies from which proteins a list of peptides can be derived, and returns an estimate of the expression level of those peptides from selected public databases.



Restrictor Analysis Tool for Epitopes (RATE)

http://tools.iedb.org/rate/

- Automated method to infer HLA restriction of a given epitope set, from immune response data of HLA typed subjects
- Based on computing the frequency of alleles expressed in in donors who had an immune response to a given epitope
- Compare those frequencies in donors that did not have a response



Deimmunization

http://tools.iedb.org/deimmunization/



T Cell Epitopes - Immunogenicity Prediction

These tool make predictions about the relative ability of a peptide/MHC complex to elicit an immune response.

T cell class I pMHC immunogenicity predictor

This tool uses amino acid properties as well as their position within the peptide to predict the immunogenicity of a class I peptide MHC (pMHC) complex.

Deimmunization:

The deimmunization tool is attempt to identify immunodominant regions in a given therapeutically important protein, and suggest amino-acid substitutions that create non-immunogenic versions of the proteins. So we have opted a two steps process; 1) In the first step, the deimmunization tool will list all the immunogenic regions or peptides based on selected threshold. These peptides will be generated from the protein with 15mer window size and 10mer overlap. 2) In the second step, the user can select one or more peptides listed in the results and final result window will display the non-immunogenic substitution of each selected peptides. The default threshold is 8.5 (which is difference in the median of percentile rank from 26 reference alleles set for MHC class II). In the final result window, the tools will also take care of the fact that non-immunogenic substitution in the immunogenic peptides, should not create new immunogenic site in the neighboring peptides. Therefore, the result window will also display the effect of substitution on the neighboring peptides.

CD4 T cell immunogenicity prediction:

The server is developed to predict the allele independent CD4 T cell immunogenicity at population level. User can predict the T cell immunogenicity using 7-allele method (Paul et. al. 2015), immunogenicity method and combined method (IEDB recommended). The combined method predicts the final score that combines the predictions from 7-allele method and immunogenicity method.

Deimmunization

http://tools.iedb.org/deimmunization/

- Generate overlapping peptides from protein sequence
- Predict HLA class II binding binding regions
- Suggest amino acid substitutions that are predicted to decrease binding
 - Also consider the effect of substitutions on neighboring peptides

	Α	В	С	D	E	F	G	Н	1	J	K	L
								C terminal	C terminal	N terminal	N terminal	
	Protein		Peptide	Start	End	Median	Median	Neighbor 1	Neighbor 2	Neighbor 1	Neighbor 2	Deimmunization
1	Number	Peptide	ID	Position	Position	Percentile Rank	Difference	(Median)	(Median)	(Median)	(Median)	Score
2	1	DTFRKLFRVYSNFLR	wild	136	150	10.255	0	14.5	49.75	47	44.25	NA
3	1	DTFRKLFRVYSNFDR	L149D	136	150	32	21.745	41	68.5	NA	NA	3
4	1	DTFRKLFRVYSNFGR	L149G	136	150	27.5	17.245	31.5	68.75	NA	NA	3
5	1	DTFRKEFRVYSNFLR	L141E	136	150	26.5	16.245	26.5	NA	60.75	NA	3
6	1	DTFRKPFRVYSNFLR	L141P	136	150	26.35	16.095	26.5	NA	52.5	NA	3
7	1	DTFRKQFRVYSNFLR	L141Q	136	150	26	15.745	25.5	NA	53.25	NA	3
8	1	DTFRKLFRVYSNFNR	L149N	136	150	26	15.745	21.75	61.75	NA	NA	3
9	1	DTFRKLGRVYSNFLR	F142G	136	150	25.075	14.82	31	NA	50.75	NA	3
10	1	DTFRKLFDVYSNFLR	R143D	136	150	24.75	14.495	35.5	NA	49.25	NA	3
11	1	DTFRKKFRVYSNFLR	L141K	136	150	24.525	14.27	23	NA	59	NA	3
12	1	DTFRKLFRVYSNFCR	L149C	136	150	24.25	13.995	36	64	NA	NA	3
13	1	DTFRKCFRVYSNFLR	L141C	136	150	23.85	13.595	23.5	NA	73	NA	3
14	1	DTFRKLFRVYSCFLR	N147C	136	150	23.75	13.495	39.75	50	NA	NA	3
15	1	DTFRKDFRVYSNFLR	L141D	136	150	23.5	13.245	27.5	NA	62.5	NA	3
16	1	DTFRKGFRVYSNFLR	L141G	136	150	23.5	13.245	27	NA	57.5	NA	3
17	1	DTFRKLFRVYSNFKR	L149K	136	150	23.5	13.245	28	59	NA	NA	3
18	1	DTFRKLFRVYSNFER	L149E	136	150	22.75	12.495	34	62	NA	NA	3
19	1	DTFRKLERVYSNFLR	F142E	136	150	22.7	12.445	31	NA	48	NA	3
20	1	DTFRKLCRVYSNFLR	F142C	136	150	22.4	12.145	31	NA	50.25	NA	3
21	1	DTEDVITOVVCNIELD	E1//OT	126	150	22 175	11.02	20	NIA	10 75	NIA	9

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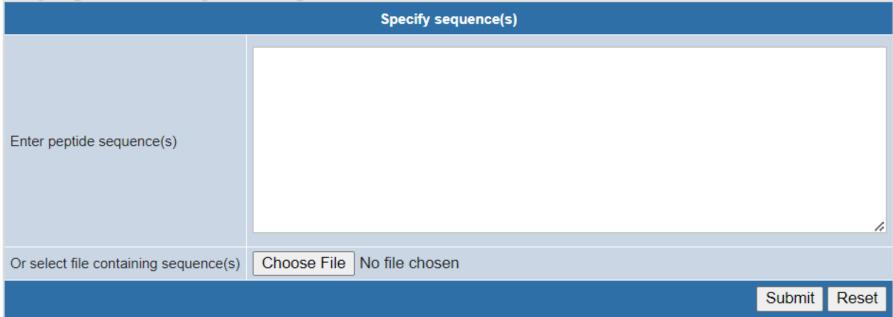


Peptide Synthesis Score (PepSySco)

http://tools.iedb.org/pepsysco/

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PepSySco - Peptide Synthesis Score



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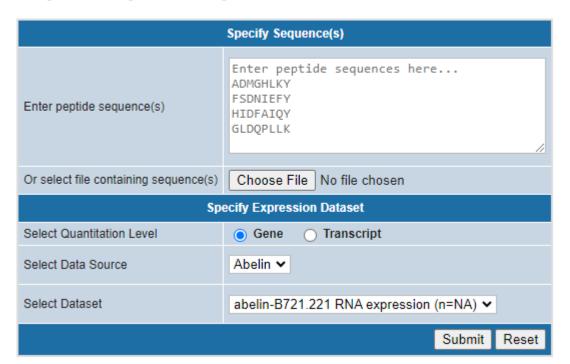


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http://tools.iedb.org/pepx/

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- Returns an estimate of the expression level of those peptides from selected public databases

PepX - Peptide Expression Annotation



Analysis Tools Recap

 Help to examine existing sets of epitopes and gain new knowledge across a broad array of applications

Population Coverage

Analyze T cell epitopes with known HLA restriction that are recognized in a population based on HLA frequencies

Conservancy

Investigate epitope conservancy across different protein sequences.

Cluster

Cluster epitopes on the basis of homology

RATE

Infer HLA restrictions for epitopes of T cell response frequency in HLA typed subjects

Deimmunization

Identify immunodominant regions in a given protein, and suggest aminoacid substitutions that create non-immunogenic versions of the protein

PepSySco

Predict the likelihood that a set of peptides can be synthesized successfully

PepX

Identify peptides that can be derived from which proteins, and estimate the expression level of those peptides from selected public databases