

Immune Epitope Database NEWSLETTER

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DiscoTope - A New Structure-based Antibody Epitope Prediction Tool

A new tool is available in the IEDB's Analysis Resource . This tool, Discotope, predicts discontinuous B cell epitopes from three-dimensional protein structural data represented in the Protein Data Bank (www.pdb.org). The method utilizes calculation of surface accessibility (estimated in terms of contact numbers) and a novel epitope propensity amino acid score. The final scores are calculated by combining the propensity scores of residues in spatial proximity and the contact numbers. Output from DiscoTope appears in three different forms. In the Chart view, the DiscoTope score is plotted against residue number. The user can change the score threshold for determining positive predictions. The Table view displays Chain ID, Residue ID, Residue Name, Contact Number, Propensity Score, and DiscoTope Score. Positive predictions are indicated by red font. The 3D view uses Jmol to display the structure positive predictions high-

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Curation Update

Curation of data relating to NIAID Category A, B, and C priority pathogens, NIAID emerging and re-emerging infectious diseases (<http://www3.niaid.nih.gov/research/topics/emerging/list.htm>), Malaria, Hepatitis B, Clostridium tetani, Leishmania, and Candida albicans is current for articles appearing in PubMed as of the end of June 2007. These results will be updated in October to cover newer published articles and pertinent references recently brought to our attention. The IEDB curation team has curated the majority of the relevant herpesvirus references and has started on allergen references. Curation of autoimmune diseases will start in 2008.

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New Format for "Browse Records by Allele"

The IEDB contains MHC Allele data for over ten species. Users can access these data via the Quick Search, Simple Search, and Advanced Search, but users might prefer to browse the data with one of the three IEDB browse features. The interface for the Browse by Allele has recently changed from a very long table of MHC alleles and their corresponding species to a tree structure that makes it much easier for users to find and investigate information on specific MHC alleles. As Figure 1 shows, the tree structure expands (and collapses) so users can drill down on species, MHC type, and allele to find the number of records in the IEDB for their MHC allele of interest.

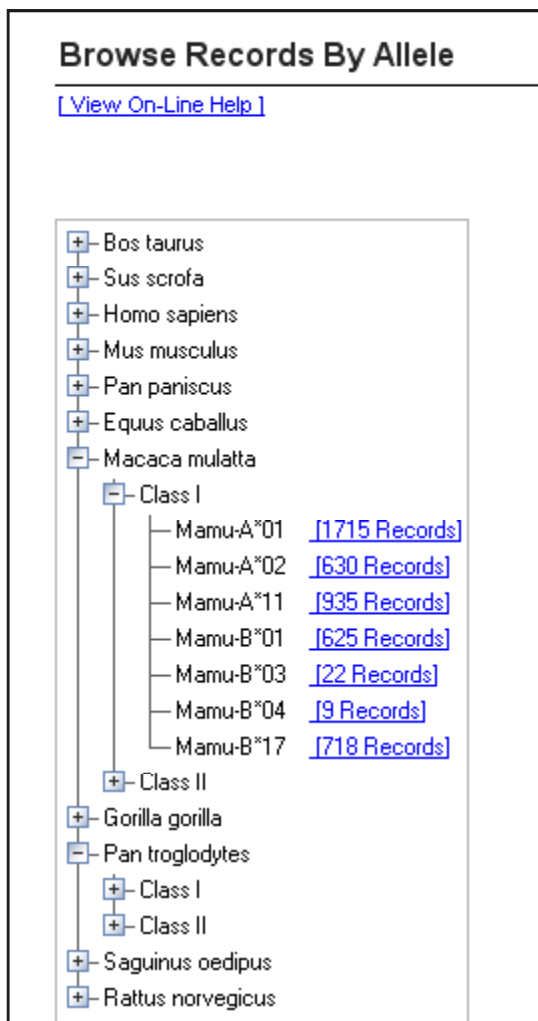


Figure 1: The new format of the Browse by MHC Allele allows users to drill down on species, MHC type, and allele to find the data of interest.

Recommended Reading

Disruption of *Plasmodium falciparum* development by antibodies against a conserved mosquito midgut antigen.

Rhoel R. Dinglasan, Dario E. Kalume, Stefan M. Kanzok, Anil K. Ghosh, Olga Muratova, Akhilesh Pandey, and Marcelo Jacobs-Lorena

Proc Natl Acad Sci USA 104: 13461-13466.

PMID: 17673553

Debbie's review: Malaria parasites must complete development in the *Anopheles* mosquito before transmission to a new host. Scientists at Johns Hopkins University have identified an *Anopheles* protein as a potential target for transmission-blocking interventions. The lectin-binding protein, aminopeptidase N (AgAPN 1), is constitutively expressed in the midgut of *Anopheles gambiae* and a cross-reactive protein is recognized in four other *Anopheles* species. AgAPN1 appears to be involved in mediating *Plasmodium* ookinete invasion of the mosquito midgut, which leads to oocyst formation and release of sporozoites that invade the mosquito salivary glands. Polyclonal antiserum to AgAPN1 inhibited up to 80% formation of *Plasmodium berghei* oocysts in *A. gambiae* that were fed on infected mice passively immunized with the antibody. Anti-AgAPN1 antibodies also blocked transmission of *Plasmodium falciparum*, which infects humans. Parasite oocyst development could be blocked up to 95% with a combined treatment of anti-AgAPN1 antibody and the salivary gland and midgut peptide 1 (SM1), which targets a different ookinete ligand. SM1 is a 12-amino acid peptide that alone inhibits transmission of *P. berghei* by 60-70%, but does not inhibit *P. falciparum*. The authors stress the need to target multiple ligands to interfere with malaria parasite transmission and suggest that AgAPN1 is one potential target because it appears to have a conserved role in midgut cell invasion by ookinetes. The authors also caution that the mouse model of *P. berghei* transmission may not be adequate to model *Plasmodium falciparum* transmission in humans.

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Large Scale Antibody & T Cell Epitope Discovery Program

David Lewinsohn, Ph.D.

Oregon Health & Science University



Top left: David & Deborah Lewinsohn. Top right: Megan Null & Meghan Cansler. Bottom Left: (back row, left to right) Lynne Swarbrick, Laura Byrd, Jake Delapine, Shannon McWeeney, (front row, left to right) Tomi Mori, Marisa Frieder, Megan Null, Byung Park. Right center: Veena Rajaraman. Bottom right: Megan Null & Meghan Cansler

The goal of Dr. Lewinsohn's contract is to define the repertoire of immunodominant CD8 antigens and epitopes in Mycobacterium tuberculosis (Mtb). Mtb infection resulting in tuberculosis (TB) remains an important cause of infectious disease morbidity and mortality worldwide. Furthermore, the recent emergence of highly resistant forms of TB has highlighted the need for improved vaccines for tuberculosis. Mtb-specific CD8+ T lymphocytes are important in the host response to infection. Both classically and non-classically restricted CD8+ T cells preferentially recognize heavily infected cells and are present at high frequency in those infected with Mtb. Hence, they may represent a surrogate for bacterial burden and/or disease progression. However, the repertoire and dominance pattern of human CD8 antigens remains poorly characterized. Dr. Lewinsohn's contract proposes to identify important CD8 antigens and epitopes in Mtb. CD8 antigens are defined using three complementary methods employing Mtb-specific classically and non-classically HLA restricted T cell clones. The first method utilizes a synthetic over-

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The following table lists some of the TB epitopes that have been defined to date using these techniques. For each T cell clone, the minimal epitope, HLA restriction, MHC binding affinity, ex-vivo frequency and TCR V-beta region have all been defined.

Clone ^a	Gene	Accession Number	HLA-Restricting Allele	Epitope Location	Epitope Sequence	#SFU/250,000 CD8+ T-cells	MHC Binding Affinity (IC50 nm)	V beta region
D 160 1-1B ^b (0)	CFP10	Rv3874	B44	2-11	AEMKTDAATL	360	38	IND
D160 1-6F ^b (0)	CFP10	Rv3874	B14	85-94	RADEEQQAL	120	NA	TBD
D432 H12 (1)	CFP10	Rv3874	B3514	49-58	TAAQAAVVRF	258	2011 ^c	5.3
D466 A10 (9)	CFP10	Rv3874	B4501	2-9	AEMKTDA	2458	48	IND
D466 D6 (0)	CFP10	Rv3874	B4501	2-12	AEMKTDAATLA	1993	6.2	22
D481 C10 (8)	CFP10	Rv3874	B1502	75-83	NIRQAGVQY	1715	14 ^d	9
D481 C11 (0)	CFP10	Rv3874	B1502	75-83	NIRQAGVQY	1715	14 ^d	13.6
D480 F6 (5)	CFP10	Rv3874	B0801	3-11	EMKTDAATL	387	79	13.1
D571 B12 (2)	CFP10	Rv3874	B4402	2-11	AEMKTDAATL	31	38	IND
D571 E9 (3)	CFP10	Rv3874	B4402	2-11	AEMKTDAATL	31	38	14
D504 E4 (0)	Mtb9.8	Rv0287	A0201	3-11	LLDAHIPQL	72	0.39	8
D454 B10 (0)	Mtb9.8	Rv0287	B0801	53-61	AAHARFVAA	88	0.22	IND
D454 H1-2 (0)	Mtb8.4	Rv1174c	B1501	33-43	AVINTTCNYGQ	24	10	7.1
D432 A3 (1)	Mtb 8.4	Rv1174c	B3514	61-69	ASPVAQSYL	210	127 ^c	14
D443 H9 (0)	Ag85B	Rv1886c	B4102	144-153	ELPQWLSANR	<10	N/A	22

^aNumber of sister clones in parentheses

^bPublished Previously J Immunol. 2001 Jan 1;166(1):439-46.

^cMeasured binding affinity to B3501 shown

^dMeasured binding affinity to B1501 shown

NA Not available

IND=Indeterminate

TBD= To be determined

Upcoming Events

2nd International Biocuration Meeting

Hayes Mansion
San Jose, California
October 25 - 28, 2007

Cytokines 2007

Hyatt Regency
San Francisco, California
October 26-30, 2007

Autumn Immunology Conference

Chicago Marriott Downtown
Chicago, Illinois
November 16-19, 2007

Midwinter Conference of Immunologists

Asilomar Conference Grounds
Pacific Grove, California
January 26-29, 2008

The Keystone Viral Immunity

Keystone Resort
Keystone Colorado
January 22-27, 2008.

Keystone Symposia

Keystone Resort
Keystone, Colorado
February 24-29, 2008

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lighted in yellow. An example of this output for PDB ID 1z40 is shown in Figure 2. Further information on DiscoTope can be found in the publication Prediction of residues in discontinuous B cell epitopes using protein 3D structures, Pernille Haste Andersen, Morten Nielsen and Ole Lund, Protein Science, 15:2558-2567, 2006 (PMID: 17001032). Assistance in using DiscoTope in the IEDB Analysis Resource can be found at :

<http://tools.immuneepitope.org/stools/html/DiscoTopeHelp.html>

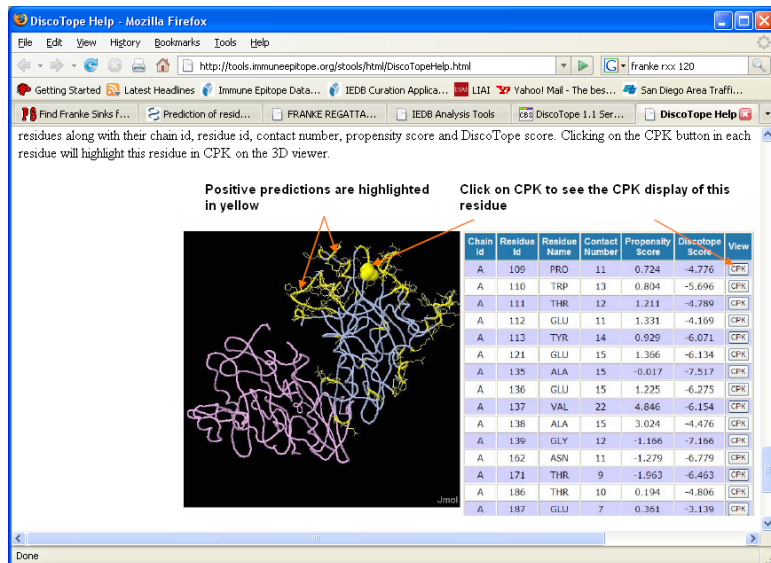


Figure 2 3D View output from the DiscoTope discontinuous antibody epitope prediction tool.

Major Redesign of the IEDB Website Coming in Spring 2008

As a result of feedback collected from users and from human-computer interface usability experts, the IEDB team is currently undertaking a major redesign of the IEDB. Come next spring, users will see a new home page that more clearly guides users to the IEDB's many features, more intuitive searching and reporting, and faster response times on queries submitted. Website navigation will be improved so users will know where they are on the site and will be able to access and analyze data more easily. More details will be available in the next IEDB Newsletter.

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Clinical and immunologic effects of component peptides in Allervax Cat.

Norman PS, Nicodemus CF, Creticos PS, Wood RA, Eggleston PA, Lichtenstein LM, Kagey-Sobotka A, Proud D

Int Arch Allergy Immunol. 1997 May-Jul;113(1-3):224-6

PMID: 9130529

Leora's Review: Peptides were designed for the purpose of tolerizing patients with cat allergy. It has been shown that mice can become tolerized if they were treated with peptides, and this approach was attempted in humans. Cat allergy is caused mainly by one protein, Fel d 1, found in cat epithelium and salvia. Two 27 amino acid peptides were selected for study. At baseline, patients allergic to cats were exposed for 30 minutes to a room inhabited by 2 live cats. On another day, a nasal challenge with cat extract was given. Patients allergic to cats were treated with the epitope 4 times, then exposed to a room inhabited by live cats, and/or given a nasal challenge with cat extract. Treatment with the epitope led to a significant reduction of symptoms compared to pretreatment results. These results led to larger clinical trials with the 2 peptides as a means to reduce allergic symptoms in cat-allergic patients.

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lapping peptide library to identify the cognate antigen recognized by either CD8+ T cell clones or ex vivo CD8+ T cells from Mtb-infected individuals. The second method uses autologous dendritic cells pulsed with M. smegmatis expressing Mtb-genomic DNA to identify antigen recognized by CD8+ T cell clones. The third method represents a proteomic approach to identifying antigens contained in Mtb cell wall recognized by non-classically restricted T cell clones. Minimal epitopes for these antigens are then defined using additional synthetic peptide pools, nested synthetic peptides, and T cell clones. Finally, the clinical utility of these newly defined CD8 antigens/epitopes are studied in a TB-endemic population. These findings will have significance for the development of an effective TB vaccine that includes targeting of CD8 antigens and may also have relevance for the development of new TB diagnostics.

Contact Information

The Immune Epitope Database & Analysis Resource is supported by a contract from the National Institute of Allergy & Infectious Disease, NIH, DHHS (Contract HHSN266200400006C). The newsletter is distributed four times a year. We welcome communication from the users of the IEDB database and invite suggestions for articles in future issues. To subscribe to the IEDB newsletter or to contact project staff, send your email information to the email address below.

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