

Immune Epitope Database NEWSLETTER

Volume 3, Issue 2

<http://www.immuneEPITOPE.org>

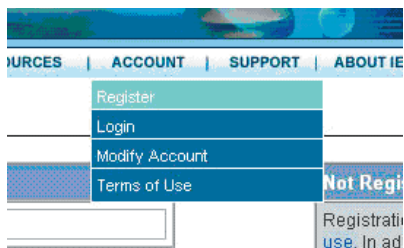
July 2006

Become a Registered IEDB User

Users of the IEDB are encouraged to register. The registration process is quick and simple, and registered users have access to several additional features:

- Submit a help request to the help desk
- Save advanced queries to be used at a later time
- Submit a discussion topic to the on-line discussion forum
- Reply to a previously submitted discussion topic in the forum

You can register by selecting Register from the Account menu (image below).



On the user registration page, the system will prompt you for your account information. Be sure that the email address you provide is accurate. Click the Submit button when you are done entering your account information. The system will prompt you to confirm your entry to ensure there are no typos. Click the Submit button to continue or the Back button to make a correction. After you have submitted your account information, the system will email an account activation key to you, but it may take a few minutes for the account activation message to arrive. You must click the link inside the email message to activate your account. Once your account has been activated, you can login and use the functions reserved for registered users.

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A Tool Developer's Resource

Benchmarking MHC-I Binding Predictions

A new resource for developers of MHC Class I binding prediction tools has been added to the IEDB website. The homepage now has a link under the News/Update section to <http://mhcbindingpredictions.immuneepitope.org/>. From this linked page, the user can access a manuscript describing the resource in detail, a dataset of experimental affinities of peptide to MHC molecules, and a description of the framework used for the evaluation of prediction methods.

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As described in the manuscript, predictions were obtained from public web-servers for all relevant peptide-MHC affinities in the dataset. The correlation between predicted and measured affinities was evaluated using scatter plots, linear regression, and ROC analyses. The evaluation of these external tools can be accessed by the name of the method or the MHC allele. As described in detail in the manuscript, this is not a fair evaluation of the value of each method, primarily because the data available to each method are highly divergent.

A similar evaluation of prediction performance of three prediction methods routinely used by the IEDB team was carried out using cross-validation on the dataset. In contrast to the comparison of external predictions, this is a fair evaluation of prediction performance of the three methods, as training and testing data were the same for each method. Again, the evaluations of these three internal methods can be accessed by the name of the method or the MHC allele.

Curation

Status & Update

The curation of essentially all relevant epitope literature listed in PubMed as of 26 May 2006 on NIAID Category A-C priority pathogens (http://www3.niaid.nih.gov/biodefense/bandc_priority.htm) has been curated by the IEDB curation staff. About 30% of this literature pertains to influenza. We are now focusing on curating literature related to the NIAID list of emerging and reemerging infectious diseases (<http://www.niaid.nih.gov/dmid/eid/erd.htm>) and will continue to update references on Category A-C pathogens periodically.

IEDB Data Content and Priorities

The IEDB project team curates immune epitope data based on priorities provided by NIAID. The current priorities are:

1. Category A, B, and C priority pathogens (http://www2.niaid.nih.gov/biodefense/bandc_priority.htm)
2. Emerging and Re-emerging diseases
3. Transplant rejection antigens and other alloantigens, allergens, and self antigens involved in autoimmunity
4. Infectious diseases not listed included in priorities 1 and 2
5. Epitopes associated with cancer

The IEDB is scheduled to be current with regard to Category A-C priority pathogen scientific literature by July 2006. The IEDB curation staff will then concentrate on literature pertaining to emerging and re-emerging infectious diseases, while periodically updating the Category A-C literature. Curation activities will continue throughout the IEDB contract's period of performance, which ends in December 2010.

The list of potentially relevant articles is generated with a query of PubMed (<http://www.pubmed.gov>). In order for a scientific article to be included in the IEDB, it must meet several objective criteria as described in Section 2 of the IEDB Curation Manual, available at <http://www.immuneepitope.org/downloadDocuments.do>. While the IEDB staff endeavors to curate all articles that contain relevant epitope information, some literature will invariably be missed. Users are invited to bring appropriate references to the attention of the IEDB project staff using the Feedback feature, accessible on the IEDB home page in the Quick Links box. Such references will be considered in accordance with the stated curation priorities.

Summary Metrics as of June 19, 2006

As of 19 June 2006, the IEDB contained data from 2112 references and 33,569 records. A record is defined as a single molecular structure or entity within a single reference. The term "structure" is used because the IEDB collects data with both positive and negative binding values, but only those structures that positively bind can truly be called "epitopes". Structures can appear in multiple references, so the number of distinct structures (26,934) is always less than the number of records. When the structures with negative binding are disregarded, the number of distinct epitopes remaining is 16,536.

Large Scale Antibody & T Cell Epitope Discovery Program

Clemencia Pinilla, Ph.D.



Front (Left to Right): Clemencia Pinilla, Atima Sharma
Back (Left to Right): Claudia Raja Gabaglia, Richard A. Houghten, Lisa Osthues, Patricia Norori, Jon R. Appel

Background

Dr. Pinilla's Epitope Discovery contract is focused on the characterization of relevant peptide sequences (epitopes) involved in the protective immune response following vaccination against vaccinia infections. Smallpox, a highly contagious and sometimes lethal disease, is caused by the variola virus. Due to a successful vaccination program conducted worldwide, smallpox was eradicated in 1979. Recent events have raised concerns regarding the possible use of smallpox, as well as new emerging infections such as monkeypox, as bioterrorism agents. Routine immunization against smallpox was discontinued during the 1970's, and the remaining live vaccinia to be used for immunization does not meet the current safety standards. Furthermore, although this type of immunization was efficacious for extinguishing smallpox, the relevant vaccine antigens capable of expanding appropriated humoral and T cell immune responses are only now beginning to be addressed. Clearly, there is a strong need for the development of better vaccine candidates. Dr. Pinilla's contract proposes to identify T cell epitopes recognized by vaccinia-immunized donors who are participating in a clinical trial designed to evaluate the safety and efficacy of two different vaccines, namely MVA and Dryvax. Human T cell lines and clones derived from immunized human donors are being gener-

ated. These cell lines and clones will be used to screen combinatorial peptide libraries as well as overlapping panels of peptides of pox virus proteins.

Positional Scanning Libraries

Positional scanning libraries representing trillions of peptides of different lengths are unbiased sources of peptide antigens in T cell activation assays for the identification of T cell epitopes. These libraries are composed of systematically arranged sub-libraries that address each position of the peptide with a defined amino acid. The screening data of a given PS-SCL permit the identification of key residues at each diversity position. It is important to note, however, that the activity found for any given mixture is due to the presence of specific active peptide(s) within the mixture, and not to the individual amino acids as separate entities. The information derived from the screening of these libraries with T cell clones, in conjunction with a recently developed biometrical analysis, allows the identification of T cell ligands from proteins in public databases. The combination of two different antigenic sources, overlapping individual peptides and positional scanning libraries, will facilitate and expedite the identification of the T cell epitopes recognized by a large number of human lines and clones reactive to vaccinia virus.

Integration of positional scanning libraries and biometrical analysis to identify new ligands

The studies utilizing positional scanning libraries with T cells of known specificity led to the development of a new strategy: a PS-SCL-based biometrical analysis that integrates the data acquisition from the screening of PS-SCL with protein sequence databases in order to predict and identify naturally occurring peptide ligands. This biometrical analysis compares the information derived from libraries composed of trillions of peptides with the millions of decapeptide segments of proteins contained in a protein database to rank and predict the most stimulatory peptides ligands. The table below summarizes some results obtained for pathogenic T cell clones (CD4+ and CD8+), for which their peptide epitope specificity was unknown, and through the use of PS-SCL based biometrical analysis, the specificities were elucidated. This approach has also been shown to predict the known epitope among the top 50 to 100 highest ranking sequences and has allowed the identification of crossreactive peptides for clones of known specificity. In Dr. Pinilla's contract, the PS-SCL-based biometrical analysis will be carried out pri-

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2006 American Association of Immunology (AAI) Meeting

IEDB Exhibition Summary

Purpose of Exhibition

The purpose of participating in the 2006 AAI meeting was to formally introduce the beta version of the IEDB to immunologists and other potential users. The two broad objectives were to 1) promote the use of the IEDB and 2) generate feedback from users with subject matter expertise to be considered for future IEDB improvements. Representing the IEDB were Bjoern Peters (Co-P.I., Tools Specialist), Kerrie Vaughan (Curator), and Nima Salimi (Curator). The IEDB exhibit consisted of a backdrop providing a brief overview of the IEDB, a projected feed of the IEDB website on which live demonstrations of the IEDB were provided, and an additional laptop connected to the IEDB website. Literature summarizing the database and its capabilities was distributed and contact information was gathered from visitors to the booth.

User Interest in IEDB

Visitors to the IEDB exhibit were guided through live sample queries and analysis tool usage, on the projected screen. This method proved extremely effective, as it fostered an interactive environment amongst the attendees and the IEDB representatives, and promoted a question and answer forum. On the additional laptop, one-on-one tutorials were given for those who desired more extensive demonstrations. The database and analysis tools were very well received. Visitors to the IEDB booth were pleased with the overall objective of the project and the accessibility of the data to the general community. Users successfully searched for, and found data pertinent to their current work or interests.

IEDB Issues that were identified

Several of the visitors to the booth communicated a general frustration with not knowing how to make sense of IC50 values (and others) from MHC binding prediction tools. The consensus was that it was difficult to rate binding based on what seem like arbitrary values.



(Left to right) Booth exhibitors: Kerrie Vaughan, Bjoern Peters, Nima Salimi. The booth consisted of an 8 foot pop-up display and a portable LCD display screen for guests to navigate the booth and ask questions about the database. Pamphlets about the project and t-shirts were also handed out.

The IEDB may be able to address this by providing a straightforward way for the user to understand the predictive values generated and what they mean.

IEDB Feedback

In general, user feedback was very good. One suggestion was that the IEDB homepage could display an overview of what the database currently contains by pathogen or broad category (A-C, cancer, autoimmunity, etc.). Many potential users were interested in retrieving autoimmunity and cancer data (curation of autoimmunity references is scheduled for 2007). Other suggestions included adding more quantitative values, incorporating Endnote export functionality, and a "Share Results with Friends" functionality.

Annual Compendium

Where to find it

The 2005 Annual Compendium can now be viewed and downloaded as a PDF file on the IEDB website. The link appears on the home page and on the download page under the Resources pull-down menu. This first Annual Compendium of the Immune Epitope Database and Analysis Resource consists of three sections. The first section lists and describes the various features of the IEDB website implemented by the end of 2005. The second section contains a list of the antibody and T cell epitope information in the database as of 31 December 2005. Although the IEDB collects data from three primary sources – published literature, patents, and direct data submissions from researchers, only literature data were curated in 2005. The third section lists the scientific publications in 2005 for which the IEDB played a contributory role. This list is limited to articles published by IEDB contractor team members given that it was not publicly available in 2005.

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marily with custom poxvirus databases. This analysis will allow the identification of epitopes in the vaccinia preparation as well as possible crossreactive epitopes in other poxviruses, including variola.

Altogether, the goal is to identify the key CD4+ and CD8+ T cell epitopes essential for a protective immune response testing vaccinia-immunized donors. These studies will lead to a better understanding of human immune responses to vaccinia infections.

Table 1: PS-SCL-based biometrical analysis used for characterization of previously unknown relevant antigens in different pathogenic systems.

Table 1

Disease	T cell clones generated with	PS-SCL Biometrical analysis	Publication
Lyme	CD4 Borrelia	Borrelia and human peptides	Nature Med 1999
Melanoma	CD8 PHA	Tumor antigen-SSX2	European Journ of Immunol 2002
Multiple Sclerosis	CD4 PHA	Viral and human peptides	Plos Pathogens 2005
Diabetes	-	Bacterial and viral peptides	Diabetes 2004
Smallpox Vaccinated Donors	CD4 & CD8 Vaccinia Virus	In progress	

Contact Information

The Immune Epitope Database 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. Upon deployment of the database, we will actively solicit tool and epitope submissions. To subscribe to the IEDB newsletter or contact project staff, send your email information to the email address below.

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