

Immune Epitope Database

NEWSLETTER

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June 2010

IEDB has First-Time Exhibit Booth at AAAAI Conference

The IEDB attended this year's American Academy of Allergy, Asthma and Immunology (AAAAI) Conference in New Orleans on February 26 - March 2. This was our first endeavor for allergy-specific outreach. Not only was the IEDB well-received, a great deal was learned with respect to this particular user community. The conference was a unique opportunity to gain new insights into database usability for this user community. In this respect we learned that many users are interested in being able to search by disease. Constructive criticism included IEDB search complexity and jargon. Several users expressed a desire to be able to search more easily by allergy type. The IEDB team has started to address this issue and will have an upgraded disease finder deployed in the fourth quarter 2010.

In addition to learning what the IEDB contained and how to use it, other inquiries included:

- companies that use the IEDB for epitope identification or prediction
- clinicians who want to be able to associate clinical signs with data in the IEDB
- clinicians and allergists performing clinical studies who wanted to use the IEDB to see what has been done previously with various allergens for comparison
- researchers wishing to collaborate for epitope-predictive tool building

The IEDB will be attending the FOCIS (Federation of Clinical Immunology Societies) 2010 conference in Boston on June 24 – 27 with its exhibit booth. Two curators will be staffing it and will be available to demonstrate its features and answer questions.

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Allergy Meta-analysis and IEDB Presented at AAAAI Meeting

LIAI performed a preliminary meta-analysis on allergy and asthma epitope data that were available in the IEDB as of January 2010. Dr. Kerrie Vaughan presented the results at the American Academy of Allergy, Asthma and Immunology (AAAAI) Conference in January at a poster session. The analysis identified nearly 5,000 allergy-related epitopes derived from over 500 different allergens. This included epitopes from protein allergens (4,646), and for the first time, epitopes derived from non-peptidic allergens (257). Protein allergens were categorized according to their source organism, which included plants, animals, insects, food, parasites, and fungi. Non-peptidic allergens were categorized into five groups including drugs and biologicals, industrial compounds or those related to occupational exposure, metals, model haptens, and carbohydrates from plants.

The vast majority of allergy epitopes (both peptidic and non-peptidic) were defined for B cells/antibodies in humans. In these records, IgE figured prominently; however, IgG, IgG1, IgG4, IgA, IgM, Ig2b, IgG2a, and IgG3 were also reported. Other hosts included monkeys, pigs, dogs, rabbits, guinea pigs, rats, and mice. The majority of peptidic epitopes were defined for foods (cow's milk, wheat, and peanuts) and plants (tree and grass pollens), while the majority of non-peptidic epitopes were defined for drugs and biologicals (antibiotics). The majority of T cell epitopes were defined as CD4+/class II, with very few being defined for CD8+/class I. MHC-restriction was also captured for T cell reactivity when reported. The vast majority of human epitopes were restricted by HLA-DQ and HLA-DR. Other reported alleles included HLA-A2, HLA-DP, HLA-DRB1, HLA-DRA, HLA-DRB3, HLA-DRB4, and HLA-DRB5. A much more narrow range of mouse alleles was defined. Lacking from both peptidic and non-peptidic data are allergy epitopes defined for class II and/or CD8+ T cells. Also lacking from the human data are epitopes identified as being therapeutic in vivo. It is anticipated that this would be of significant interest for the field going forward.

Future directions include an expansion of the analysis to investigate potentially therapeutic peptidic epitopes. To date, we have identified a number of peptides that have been reported to decrease allergic reactivity as measured either in vitro or in vivo. However, a standard definition of 'therapeutic' is lacking and we plan to engage the community for guidance. We are also in the process of expanding the analysis of non-peptidic allergy epitopes. In the coming months the IEDB will be adding data representing several hundred new non-peptidic compounds related to allergy. Another area of interest and need is the classification of epitope data into standardized disease categories. At present, clinical disease manifestations of allergy are reported differently among the allergy types making it difficult to analyze like data. More broadly, we wish to investigate the relationship of epitope data research (in terms of numbers) with global allergic disease incidence (morbidity).

In addition to the meta-analysis poster presentation, Dr. Alessandro Sette was a speaker at an NIAID afternoon course, Multiple Functions of Allergens and Understanding Allergenicity, on Friday, February 26. The three major goals of the course as stated in the program were to enable participants to:

- explain that allergens have special functions, such as adjuvant activities, that are critical to their allergenic activity
- discuss the capacity of different sources of allergens to modulate allergenic properties
- identify new information on allergen epitopes

Dr. Sette's presentation was entitled "Allergen Epitope Discovery and the NIAID Immune Epitope Database Resource."

IEDB 2.4 to be Released in June

The latest version of the IEDB website is scheduled for release near the end of June. Two major improvements will be introduced affecting the Simple Search on the home page. The first is an autocomplete feature for the Molecule, Organism, and Allele Finders. For example, as the user types “human” in the Source Organism field, possible matches will be displayed. The list of matches will include scientific names and synonyms. This will expedite the selection process for the user.

The second improvement affects the defining of epitope structure. In the current version of the Simple Search, the user can select from a long list of Structure Types in a pull-down menu. In the new version, the user can select from four choices controlled by radio buttons. The Molecule Finder is being re-designed to provide a tree hierarchy similar to the one found in the existing Organism Finder and to incorporate the non-peptidic structures curated by the Chemical Entities of Biological Interest (ChEBI) database.

The screenshot shows the IEDB 2.3 Simple Search interface. It is organized into three main sections: Epitope Structure, Epitope Source, and Immune Recognition Context. In the Epitope Structure section, there is a dropdown menu for Structure Type and a text input for Linear Sequence with an Exact Matches dropdown. The Epitope Source section includes text inputs for Source Organism and Source Antigen, each with an associated button (Organism Finder and Molecule Finder). The Immune Recognition Context section features four checked checkboxes: B Cell Response, T Cell Response, MHC Binding, and MHC Ligand Elution, accompanied by a target icon. Below these are text inputs for Host Organism and MHC Restriction, each with a button (Organism Finder and Allele Finder), and a dropdown for MHC Class. At the bottom are Search and Clear buttons.

Figure 1 Simple Search as it appears on the IEDB 2.3 home page

The screenshot shows the IEDB 2.4 Simple Search interface. It is organized into three main sections: Epitope Structure, Epitope Source, and Immune Recognition Context. In the Epitope Structure section, there are radio buttons for Any, Linear Peptide, and Discontinuous Peptide. The Linear Peptide option has a text input and an Exact Matches dropdown. The Non-Peptidic option has a text input and a Molecule Finder button. The Epitope Source section includes text inputs for Source Organism and Source Antigen, each with an associated button (Organism Finder and Molecule Finder). The Immune Recognition Context section features four checked checkboxes: B Cell Response, T Cell Response, MHC Binding, and MHC Ligand Elution, accompanied by a target icon. Below these are text inputs for Host Organism and MHC Restriction, each with a button (Organism Finder and Allele Finder), and a dropdown for MHC Class. At the bottom are Search and Clear buttons.

Figure 2 Simple Search as it will appear on the IEDB 2.4 home page

Recent Publications

Limitations of Ab initio predictions of peptide binding to MHC class II molecules.

Zhang H, Wang P, Papangelopoulos N, Xu Y, Sette A, Bourne PE, Lund O, Ponomarenko J, Nielsen M, Peters B.

PLoS One. 2010 Feb 17;5(2):e9272.

PMID: 20174654

Successful predictions of peptide MHC binding typically require a large set of binding data for the specific MHC molecule that is examined. Structure based prediction methods promise to circumvent this requirement by evaluating the physical contacts a peptide can make with an MHC molecule based on the highly conserved 3D structure of peptide:MHC complexes. While several such methods have been described before, most are not publicly available and have not been independently tested for their performance. We here implemented and evaluated three prediction methods for MHC class II molecules: statistical potentials derived from the analysis of known protein structures; energetic evaluation of different peptide snapshots in a molecular dynamics simulation; and direct analysis of contacts made in known 3D structures of peptide:MHC complexes. These methods are ab initio in that they require structural data of the MHC molecule examined, but no specific peptide:MHC binding data. Moreover, these methods retain the ability to make predictions in a sufficiently short time scale to be useful in a real world application, such as screening a whole proteome for candidate binding peptides. A rigorous evaluation of each methods prediction performance showed that these are significantly better than random, but still substantially lower than the best performing sequence based class II prediction methods available. While the approaches presented here were developed independently, we have chosen to present our results together in order to support the notion that generating structure based predictions of peptide:MHC binding without using binding data is unlikely to give satisfactory results.

Design and utilization of epitope-based databases and predictive tools.

Salimi N, Fleri W, Peters B, Sette A.

Immunogenetics. 2010 Apr;62(4):185-96. Epub 2010 Mar 6.

PMID: 20213141

In the last decade, significant progress has been made in expanding the scope and depth of publicly available immunological databases and online analysis resources, which have become an integral part of the repertoire of tools available to the scientific community for basic and applied research. Herein, we present a general overview of different resources and databases currently available. Because of our association with the Immune Epitope Database and Analysis Resource, this resource is reviewed in more detail. Our review includes aspects such as the development of formal ontologies and the type and breadth of analytical tools available to predict epitopes and analyze immune epitope data. A common feature of immunological databases is the requirement to host large amounts of data extracted from disparate sources. Accordingly, we discuss and review processes to curate the immunological literature, as well as examples of how the curated data can be used to generate a meta-analysis of the epitope knowledge currently available for diseases of worldwide concern, such as influenza and malaria. Finally, we review the impact of immunological databases, by analyzing their usage and citations, and by categorizing the type of citations. Taken together, the results highlight the growing impact and utility of immunological databases for the scientific community.

Curation Update

Curation of data relating to peptidic epitopes for all infectious diseases and peptidic and non-peptidic epitopes for allergens is current for references appearing in PubMed as of the end of December 2009. A query for new potentially relevant epitope references is run quarterly to update the database. Curation of peptidic epitopes for diabetes, rheumatoid arthritis, multiple sclerosis, and lupus is essentially complete. Curation of peptidic epitopes of all other autoimmune diseases and non-peptidic epitopes for all infectious diseases is in progress and will be completed later in 2010. As of May 2010, data from approximately 10,000 references have been incorporated into the IEDB. Users are invited to bring references to our attention that are potentially relevant to the IEDB but do not appear in the database. References that are deemed to meet the IEDB criteria for curation will be queued for processing in accordance to our NIAID-directed priorities (Category A-C priority pathogens, emerging and re-emerging infectious diseases, other infectious diseases, allergies, autoimmune diseases, transplantation, and cancer). Citations should be sent to help@iedb.org.

Non-peptidic Curation

The IEDB has been working with the Chemical Entities of Biological Interest (ChEBI) database since June of 2009. ChEBI is providing a formal name, synonyms, ontologic relationships, hierarchical tree placement within the ChEBI system, SMILES notation, and a fully annotated entry in their website for every non-peptidic structure required to curate a relevant manuscript. ChEBI has been adding or assigning approximately 100 IEDB structures once a month on their regular build schedule, starting in September 2009. Utilizing this process, 95% of allergy non-peptidic references have been curated.

The IEDB team is in the process of implementing a non-peptidic molecule finder to enhance the searchability of these structures. The finder redesign features the incorporation of the ChEBI hierarchical tree which groups the structures by molecular families such as beta lactam antibiotics or carbohydrates. This feature will be available in the IEDB 2.4 release scheduled for June 2010.

Contact Information

The Immune Epitope Database and Analysis Resource is supported by a contract from the National Institute of Allergy and 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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