Immune Epitope Database NEWSLETTER

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IEBD 2.3 Released January 19

The latest version of the IEDB website was released on January 19. A list of the new features and changes in IEDB 2.3 are listed below. Several of these will be highlighted in future newsletters. Further information can also be found in the 2009 Annual Compendium that will be posted on the website shortly.

- The ability to perform "fuzzy" (BLAST) searches on linear sequences has been added on the homepage and on Epitope Search.
- Linear Sequence input on the homepage has been modified to allow longer sequences and prevent string truncation issues.
- MHC Allele Information page has been modified to display Peptide MHC Binding Motif diagrams and Amino Acid Binding Charts for a subset of MHC Allele records.
- The news section on the homepage has been redesigned to organize posts under a collapsible category structure.
- The Allergen tree on Organism Finder has been updated with current NCBI information and some lower ranks have been collapsed to conserve navigation clicks.
- The Epitope Source Organisms link on Summary Metric has been changed to link to Source Organism list view.
- The Molecule Accession links on the Molecule finder for ChEBI molecules have been added which link to the ChEBI site.
- ChEBI images and Synonyms have been added to Epitope Information page.
- Excel export capability has been added to the Reference List page.

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- The Epitope Viewer has been modified to provide the choice between calculated and curated contact data when launching.
- The Curation Last Updated date has been added to Reference Information page.
- Synonym pop-up/mouse over functionality has been added to Browse-by-3D Structure for organisms and alleles.
- The Acknowledgements, Publications Relevant to the IEDB, and Citing the IEDB pages have been updated.
- Improved usability and several defects and inconsistencies throughout the site were corrected.

New B and T Cell Epitope Discovery Kick-Off Meeting Held

A contract initiation meeting was held January 25 – 26 in the Bethesda, Maryland area for the five newly awarded B Cell Epitope and Mechanisms of Antibody Protection contracts and the six newly awarded Large Scale T Cell Epitope Discovery contracts. These contracts come on the heels of the fourteen recently completed Large Scale Antibody and T Cell Epitope Discovery contracts. All principal investigators for the current round of T Cell Epitope Discovery contracts had been previously awarded five-year contracts in the first round, which was not the case for the five Antibody Epitope Discovery contracts.

The kick-off meeting started with a welcome and introduction by Drs. Stacy Ferguson and Timothy Gondré-Lewis, the Contracting Officer's Technical Representatives (COTRs) for the new B Cell and T Cell contracts, respectively. The morning session included a talk on the Immune Epitope Database and Analysis Resource in which Drs. Bjoern Peters and Alex Sette presented an overview of the database structure and ontology, the analysis resource, the curation effort, and the ongoing meta-analyses. Nima Salimi ended the presentation with a discussion of the data submission process since all epitope discovery contractors are obligated to deposit their findings in the IEDB. This was followed by Dr. Alison Deckhut Augustine discussing the NIH Tetramer Core Facility and Dr. Susan Peacock discussing the Biodefense and Emerging Infections Research Resource Repository (BEI), both resources of potential value to the contracting teams.

During the remainder of the meeting, each epitope discovery contract presented its plans. The titles of the contracts and their respective principal investigators for the antibody contracts are listed below alphabetically by organizational affiliations grouped by antibody and T cell.

Antibody Epitope Discovery Contracts:

- B Cell Epitope Discovery in Tularemia, Jacqueline Sharon, Boston University
- Mapping of the Antibody Epitopes and Functional Regions of Dengue, Hepatitis C, and Chikungunya Virus Envelope Proteins, Benjamin Doranz, Integral Molecular, Inc.
- Vaccinia Virus B Cell Epitope Discovery and Mechanisms of Antibody Protection, Bjoern Peters, La Jolla Institute for Allergy and Immunology
- Roles of Protective or Pathogenic B Cell Epitopes in Human Lassa Fever, James Robinson, Tulane University
- Genetic and Structural Basis for Virus Neutralization, James Crowe, Vanderbilt University

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T Cell Epitope Discovery Contracts:

- Identifying Epitopes Recognized by Influenza and Flavivirus Responsive CD4+ T Cell Following Vaccination or Natural Infection, William Kwok, Benaroya Research Institute at Virginia Mason
- T Cell Epitopes from Burkholderia pseudomallei, Daniel Altman, Imperial College
- The Identification of Class I and Class II T Cell Epitopes from Benue Viruses, Alessandro Sette, La Jolla Institute for Allergy and Immunology
- The Identification of Class II T Cell Epitopes from Mycobacterium tuberculosis, Alessandro Sette, La Jolla Institute for Allergy and Immunology
- Using Human CD8+ T Cells to Define Mtb-specific Immunodominant Epitopes, David Lewinsohn, Oregon Health & Science University
- Complete Analysis of T Cell Epitopes in Yellow Fever Virus, Søren Buus, University of Copenhagen

Recent Publications

Pre-existing immunity against swine-origin H1N1 influenza viruses in the general human population.

Greenbaum JA, Kotturi MF, Kim Y, Oseroff C, Vaughan K, Salimi N, Vita R, Ponomarenko J, Scheuermann RH, Sette A, Peters B.

Proc Natl Acad Sci U S A. 2009 Dec 1;106(48):20365-70. Epub 2009 Nov 16.

PMID: 19918065

A major concern about the ongoing swine-origin H1N1 influenza virus (S-OIV) outbreak is that the virus may be so different from seasonal H1N1 that little immune protection exists in the human population. In this study, we examined the molecular basis for pre-existing immunity against S-OIV, namely the recognition of viral immune epitopes by T cells or B cells/antibodies that have been previously primed by circulating influenza strains. Using data from the Immune Epitope Database, we found that only 31% (8/26) of B-cell epitopes present in recently circulating H1N1 strains are conserved in the S-OIV, with only 17% (1/6) conserved in the hemagglutinin (HA) and neuraminidase (NA) surface proteins. In contrast, 69% (54/78) of the epitopes recognized by CD8(+) T cells are completely invariant. We further demonstrate experimentally that some memory T-cell immunity against S-OIV is present in the adult population and that such memory is of similar magnitude as the pre-existing memory against seasonal H1N1 influenza. Because protection from infection is antibody mediated, a new vaccine based on the specific S-OIV HA and NA proteins is likely to be required to prevent infection. However, T cells are known to blunt disease severity. Therefore, the conservation of a large fraction of T-cell epitopes suggests that the severity of an S-OIV infection, as far as it is determined by susceptibility of the virus to immune attack, would not differ much from that of seasonal flu. These results are consistent with reports about disease incidence, severity, and mortality rates associated with human S-OIV.

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The Immune Epitope Database 2.0.

Vita R, Zarebski L, Greenbaum JA, Emami H, Hoof I, Salimi N, Damle R, Sette A, Peters B.

Nucleic Acids Res. 2009 Nov 11.

PMID: 19906713

The Immune Epitope Database (IEDB, www.iedb.org) provides a catalog of experimentally characterized B and T cell epitopes, as well as data on Major Histocompatibility Complex (MHC) binding and MHC ligand elution experiments. The database represents the molecular structures recognized by adaptive immune receptors and the experimental contexts in which these molecules were determined to be immune epitopes. Epitopes recognized in humans, nonhuman primates, rodents, pigs, cats and all other tested species are included. Both positive and negative experimental results are captured. Over the course of 4 years, the data from 180 978 experiments were curated manually from the literature, which covers approximately 99% of all publicly available information on peptide epitopes mapped in infectious agents (excluding HIV) and 93% of those mapped in allergens. In addition, data that would otherwise be unavailable to the public from 129 186 experiments were submitted directly by investigators. The curation of epitopes related to autoimmunity is expected to be completed by the end of 2010. The database can be queried by epitope structure, source organism, MHC restriction, assay type or host organism, among other criteria. The database structure, as well as its querying, browsing and reporting interfaces, was completely redesigned for the IEDB 2.0 release, which became publicly available in early 2009.

Derivation of an amino acid similarity matrix for peptide: MHC binding and its application as a Bayesian prior.

Kim Y, Sidney J, Pinilla C, Sette A, Peters B.

BMC Bioinformatics. 2009 Nov 30;10:394.

PMID: 19948066

BACKGROUND: Experts in peptide:MHC binding studies are often able to estimate the impact of a single residue substitution based on a heuristic understanding of amino acid similarity in an experimental context. Our aim is to quantify this measure of similarity to improve peptide:MHC binding prediction methods. This should help compensate for holes and bias in the sequence space coverage of existing peptide binding datasets.

RESULTS: Here, a novel amino acid similarity matrix (PMBEC) is directly derived from the binding affinity data of combinatorial peptide mixtures. Like BLOSUM62, this matrix captures well-known physicochemical properties of amino acid residues. However, PMBEC differs markedly from existing matrices in cases where residue substitution involves a reversal of electrostatic charge. To demonstrate its usefulness, we have developed a new peptide:MHC class I binding prediction method, using the matrix as a Bayesian prior. We show that the new method can compensate for missing information on specific residues in the training data. We also carried out a large-scale benchmark, and its results indicate that prediction performance of the new method is comparable to that of the best neural network based approaches for peptide:MHC class I binding.

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CONCLUSION: A novel amino acid similarity matrix has been derived for peptide:MHC binding interactions. One prominent feature of the matrix is that it disfavors substitution of residues with opposite charges. Given that the matrix was derived from experimentally determined peptide:MHC binding affinity measurements, this feature is likely shared by all peptide:protein interactions. In addition, we have demonstrated the usefulness of the matrix as a Bayesian prior in an improved scoring-matrix based peptide:MHC class I prediction method. A software implementation of the method is available at: http://www.mhc-pathway.net/smmpmbec.

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 September 2009. A query for new potentially relevant epitope references is run quarterly to update the database. Curation of peptidic epitopes for diabetes, rheumatoid arthritis, and multiple sclerosis is essentially complete and about half of lupus peptidic references have been curated. Curation of peptidic epitopes of all other autoimmune diseases and non-peptidic epitopes for all infectious diseases will commence in the second quarter of 2010. As of February 2010, data from approximately 9,000 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.

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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