

Immune Epitope Database NEWSLETTER

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<http://www.immuneepitope.org>

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IEDB Goes Into Public Beta: February 2006

The Immune Epitope Database and Analysis Resource (IEDB) is scheduled to go into a public beta release on February 15, 2006. We anticipate that the database will contain approximately 1,600 literature references, 15,000 records, and over 5,000 distinct epitopes, which will be available to users on the IEDB website. In the spirit of scientific collaboration, the IEDB imported data from three other epitope databases—FIMM, HLA Ligand, and TopBank.

Users can search the IEDB with three different

query modes—a Google-like text search, an immunologist-friendly simple search, and an advanced query-by-example search. A variety of analysis tools will also be available, including tools for predicting MHC Class I T cell epitopes, MHC Class II T cell epitopes, and linear B cell epitopes; as well as analysis tools for epitope structure visualization, population coverage, and epitope conservancy.

Community Outreach: An Important Component of the IEDB project

An important goal of the IEDB project is to involve the scientific community. In an effort to do so, a community outreach plan has been put in place. The plan includes ways to promote access to the database and encourage the community to get involved. This includes instructions for the community to obtain database documents and guidelines, access the online forum module, and become recipients of quarterly newsletters and other email content.

To encourage community involvement and enhance usability, the IEDB team will make database documents and guidelines freely available to the research community for use, improvement and publication purposes. Users are encouraged not only to use these available resources, but also to provide feedback and contribute data or analysis resources to the database. Any data and analysis resource contributions will be cited by authorship or acknowledgment on the IEDB website.

The website will have a registration capability, which will provide users with many advantages. Registered users can post and comment on topics in a forum module, enabling discussions with other users of the database. They can also subscribe to the quarterly newsletter and other email broadcasts. One major advantage is the ability to save personal-

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Science in the News

Journals and Articles: Recommended Reading

Looking at the History and Evolution of the Influenza Viruses

Influenza has been a dominant topic lately due to human infections of the bird flu throughout Southeast Asia and parts of Europe. The pandemic threat has caused in researchers and leaders alike to place it as a priority on their agendas. Below are a few articles recommended by Drs. David Tschärke, Erika Assarson and other scientists on influenza:

1. Characterization of the reconstructed 1918 Spanish influenza pandemic virus.

Tumpey TM, Basler CF, Aguilar PV, Zeng H, Solorzano A, Swayne DE, Cox NJ, Katz JM, Taubenberger JK, Palese P, Garcia-Sastre A.

PMID: 16210530

Influenza Branch, Mailstop G-16, Division of Viral and Rickettsial Diseases (DVRD), National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, Atlanta, GA 30333, USA. tft9@cdc.gov

The pandemic influenza virus of 1918-1919 killed an estimated 20 to 50 million people worldwide. With the recent availability of the complete 1918 influenza virus coding sequence, we used reverse genetics to generate an influenza virus bearing all eight gene segments of the pandemic virus to study the properties associated with its extraordinary virulence. In stark contrast to contemporary human influenza H1N1 viruses, the 1918 pandemic virus had the ability to replicate in the absence of trypsin, caused death in mice and embryonated chicken eggs, and displayed a high-growth phenotype in human bronchial epithelial cells. Moreover, the coordinated expression of the 1918 virus genes most certainly confers the unique high-virulence phenotype observed with this pandemic virus.

2. Large-scale sequencing of human influenza reveals the dynamic nature of viral genome evolution.

Ghedini E, Sengamalay NA, Shumway M, Zaborsky J, Feldblyum T, Subbu V, Spiro DJ, Sitz J, Koo H, Bolotov P, Dernovoy D, Tatusova T, Bao Y, St George K, Taylor J, Lipman DJ, Fraser CM, Taubenberger JK, Salzberg SL.

PMID: 16208317

The Institute for Genomic Research, 9712 Medical Center Dr., Rockville, Maryland 20850, USA.

Influenza viruses are remarkably adept at surviving in the human population over a long timescale. The human influenza A virus continues to thrive even among populations with widespread access to vaccines, and continues to be a major cause of morbidity and mortality. The virus mutates from year to year, making the existing vaccines ineffective on a regular basis, and requiring that new strains be chosen for a new vaccine. Less-frequent major changes, known as antigenic shift, create new strains against which the human population has little protective immunity, thereby causing worldwide pandemics. The most recent pandemics include the 1918 'Spanish' flu, one of the most deadly outbreaks in recorded history, which killed 30-50 million people worldwide, the 1957 'Asian' flu, and the 1968 'Hong Kong' flu. Motivated by the need for a better under-

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Large Scale Antibody & T Cell Epitope Discovery Program

The Technical University of Denmark; Ole Lund, Ph.D.



Dr. Lund's lab members: (left to right) Pemille Haste Andersen, Morton Nielsen, Annie Molgaard, Jens Pontoppidan, Sune Frankild, Thomas Blicher, Claus Lundegaard, Xiuxiu Ye

Introduction

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), awarded 14 contracts totaling more than \$73 million to fund the Large-Scale Antibody and T Cell Epitope Discovery Program, an initiative aimed at quickly identifying the regions of selected infectious agents that elicit immune reactions. The study of these regions, known as epitopes, promises to uncover targets for new and improved vaccines, therapies and diagnostic tools against potential bio-terror agents as well as emerging/re-emerging infectious diseases such as West Nile virus and influenza. Dr. Ole Lund is among the list of award recipients. For a full list of awardees, visit: http://www3.niaid.nih.gov/Biodefense/Research/2004awards/discovery_awards.htm

Epitope Discovery Principal Investigator

The goal of Dr. Lund's 5-year Epitope Discovery contract is to identify parts of disease causing microorganisms (pathogens) that can be recognized by the human immune system. Infected cells are recognized and killed by the immune system when they display fragments of the infecting agent, called epitopes, on their cell surface. Enumerating and describing epitopes may be used to design vaccines that protect against disease. Dr. Lund's project will develop improved methods to predict cytotoxic T cell (CTL) epitopes and use these methods to scan 15 different

pathogens, listed in Table 1, from the NIAID Category A, B, and C Priority Pathogens.

IEDB Subcontractor

Dr. Lund, in collaboration with Dr. Soren Buus from the University of Copenhagen, is a subcontractor on the IEDB project. They focus on developing new tools for epitope prediction through the use of neural networks and participate in the evaluation of predictive tools using standardized data sets.

Background

The Immunological Bioinformatics group that Dr. Lund leads is part of the Center for Biological Sequence Analysis (CBS), which is one of the large bioinformatics groups in academia in Europe. The interest of CBS includes basic research in the general fields of bioinformatics and systems biology. The group has pioneered the use of machine learning techniques, in particular for prediction of protein localization, secretion pathways, post-translational modifications, non-homology based protein function prediction (for example for identification of cell cycle regulated genes), membrane protein topology, and protein distance matrix predictions. In the field of immunology, the group has developed a method for prediction of binding of peptides to HLA class I and II molecules and prediction of TAP binding and proteasomal cleavage sites.

Table 1

Pathogen	HLA binding	CTL
Influenza	X	X
Variola major (smallpox) vaccine strain	X	X
Yersinia pestis	X	
Francisella tularensis (tularemia)	X	
Lymphocytic choriomeningitis virus(LCM)	X	
Lassa Fever	X	
Hantaan virus (Korean hemorrhagic fever virus)	X	
Rift Valley Fever	X	
Dengue	X	
Ebola	X	
Marburg	X	
Multi-drug resistant TB (BCG vaccine)	X	X
Yellow fever	X	
Typhus fever (Rickettsia prowazekii)	X	
West Nile Virus	X	

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standing of influenza evolution, we have developed flexible protocols that make it possible to apply large-scale sequencing techniques to the highly variable influenza genome. Here we report the results of sequencing 209 complete genomes of the human influenza A virus, encompassing a total of 2,821,103 nucleotides. In addition to increasing markedly the number of publicly available, complete influenza virus genomes, we have discovered several anomalies in these first 209 genomes that demonstrate the dynamic nature of influenza transmission and evolution. This new, large-scale sequencing effort promises to provide a more comprehensive picture of the evolution of influenza viruses and of their pattern of transmission through human and animal populations. All data from this project are being deposited, without delay, in public archives.

3. Avian and pandemic influenza-Five questions for 2006

Nicoll A.

PMID: 16371697

European Centre for Disease Prevention and Control (ECDC), London, United Kingdom.

In January this year it was observed that 2005 was going to be the Year of the Rooster in the Chinese calendar, and that perhaps was an ill omen for bird (avian) and pandemic influenza. Certainly, influenza was the infection that then dominated the popular press in 2005, and so in a certain way this was a very good year for influenza and those who study it. The infection has been getting the attention it deserves as a human threat.

Other articles to consider:

Resurrected Influenza Virus Yields Secrets of Deadly 1918 Pandemic

<http://www.sciencemag.org/cgi/content/summary/310/5745/28>

Pandemic Influenza: Global Update

<http://www.sciencemag.org/cgi/content/summary/309/5733/370>

Full Restoration of Viral Fitness by Multiple Compensatory Co-Mutations in the Nucleoprotein of Influenza A Virus Cytotoxic T-Lymphocyte Escape Mutants

<http://vir.sgmjournals.org/cgi/content/abstract/86/6/1801>

Genetic Analyses Suggest Bird Flu Virus Is Evolving

<http://www.sciencemag.org/cgi/content/summary/308/5726/1234a>

Pandemic Influenza: Global Update

<http://www.sciencemag.org/cgi/reprint/309/5733/370.pdf>

Recapitulating the *Workshops of 2005*

Annual Workshop



Left to right: Scott Way, Alex Sette, and Arturo Casadevall

The Second Annual Immune Epitope Database and Discovery Workshop was held on November 2 and 3, 2005 in Bethesda, Maryland. The meeting provided an opportunity for the contractors to present their project status and plans and to discuss common interests.

The IEDB presentation, which included a review of project timelines, community outreach activities, and future plans was followed by thirteen 30-minute presentations by the Large-Scale Antibody and T Cell Epitope Discovery contractor teams. Two discussion sessions were also held during the workshop on the topics of assay standardization among the Discovery groups and data submission from the Discovery groups to the IEDB. The Third Annual Immune Epitope Database and Discovery Workshop will be held in Bethesda, MD, on November 7 and 8, 2006.

Analysis Tools Workshop

An IEDB Analysis Tool Workshop was held in Bethesda, MD, on November 4, 2005. The purpose of the meeting was to engage tool developers and users to provide critical feedback regarding the utility of the T cell and antibody epitope prediction and analysis tools being developed for the IEDB Analysis Resource. After welcoming comments from Dr. Alison Deckhut Augustine, NIAID program officer, the IEDB staff provided an introduction of the IEDB and Analysis Resource, followed by presentations describing the prediction tools, the population coverage and epitope conservancy analysis tools, and the homology mapping and epitope visualization tools. The fifty participants then had an opportunity to exercise the analysis tools using test data provided by the project, as well as their own data sets. Many valuable comments and suggestions were received and are currently being evaluated for improving the resources. A number of the recommendations have already been implemented and will be available in the public release of the IEDB in February, 2006.

1st International Biocurator Meeting

Pacific Grove, CA: Dec. 8-11, 2005

The goal of this meeting was to create a forum for curators and developers of biological databases to discuss their work, promote collaborations, and foster a sense of community in this very active



Left to right: Nima Salimi and Randi Vita are curators who attended the meeting.

and growing area of research. The Immune Epitope Database and Analysis Resource (IEDB) curators Randi Vita and Nima Salimi represented the IEDB at the meeting, where they presented a poster entitled, "The Design and Implementation of the Immune Epitope Database and Analysis Resource (IEDB)." In addition to serving as an opportunity for outreach, the meeting afforded IEDB curators the opportunity to learn from the experiences of other biological databases. Issues that arose from the meeting that apply to the IEDB are the potential for use of text mining programs, discussion regarding the curation process, the relationship that curators have with database programmers, collaboration opportunities between databases, and the need for outreach to the scientific community.

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ized query searches and data output via the reporting module. The newsletter will contain current IEDB related news, community news, system updates, significant database additions, and other important information.

To promote the database, the IEDB team plans to represent the IEDB resource at selected scientific meetings and workshops, invite authors of curated papers to visit the official website to promote interest, publish available information, and hold press releases when opportunities arise. Awareness of the database will expose it to a larger number of potential users.

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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