

Immune Epitope Database

NEWSLETTER

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Swine Flu Analysis

In response to concerns of a swine flu epidemic, the IEDB Curation team updated the database's collection of influenza references and conducted an analysis of epitopes found in the newly emerging influenza A (H1N1) virus. In order to make the analysis available on a timely basis, the report was posted on the IEDB website's Solutions Center as a separate forum topic. A data set of epitopes in swine flu with potential for pre-existing immunity was also posted on the forum. All this information can be found at <http://iedb.zendesk.com/forums/45499/entries>, and the abstract of the analysis report is presented below. An additional study was conducted by Richard Scheuermann and his colleagues at the BioHealthBase database. Their analysis of H1N1 antibody epitopes can be found at <http://www.biohealthbase.org/GSearch/homeExtraPage.do?decorator=influenza&extraPage=seperate>.

What Epitopes Does the Human Immune System Recognize in Swine Flu?

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Abstract

A primary concern about the H1N1 swine flu outbreak is that the genetic sequence of this virus is so different from seasonal influenza that little immune protection is present in the human population. To analyze how different the H1N1 swine flu virus is to the

immune system, we examined the parts of the virus which are recognized by antibodies or T cells and are called epitopes. Memory immune protection is based on the presence of antibodies and T cells already primed to recognize epitopes in the virus due to past infections or previous vaccination. Indeed, while a virus can change substantially in some sequences/regions, it can still be recognized by the immune system if its epitopes are conserved. Herein we report on analysis of influenza epitopes cataloged in the Immune Epitope Database (<http://www.iedb.org>), in the context of recent H1N1 swine flu outbreak. Only 35% (11/31) of antibody epitopes for which immune memory is expected to be present in the general human population are conserved in the H1N1 swine flu, while 67% (52/78) of the epitopes recognized by cytotoxic CD8+ T cells are completely invariant. The difference is due to the concentration of antibody epitopes in the more variable surface HA and NA proteins, while T cell epitopes are concentrated in the

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more conserved internal proteins. It is therefore likely that some degree of immunity against swine flu is already present in a significant fraction of the adult population and that such memory predominantly recognizes T cell epitopes. Since protection from infection is antibody-mediated, a vaccine based on the specific H1N1 swine HA and NA proteins would be required. However, since T cells are known to blunt disease severity, the conservation of a large fraction of T cell epitopes suggest that the severity of the infection, at least as it relates to susceptibility to immune attack, would not differ from common seasonal flu. These results are consistent with recent reports relating to disease severity and mortality rates associated with the H1N1 swine influenza outbreak in humans.

IEDB 2.1 and Beyond

On June 8, a new version of the IEDB was released to the public at <http://www.iedb.org>. The release corrected several defects and introduced a number of new features. Some of the major new features include displaying SMILES images for non-peptidic epitopes, adding the epitope ID to the advanced search, and updating the sorting of the MHC binding quantitative measure. The News section on the home page now pulls content from the six most recently posted articles in the General Announcements forum of the Support Center. In addition, users can link to the IEDB ontology under the “More IEDB” menu.

IEDB 2.2 has a planned release date in the fall of 2009. Some of the highlighted features it will contain are a SQL database export, browse by 3D structure, and “fuzzy” record searching/clustering by epitope sequence and source organism. Users will also be able to easily go to a record using its ID and export all values of a query result into a spreadsheet via a CSV format file. Subsequent releases of the IEDB will have revised finders that improve usability, new source antigen details page, browse by source antigen, the ability to create custom search result formats, and a new custom data export feature.

Curation Update

Curation of data relating to peptidic epitopes for all infectious diseases and allergens is current for references appearing in PubMed as of the end of March 2009. Articles published in the second quarter of 2009 are currently being curated. These reference categories will continue to be updated quarterly. Curation of autoimmune diseases, with an emphasis on diabetes, has started. 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 iedb_help@liai.org.

Recent Publications

NetMHCpan, a method for MHC class I binding prediction beyond humans.

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Binding of peptides to major histocompatibility complex (MHC) molecules is the single most selective step in the recognition of pathogens by the cellular immune system. The human MHC genomic region (called HLA) is extremely polymorphic comprising several thousand alleles, each encoding a distinct MHC molecule. The potentially unique specificity of the majority of HLA alleles that have been identified to date remains uncharacterized. Likewise, only a limited number of chimpanzee and rhesus macaque MHC class I molecules have been characterized experimentally. Here, we present NetMHCpan-2.0, a method that generates quantitative predictions of the affinity of any peptide-MHC class I interaction. NetMHCpan-2.0 has been trained on the hitherto largest set of quantitative MHC binding data available, covering HLA-A and HLA-B, as well as chimpanzee, rhesus macaque, gorilla, and mouse MHC class I molecules. We show that the NetMHCpan-2.0 method can accurately predict binding to uncharacterized HLA molecules, including HLA-C and HLA-G. Moreover, NetMHCpan-2.0 is demonstrated to accurately predict peptide binding to chimpanzee and macaque MHC class I molecules. The power of NetMHCpan-2.0 to guide immunologists in interpreting cellular immune responses in large out-bred populations is demonstrated. Further, we used NetMHCpan-2.0 to predict potential binding peptides for the pig MHC class I molecule SLA-1*0401. Ninety-three percent of the predicted peptides were demonstrated to bind stronger than 500 nM. The high performance of NetMHCpan-2.0 for non-human primates documents the method's ability to provide broad allelic coverage also beyond human MHC molecules. The method is available at <http://www.cbs.dtu.dk/services/NetMHCpan>.

The New IEDB Solutions Center

The IEDB Solutions Center is the primary resource for information on using the website's features. It can be accessed from the "Support" pull-down menu and from the Support section in the middle-right-hand section of the home page. The user can submit help requests, check on the status of requests, browse and search the knowledge base and forums, and link to help documentation, such as the Curation Manual. In order to submit and subsequently track a help request via the Solutions Center, users must follow a simple registration procedure in order to provide an email address, name, and password.

The Solutions Center is powered by Zendesk (www.zendesk.com), a web-based help desk system in a hosted environment. A major advantage of this new system is the flexibility and timeliness it provides the IEDB team to post articles and documents of interest and generate new forum topics. For example, newsletters can now be made available through the Solution Center without the need of an update release of the IEDB website. As content is added to the IEDB Solutions Center, the search knowledge base grows and its utility for users to find helpful information increases. There are currently forums for general announcements, queries and reporting, analysis tools, the H1N1 swine flu virus analysis, and tool and database developers who wish to link to the IEDB.

IEDB 2.0 Press Release Has Wide Distribution

On May 5, LIAI released a press announcement about the new IEDB 2.0 entitled “La Jolla Institute Announces 2.0 Launch of Major Database to Aid Vaccine Development Worldwide - Database to assist researchers around the globe in combating infectious disease”. It was carried on numerous websites, including EurekaAlert (www.eurekaalert.org), Medical News Today (www.medicalnewstoday.com), Canada’s National Collaborating Centre for Infectious Diseases (www.nccid.ca), NewsRx (www.newsrx.com), Life Science Blog (www.lsblog.org), West African Doctors Network (www.wadn.org), and First Science (www.firstscience.com). The text of the announcement follows:

Key improvements in a major infectious disease database that will aid vaccine development worldwide were unveiled today with the 2.0 launch of the National Institutes of Health-sponsored Immune Epitope Database and Analysis Resource (IEDB). The 2.0 launch was announced by a research team from the La Jolla Institute for Allergy & Immunology, who designed, developed and continue to host the database under a multi-million dollar NIH contract.

The IEDB is the world’s largest collection of scientific data on how the immune system responds to infectious diseases. It is freely available online to researchers worldwide at: www.iedb.org.

“With this new version, we have curated hundreds of thousands of experimental data points and created a simplified search process that will significantly assist researchers around the globe in their efforts to develop new and better vaccines,” said Alessandro Sette, Ph.D., the IEDB’s lead scientist and director of the La Jolla Institute’s Center for Infectious Disease.

While the 2.0 launch was not timed to coincide with the swine flu outbreak, it nonetheless points up the importance of such public health tools, said Bjoern Peters, Ph.D., the database’s co-principal investigator for bioinformatics. “The IEDB provides data on more than 50,000 epitopes, which are the sites on a virus that the immune system targets for attack. This information is key for researchers in developing new treatments, vaccines and diagnostics,” said Dr. Peters. “Researchers will undoubtedly tap into the database in working to combat swine flu as well as other emerging or re-emerging infectious diseases such as tuberculosis, West Nile virus and dengue fever.” Dr. Peters will present a workshop on the IEDB on Saturday during the American Association of Immunologists Annual Meeting in Seattle.

The IEDB was originally launched in 2006 in the midst of bioterrorism concerns and was financed via the federal biodefense research program. “The idea was to create a central, searchable information resource that would allow researchers worldwide to quickly share and analyze data in an unprecedented manner,” said Stephen Wilson, Ph.D., the IEDB’s project director. “In doing so, it would accelerate the development of new and better vaccines. Researchers would not have to reinvent the wheel when conducting experiments. Instead, they could go to the IEDB and view and analyze all immune epitope data previously published, which relates to their work.”

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The La Jolla Institute received the contract for developing the database in 2004 under a competitive bid process via the National Institutes of Allergy & Infectious Diseases, part of the National Institutes of Health. Creating the database meant culling information from thousands of separate research articles published over several decades. It also meant designing a first-ever format. “We were creating a repository and method of data sharing that had never existed before,” Dr. Wilson said. In its first iteration, released in 2006, Institute developers took a more bioinformatics approach, presenting the data in a heavily analytical format. With the 2.0 launch, the Institute now had the benefit of user feedback, Dr. Wilson said, and could make the database easier to search, focusing more specifically on key terms and concepts used by biologists to mine data.

One critical element of this, said Dr. Sette, was ensuring that the database used shared terms, labeling and presentation formats common across various scientific databases now in use by researchers around the globe. “The modern researcher needs to be able to access all this information and to be able to jump from the genome database to the chemical structure database to the immune epitope database quickly with the assurance that the data are presented using similar formats for easy understandability,” he said.

To accomplish this goal, Dr. Peters said the Institute sought input from bioengineering computer experts and scientific leaders in the field. “This version taps into how the user really thinks and how they universally access data,” he said. “In addition, we’ve provided more computational tools that enable researchers to quickly analyze their data.”

Along with increased usability, the database’s information resources have grown vastly over the last several years. “The 2.0 version catalogues over 95% of the published information currently available on the immune epitope response to infectious diseases, and is continuously updated,” Dr. Peters said.

In addition, Institute researchers are currently adding data on epitope responses to allergies and autoimmune diseases that will benefit researchers in those areas.

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.

Email: contact@iedb.org
Web: <http://www.iedb.org>

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