*24 February 2009*

*This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.*

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# Chem-Bio News - Pandemic Influenza Edition #49

**1. SCIENTISTS IDENTIFY HUMAN MONOCLONAL ANTIBODIES EFFECTIVE AGAINST BIRD AND SEASONAL FLU VIRUSES:** *"Researchers at the Dana-Farber Cancer Institute, Burnham Institute for Medical Research and the Centers for Disease Control and Prevention have reported the identification of human monoclonal antibodies (mAb) that neutralize an unprecedented range of influenza A viruses, including avian influenza A (H5N1) virus, previous pandemic influenza viruses, and some seasonal influenza viruses."*

**2. NOVARTIS FINDS FASTER WAY TO TEST BIRD FLU VACCINE:** *"Scientists at Swiss drugmaker Novartis have found a faster way to test H5N1 bird flu vaccines in people, in a move that should speed preparations for mass immunisation in the event of a global pandemic."*

**3. MENTAL HEALTH SERVICES AND THEIR ROLE IN PANDEMIC PLANNING, RESPONSE AND RECOVERY WEBCAST:** *"Archive of February 18, 2009 Webcast on mental health services and their role in pandemic planning, response and recovery."*

**4. DRAFT GUIDANCE FOR INDUSTRY AND FDA STAFF: ESTABLISHING THE PERFORMANCE CHARACTERISTICS OF IN VITRO DIAGNOSTIC DEVICES FOR THE DETECTION OR DETECTION AND DIFFERENTIATION OF INFLUENZA VIRUSES:** "*Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the Federal Register of the notice announcing the availability of the draft guidance."*

**5. RECOMBINANT MODIFIED VACCINIA VIRUS ANKARA EXPRESSING THE HEMAGGLUTININ GENE CONFERS PROTECTION AGAINST HOMOLOGOUS AND HETEROLOGOUS H5N1 INFLUENZA VIRUS INFECTIONS IN MACAQUES:** *"Therefore, MVA-HA-VN/04 is a promising vaccine candidate for the induction of protective immunity against highly pathogenic H5N1 avian influenza viruses in humans."*

**6. INFLUENZA SEQUENCE AND EPITOPE DATABASE:** *"ISED provides users with prebuilt application tools to analyze sequence alignment and different patterns and allows users to visualize epitope-matching structures, which is freely accessible at http://influenza.korea.ac.kr and http://influenza.cdc.go.kr."*

**7. STRUCTURE OF NS1A EFFECTOR DOMAIN FROM THE INFLUENZA A/UDORN/72 VIRUS:** *"A hypothetical model of the intact NS1 dimer is presented."*

# CB Daily Report

## *Chem-Bio News*

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**SCIENTISTS IDENTIFY HUMAN MONOCLONAL ANTIBODIES EFFECTIVE AGAINST BIRD AND SEASONAL FLU VIRUSES**
Physorg.com
February 22, 2009

“Researchers at the Dana-Farber Cancer Institute, Burnham Institute for Medical Research and the Centers for Disease Control and Prevention have reported the identification of human monoclonal antibodies (mAb) that neutralize an unprecedented range of influenza A viruses, including avian influenza A (H5N1) virus, previous pandemic influenza viruses, and some seasonal influenza viruses.

These antibodies have the potential for use in combination with other treatments to prevent or treat certain types of avian and seasonal flu. The study was published online on February 22 in Nature Structural and Molecular Biology.

The antibodies identified by the team of scientists neutralize a broad range of influenza A subtypes because they bind to the highly conserved stem region of H5 type hemaglutinin (HA). Binding to the stem prevents a conformational change in the protein that is necessary for viral entry into the host cell, thereby preventing further infection of host cells and the rise of escape mutants.

"The head portion of hemaglutinin is highly mutable, leading to the rise of forms of the virus that can evade neutralizing antibodies," said Robert Liddington, Ph.D., professor and director, Infectious and Inflammatory Disease Center at Burnham and one of the investigators on the study. "However, the stem region of hemaglutinin is highly conserved because it undergoes a dramatic conformational change to allow entry of viral RNA into the host cell. It's very difficult to get a mutation that doesn't destroy that function, which explains why we aren't seeing escape mutants and why these antibodies neutralize such a variety of strains of influenza."

While more costly to produce than existing influenza drugs, therapeutic antibodies can be readily manufactured and stockpiled. In the event of a pandemic, the antibodies could be used in combination with antiviral therapies to contain the outbreak until a vaccine became available. The production of a new influenza vaccine takes six to nine months using conventional methods.”

The full article can be found at: http://www.physorg.com/news154540721.html

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**NOVARTIS FINDS FASTER WAY TO TEST BIRD FLU VACCINE**
By Ben Hirschler
Reuters
February 23, 2009

“Scientists at Swiss drugmaker Novartis have found a faster way to test H5N1 bird flu vaccines in people, in a move that should speed preparations for mass immunisation in the event of a global pandemic.”

“Current clinical testing methods frequently take a year or more to measure a person's immune response. By contrast, the new technique should be able to predict after a single dose whether a vaccine offers protection.

Rino Rappuoli and colleagues, writing in the Proceedings of the National Academy of Sciences on Monday, said their work could lead to a quicker way of identifying and producing the correct vaccine for use at the start of any pandemic.”

The full article can be found at: http://www.reuters.com/article/rbssHealthcareNews/idUSLN61788120090223?rpc=401&

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**MENTAL HEALTH SERVICES AND THEIR ROLE IN PANDEMIC PLANNING, RESPONSE AND RECOVERY WEBCAST**
PandemicFlu.gov
February 18, 2009

“Overview: Archive of February 18, 2009 Webcast on mental health services and their role in pandemic planning, response and recovery.

Duration: 60 minutes (Captioned Video)
You will need Flash (http://www.adobe.com) installed on your computer in order to view the video.”

The full article can be found at: http://pandemicflu.gov/news/panflu_webinar10.html

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**DRAFT GUIDANCE FOR INDUSTRY AND FDA STAFF: ESTABLISHING THE PERFORMANCE CHARACTERISTICS OF IN VITRO DIAGNOSTIC DEVICES FOR THE DETECTION OR DETECTION AND DIFFERENTIATION OF INFLUENZA VIRUSES**

US Food and Drug Administration
February 15, 2009

“FDA is issuing this draft guidance to provide industry and agency staff with recommendations forstudies to establish the analytical and clinical performance of in vitro diagnostic devices (IVDs) intended for the detection, or detection and differentiation, of influenza viruses. These devices are used to aid in the diagnosis of influenza infection. They include devices that detect one specific type or subtype, as well as devices that detect more than one type or subtype of influenza virus and further differentiate among them, to indicate whether the specimen contains influenza A virus versus influenza B virus, or which subtype of influenza A is present.1

This guidance provides detailed information on the types of studies FDA recommends to support Class I and Class II premarket submissions for these devices. The guidance includes a list of influenza virus strains recommended for analytical sensitivity studies, a list of microorganisms recommended for analytical specificity studies, and an example of a suggested format for presenting data from cross-reactivity studies.

This document is limited to studies intended to establish the performance characteristics of devices that detect either influenza viral antigens or influenza viral genome (protein or nucleic acid). It includes rapid detection devices and nucleic acid-based devices. It does not address detection of serological response from the host to the viral antigen, nor does it address establishing performance of non-influenza components of multi-analyte or multiplex devices.

FDA’s guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidance documents means that something is suggested or recommended, but not required.”

The full document can be found at: http://www.fda.gov/cdrh/oivd/guidance/1638.html

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**RECOMBINANT MODIFIED VACCINIA VIRUS ANKARA EXPRESSING THE HEMAGGLUTININ GENE CONFERS PROTECTION AGAINST HOMOLOGOUS AND HETEROLOGOUS H5N1 INFLUENZA VIRUS INFECTIONS IN MACAQUES**
Preventive Medicine Week
March 1, 2009

“In light of the pandemic threat caused by these events, the rapid availability of safe and effective vaccines is desirable. Modified vaccinia virus Ankara (MVA) expressing the hemagglutinin (HA) gene of H5N1 viruses is a promising candidate vaccine that induced protective immunity against infection with homologous and heterologous H5N1 influenza virus in mice. In the present study, we evaluated a recombinant MVA vector expressing the HA gene of H5N1 influenza virus A/Vietnam/1194/04 (MVA-HA-VN/04) in nonhuman

primates. Cynomolgus macaques were immunized twice and then were challenged with influenza virus A/Vietnam/1194/04 (clade 1) or A/Indonesia/5/05 (clade 2.1) to assess the level of protective immunity. Immunization with MVA-HA-VN/04 induced (cross-reactive) antibodies and prevented virus replication in the upper and lower respiratory tract and the development of severe necrotizing bronchointerstitial pneumonia."

"Therefore, MVA-HA-VN/04 is a promising vaccine candidate for the induction of protective immunity against highly pathogenic H5N1 avian influenza viruses in humans."

The full article can be found at: (J.H.C.M. Kreijtz, et. al. "Recombinant Modified Vaccinia Virus Ankara Expressing the Hemagglutinin Gene Confers Protection against Homologous and Heterologous H5N1 Influenza Virus Infections in Macaques". Journal of Infectious Diseases, 2009;199(3):405-413). Link not available.

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**INFLUENZA SEQUENCE AND EPITOPE DATABASE**
Health Risk Factor Week
February 24, 2009

"Knowledge about the genomes of the seasonal influenza viruses from different countries in Asia is valuable for monitoring and understanding of the emergence, migration and evolution of strains. In order to make full use of the wealth of information from such data, we have developed an integrated user friendly relational database, Influenza Sequence and Epitope Database (ISED), that catalogs the influenza sequence and epitope information obtained in Asia. ISED currently hosts a total of 13 020 influenza A and 2984 influenza B virus sequence data collected in 17 countries including 9 Asian countries, and a total of approximately 545 amantadine-resistant influenza virus sequences collected in Korea."

"ISED provides users with prebuilt application tools to analyze sequence alignment and different patterns and allows users to visualize epitope-matching structures, which is freely accessible at http://influenza.korea.ac.kr and http://influenza.cdc.go.kr."

The full article can be found at: (S. Yang, et. al., "Influenza sequence and epitope database" Nucleic Acids Research, 2009;37(Sp. Iss.):D423-D430). Link not available.

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**STRUCTURE OF NS1A EFFECTOR DOMAIN FROM THE INFLUENZA A/UDORN/72 VIRUS**
Medical Imaging Week
February 28, 2009

"The nonstructural protein NS1A from influenza virus is a multifunctional virulence factor and a potent inhibitor of host immunity. It has two functional domains: an N-terminal 73-

amino-acid RNA-binding domain and a C-terminal effector domain," investigators in the United States report (see also Influenza).

"Here, the crystallographic structure of the NS1A effector domain of influenza A/Udorn/72 virus is presented. Structure comparison with the NS1 effector domain from mouse-adapted influenza A/Puerto Rico/8/34 (PR8) virus strain reveals a similar monomer conformation but a different dimer interface. Further analysis and evaluation shows that the dimer interface observed in the structure of the PR8 NS1 effector domain is likely to be a crystallographic packing effect."

"A hypothetical model of the intact NS1 dimer is presented."

The full article can be found at: (S.L. Xia, et. al., "Structure of NS1A effector domain from the influenza A/Udorn/72 virus" Acta Crystallographica Section D - Biological Crystallography, 2009;65(Part 1):11-17). Link not available.

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