3 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 #46

1. DETECTION OF HUMAN VIRULENCE SIGNATURES IN H5N1: *"This method can be used to screen samples for influenza and to determine if the detected virus contains mutations that may make the virus more infective or virulent to humans, potentially thwarting a pandemic outbreak."*

2. FACE MASK USE AND CONTROL OF RESPIRATORY VIRUS TRANSMISSION IN HOUSEHOLDS: *"We concluded that household use of face masks is associated with low adherence and is ineffective for controlling seasonal respiratory disease. However, during a severe pandemic when use of face masks might be greater, pandemic transmission in households could be reduced."*

3. CROSS-GLADE [SIC – CLADE?] PROTECTIVE IMMUNITY OF H5N1 INFLUENZA VACCINES IN A MOUSE MODEL: *"These results suggest that currently stockpiled pre-pandemic vaccines, especially clade 2.1-based vaccines, will likely be useful as backup vaccines in a pandemic situation, even one involving antigenic-drifted viruses."*

4. AB INITIO FRAGMENT MOLECULAR ORBITAL STUDIES OF INFLUENZA VIRUS HEMAGGLUTININ-SIALOSACCHARIDE COMPLEXES TOWARD CHEMICAL CLARIFICATION ABOUT THE VIRUS HOST RANGE DETERMINATION: *"Our theoretical approach may predict the infectious level of new viruses and point out some unknown dangerous mutation positions on HA in advance."*

5. CAPTURE OF CELL CULTURE-DERIVED INFLUENZA VIRUS BY LECTINS: STRAIN INDEPENDENT, BUT HOST CELL DEPENDENT: *"Hence, altered lectin specificities have been observed between the two cell lines, requiring process adaptations between different influenza vaccine production systems."*

CB Daily Report

Chem-Bio News

DETECTION OF HUMAN VIRULENCE SIGNATURES IN H5N1
Drug Week
January 30, 2009

A method for detecting the emergence of potential pandemic-causing influenza strains has been developed. The system first uses real-time RT-PCR to detect H5, the highly pathogenic avian influenza subtype most likely to cause a pandemic."

"Pyrosequencing is then employed to scan for codon changes encoding amino acids known to define human influenza versus avian influenza signatures. The pyrosequencing assays were developed to screen at the nucleotide level for 52 amino acid changes defined as avian- or human-specific. A library has been built to screen the sequence data generated and properly identify the strain in question as a potential threat."

"This method can be used to screen samples for influenza and to determine if the detected virus contains mutations that may make the virus more infective or virulent to humans, potentially thwarting a pandemic outbreak."

The full article can be found at: (N. Waybright, et. al., "Detection of human virulence signatures in H5N1". Journal of Virological Methods, 2008;154(1-2):200-5). Link not available.

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FACE MASK USE AND CONTROL OF RESPIRATORY VIRUS TRANSMISSION IN HOUSEHOLDS
By C. Raina MacIntyre, Simon Cauchemez, Dominic E. Dwyer, Holly Seale, Pamela Cheung, Gary Browne, Michael Fasher, James Wood, Zhanhai Gao, Robert Booy, and Neil Ferguson
Emerging Infectious Diseases
February 2, 2009

"Many countries are stockpiling face masks for use as a nonpharmaceutical intervention to control virus transmission during an influenza pandemic. We conducted a prospective cluster-randomized trial comparing surgical masks, non–fit-tested P2 masks, and no masks in prevention of influenza-like illness (ILI) in households. Mask use adherence was self-reported. During the 2006 and 2007 winter seasons, 286 exposed adults from 143 households who had been exposed to a child with clinical respiratory illness were recruited. We found that adherence to mask use significantly reduced the risk for ILI-associated infection, but <50% of participants wore masks most of the time. We concluded that household use of face masks is associated with low adherence and is ineffective for controlling seasonal respiratory disease. However, during a severe pandemic when use of face masks might be greater, pandemic transmission in households could be reduced."

The full article can be found at: http://www.cdc.gov/eid/content/15/2/233.htm

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CROSS-GLADE [SIC – CLADE?] PROTECTIVE IMMUNITY OF H5N1 INFLUENZA VACCINES IN A MOUSE MODEL
Pharma Investments, Ventures & Law Weekly
February 1, 2009

"Here, to evaluate fundamental immunogenic variations between H5N1 vaccines, we prepared four inactivated H5N1 test vaccines from different phylogenetic Glades (clade 1, 2.1, 2.2, and 2.3.4) in accordance with the WHO recommendation, and tested their cross-Glade immunity in a mouse model by vaccination followed by challenge with heterologous virulent viruses. All H5N1 vaccines tested provided full or partial cross-clade protective immunity, except one Glade 2.2-based vaccine, which did not protect mice from clade 2.3.4 virus challenge. Among the test vaccines, a clade 2.1-based vaccine possessed the broadest-spectrum cross-immunity."

"These results suggest that currently stockpiled pre-pandemic vaccines, especially clade 2.1-based vaccines, will likely be useful as backup vaccines in a pandemic situation, even one involving antigenic-drifted viruses."

The full article can be found at: (S. Murakami, et. al., "Cross-Glade protective immunity of H5N1 influenza vaccines in a mouse model". Vaccine, 2008;26(50):6398-6404). Link not available.

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AB INITIO FRAGMENT MOLECULAR ORBITAL STUDIES OF INFLUENZA VIRUS HEMAGGLUTININ-SIALOSACCHARIDE COMPLEXES TOWARD CHEMICAL CLARIFICATION ABOUT THE VIRUS HOST RANGE DETERMINATION
Biotech Law Weekly
January 30, 2009

"If we predict the host range of new or mutant influenza virus in advance, we are able to measure against pandemic human influenza immediately after the new virus emerges somewhere. Influenza viral hemagglutinin(HA)-sialoside receptor interaction is a target event for in silico chemical prediction studies about the virus host range determination."

"We theoretically studied avian and human influenza A virus HA H3 subtype complexed with avian or human type receptor Neu5Ac alpha(2-3 or 2-6)Gal analogues by ab initio fragment molecular orbital (FMO) method at the second order Muller-Plesset (MP2)/6-31G level, which can evaluate correctly not only electrostatic interactions but also lipophilic interactions based on van der Waals dispersion force. Avian H3 bound to avian alpha 2-3 11.4 kcal/mol stronger than to human alpha 2-6 in the model complexes with taking account of intermolecular lipophilic interaction. A substitution at the position 226 between Gln(avian) and Leu(human) on influenza H3 HA1 has altered its virus host range between avian and human. In the ab initio FMO studies, binding energy of avian Gln226Leu H3-human alpha 2-

6 was quite similar to that in the human H3-human alpha 2-6 complex with amino acid sequence differences at nine positions in the models. This similarity indicates that avian Gln226Leu H3 virus can infect human with the same level as human H3 virus. Opposite mutation Leu226Gln in the human H3 gave the moderate binding energies to avian alpha 2-3 with similarity to avian H3-alpha 2-3 complex that supported our previous virus-sialoside binding assay. Ab initio FMO studies have revealed the relationship between influenza H3 virus host range and H3-alpha(2-3 or 2-6) receptors binding."

"Our theoretical approach may predict the infectious level of new viruses and point out some unknown dangerous mutation positions on HA in advance."

The full article can be found at: (T. Sawada, et. al., "Ab initio fragment molecular orbital studies of influenza virus hemagglutinin-sialosaccharide complexes toward chemical clarification about the virus host range determination". Glycoconjugate Journal, 2008;25 (9):805-815). Link not available.

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CAPTURE OF CELL CULTURE-DERIVED INFLUENZA VIRUS BY LECTINS: STRAIN INDEPENDENT, BUT HOST CELL DEPENDENT
Medical Devices & Surgical Technology Week
February 1, 2009

"Therefore and due to frequent antigenic drifts, strain independent manufacturing processes are required for vaccine production. This study verifies the strain independency of a capture method based on Euonymus europaeus lectin-affinity chromatography (EEL-AC) for downstream processing of influenza viruses under various culture conditions propagated in MDCK cells. A comprehensive lectin binding screening was conducted for two influenza virus types from the season 2007/2008 (A/Wisconsin/67/2005, B/Malaysia/2506/2004) including a comparison of virus-lectin interaction by surface plasmon resonance technology. EEL-AC resulted in a reproducible high product recovery rate and a high degree of contaminant removal in the case of both MDCK cell-derived influenza virus types demonstrating clearly the general applicability of EEL-AC. In addition, host cell dependency of EEL-AC was studied with two industrial relevant cell lines: Vero and MDCK cells. However, the choice of the host cell lines is known to lead to different product glycosylation profiles."

"Hence, altered lectin specificities have been observed between the two cell lines, requiring process adaptations between different influenza vaccine production systems."

The full article can be found at: (L. Opitz, et. al., "Capture of cell culture-derived influenza virus by lectins: strain independent, but host cell dependent". Journal of Virological Methods, 2008;154(1-2):61-8). Link not available.

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