*20 January 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 #44*

**1. NEUTRALIZING HUMAN MONOCLONAL ANTIBODY AGAINST H5N1 INFLUENZA HA SELECTED FROM A FAB-PHAGE DISPLAY LIBRARY:** *"The inhibitory effects of these five antibodies were similar to those observed with a previously described neutralizing antibody specific for the 140s antigenic loop present within HA1 and highlight the exciting possibility that these antibodies may be efficacious against multiple H5N1 strains."*

**2. ELICITATION OF PROTECTIVE IMMUNE RESPONSES USING A BIVALENT H5N1 VLP VACCINE:** *"These results demonstrate that a multivalent influenza VLP vaccine representing different genetic clades is a promising strategy to elicit protective immunity against isolates from emerging clades and subclades of H5N1."*

**3. EXPERTS CONSIDER 4-STRAIN FLU VACCINE TO FIGHT B VIRUSES:** *"But the idea raises questions about the effects on vaccine manufacture and supply, cost, and side effects. Some vaccine producers are studying the possibility, but they will need a formal government recommendation before they would proceed."*

**4. FEDS OUTLINE STATE PANDEMIC PLANNING GAINS AND GAPS:** *"The report found that many scored well in areas such as protecting citizens and administering mass vaccinations, but showed major gaps in such areas as sustaining state operations, developing community mitigation plans, and maintaining key infrastructure."*

**5. RISING H9N2 INFLUENZA REPLIKIN COUNT HAS DOUBLED THAT OF H5N1:** *"H9N2 Count increases occurred in 1996, one year in advance of the 1997 H5N1 Hong Kong outbreak, and again in 1999-2000 and 2004-05, 2 years before the subsequent H5N1 Replikin Count increases and outbreaks."*

**6. SEASONAL INFLUENZA ACTIVITY INCREASING ACROSS EUROPE - H3N2 DOMINANT STRAIN:** *"Latest surveillance data coming through the European Centre for Disease Prevention and Control (ECDC) from virologists and clinicians indicates that the influenza A(H3N2) virus is the predominant strain in Europe so far this season."*

# CB Daily Report

## *Chem-Bio News*

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**INFLUENZA HA SELECTED FROM A FAB-PHAGE DISPLAY LIBRARY**
Drug Week
January 23, 2009

"Identification of neutralizing antibodies with specificity away from the traditional mutation prone antigenic regions, against the conserved regions of hemagglutinin from H5N1 influenza virus has the potential to provide a therapeutic option which can be developed ahead of time in preparation for a possible pandemic due to H5N1 viruses. In this study, we used a combination of panning strategies against the hemagglutinin (HA) of several antigenic distinct H5N1 isolates to bias selection of Fab-phage from a naive human library away from the antigenic regions of HA, toward the more conserved portions of the protein."

"All of the identified Fab clones which showed binding to multiple antigenically distinct HA were converted to fully human IgG, and tested for their ability to neutralize the uptake of H5N1-virus like particles (VLP) into MDCK cells. Five of the antibodies which showed binding to the relatively conserved HA2 subunit of HA, exhibited neutralization of H5N1-VLP uptake in a dose dependant manner."

"The inhibitory effects of these five antibodies were similar to those observed with a previously described neutralizing antibody specific for the 140s antigenic loop present within HA1 and highlight the exciting possibility that these antibodies may be efficacious against multiple H5N1 strains."

The full article can be found at: (A.P.C. Lim, et. al., "Neutralizing human monoclonal antibody against H5N1 influenza HA selected from a Fab-phage display library". Virology Journal, 2008;5():130). Link not available.
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**ELICITATION OF PROTECTIVE IMMUNE RESPONSES USING A BIVALENT H5N1 VLP VACCINE**
Biotech Week
January 21, 2009

"Currently licensed human vaccines are subtype-specific and do not protect against pandemic H5N1 viruses. Previously, our group has reported on the construction of an influenza virus-like particle (VLP) as a new generation candidate vaccine."

"A mixture of influenza H5N1 VLPs representing clade 1 and 2 viruses were examined for the ability to elicit protective immunity against isolates from various clades and subclades of H5N1. Mice were vaccinated intramuscularly with each VLP individually, the mixture of VLPs, a mixture of purified recombinant hemagglutinin (rHA), or mock vaccinated. Elicited antibodies were assayed for the hemagglutination-inhibition (HAI) activity against clades 1 and clade 2 isolates. Mice vaccinated with each VLP individually or in a mixture had robust HAI responses against homologous viruses and HAI responses against the clade 2.3 virus, Anh/05. However, these vaccines did not induce an HAI response against the clade 2.2 virus, WS/05. Interestingly, clade 2 VLP vaccinated mice were protected against both clade 1 and 2 H5/PR8 viruses, but clade 1 VLP vaccinated mice were only protected against the clade 1 virus. Mice vaccinated with a mixture of VLPs were protected against both clade 1 and 2 viruses. In contrast, mice vaccinated with a mixture of rHA survived challenge, but lost similar to 15% of original weight by days 5-7 post-challenge."

"These results demonstrate that a multivalent influenza VLP vaccine representing different genetic clades is a promising strategy to elicit protective immunity against isolates from emerging clades and subclades of H5N1."

The full article can be found at: (C.J. Crevar, et. al., "Elicitation of protective immune responses using a bivalent H5N1 VLP vaccine". Virology Journal, 2008;5():131). Link not available.
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**EXPERTS CONSIDER 4-STRAIN FLU VACCINE TO FIGHT B VIRUSES**
By Robert Roos
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
January 16, 2009

"Picking the influenza strains to put in the flu vaccine each year is always a gamble, given the unpredictable prevalence of different strains, but choosing the influenza B strain has become particularly vexing in recent years.

Since the 2001-02 flu season, two distinct lineages of influenza B—Victoria and Yamagata—have been circulating in the United States, and experts have found it impossible to predict which one would dominate in any winter. "

“Putting both B families into the vaccine would offer protection against both B strains, which is regarded as particularly important for children. But the idea raises questions about the effects on vaccine manufacture and supply, cost, and side effects. Some vaccine producers are studying the possibility, but they will need a formal government recommendation before they would proceed.”

“Offering a quadrivalent vaccine to everyone is not the only way to provide some protection against both B lineages. Several other options have been proposed, including alternating lineages from year to year, making a quadrivalent vaccine intended only for children and the elderly, and offering a supplemental B vaccine to cover the strain not in the trivalent vaccine. Couch described these in his VRBPAC presentation in 2007.

The idea of alternating lineages would be that people who get vaccinated each year might have some residual cross-protection in case the dominant strain in a given year is not in the vaccine, said Fiore. "But there's really no way to predict what the impact of that would be," he said. “

The full article can be found at:
http://www.cidrap.umn.edu/cidrap/content/influenza/general/news/jan1609flub.html
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**FEDS OUTLINE STATE PANDEMIC PLANNING GAINS AND GAPS**
By Lisa Schnirring
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
January 16, 2009

“The US Department of Health and Human Services (HHS) yesterday released an assessment of progress states have made toward planning for an influenza pandemic. The report found that many scored well in areas such as protecting citizens and administering mass vaccinations, but showed major gaps in such areas as sustaining state operations, developing community mitigation plans, and maintaining key infrastructure.”

“Evaluators found that 54 states and territories were inadequately prepared to sustain state agencies and support and protect workers and that the other 2 had many major gaps. They wrote that states that had a statewide plan or one agency that directed the planning had a better understanding of what was needed to keep state government and its workforce operating during a pandemic.

They emphasized that traditional continuation-of-operations plans do not contain all of the elements needed to support government operations during a pandemic.

The states fared better on sustaining public health operations during a pandemic: 33 of 56 states or territories had no or few major gaps. Those that scored low in this area focused mainly on external health services and prophylaxis and didn't adequately address internal public health operational continuity and protection of its workforce. Low-scoring states also lacked personnel training and exercises. “

The full article can be found at: http://www.cidrap.umn.edu/cidrap/content/influenza/biz-plan/news/jan1609gaps.html

The HHS report can be found at: http://www.pandemicflu.gov/plan/states/state_assessment.html
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**RISING H9N2 INFLUENZA REPLIKIN COUNT HAS DOUBLED THAT OF H5N1**
Medical News Today
January 20, 2009

“H9N2 Count increases occurred in 1996, one year in advance of the 1997 H5N1 Hong Kong outbreak, and again in 1999-2000 and 2004-05, 2 years before the subsequent H5N1 Replikin Count increases and outbreaks. Cyclic increases and decreases appear to be synchronous for H9N2 and H5N1, with H9N2 increases occurring in advance of, and being greater than those for H5N1. These two strains appear to have a precursor and/or competitor, evolutionary biochemical relationship. H9N2 may be an alternate candidate to H5N1 for the next influenza pandemic.

The Replikin Count® is the number of specific replikin peptides per 100 amino acids in the peak gene of each strain. All sequences published on PubMed worldwide. each year from 1992 to 2008 were studied. Increases in the Replikin Count represent rapid virus replication, and occur in advance of outbreaks (see refs).”

The full article can be found at: http://www.medicalnewstoday.com/articles/136048.php
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**SEASONAL INFLUENZA ACTIVITY INCREASING ACROSS EUROPE - H3N2 DOMINANT STRAIN**
Medical News Today
January 20, 2009

“Latest surveillance data coming through the European Centre for Disease Prevention and Control (ECDC) from virologists and clinicians indicates that the influenza A(H3N2) virus is the predominant strain in Europe so far this season. Based on the data published by ECDC Roche confirms that the oral antiviral Tamiflu (oseltamivir) is fully active against influenza A(H3N2) and influenza B, which currently comprise 94 percent of circulating viruses in Europe this year.(1)

Tamiflu resistance reported in the 2008-2009 influenza seasons is confined to H1N1. No resistance has been seen with other circulating seasonal viruses - H3N2 and influenza B.”

The full article can be found at: http://www.medicalnewstoday.com/articles/135978.php
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**Steve Tesko:** Steve.Tesko@anser.org

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