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 #47

1. TAI O [CH] FINDS FUEL FEARS OF SECRET H5N1 OUTBREAK: *"The discovery of more dead chickens in Tai O, following recent findings of goose, duck and chicken carcasses on Lantau Island, has sparked concerns of a secret avian flu outbreak in the mainland, and that dead birds may have been carried by the tides."*

2. EXPERTS WEIGH NEW H5N1 VACCINE STRATEGIES: *"Keiji Fukuda, MD, MPH, coordinator of the World Health Organization's (WHO's) global influenza program, told reporters that experts don't really know what virus will spark the next global pandemic, but given the persistent and lethal nature of the H5N1 virus, the WHO has received pledges from pharmaceutical manufacturers to develop a 150 million dose international vaccine stockpile. He said the stockpile is intended to stop or slow a pandemic if the outbreak is detected early enough."*

3. LIVE ATTENUATED INFLUENZA VIRUSES CONTAINING NS1 TRUNCATIONS AS VACCINE CANDIDATES AGAINST H5N1 HIGHLY PATHOGENIC AVIAN INFLUENZA: *"The viruses were each found to be highly attenuated in a mouse model. Vaccination with a single dose of any virus conferred complete protection from death upon challenge with a mouse lethal virus expressing H5N1 hemagglutinin and neuraminidase proteins."*

4. PLANT-DERIVED HEMAGGLUTININ PROTECTS FERRETS AGAINST CHALLENGE INFECTION WITH THE A/INDONESIA/05/05 STRAIN OF AVIAN INFLUENZA: *"Immunization of mice and ferrets with plant-derived hemagglutinin elicited serum hemagglutinin-inhibiting antibodies and protected the ferrets against challenge infection with a homologous virus."*

5. BROAD CROSS-PROTECTION AGAINST H5N1 AVIAN INFLUENZA VIRUS INFECTION BY MEANS OF MONOCLONAL ANTIBODIES THAT MAP TO CONSERVED VIRAL EPITOPES: *"H5 MAbs such as 13D4 may prove to have therapeutic value in controlling infection due to current and future H5N1 variants."*

CB Daily Report

Chem-Bio News

TAI O [CH] FINDS FUEL FEARS OF SECRET H5N1 OUTBREAK
By Adele Wong
The Standard [HK]
February 6, 2009

"The discovery of more dead chickens in Tai O, following recent findings of goose, duck and chicken carcasses on Lantau Island, has sparked concerns of a secret avian flu outbreak in the mainland, and that dead birds may have been carried by the tides.

Two chickens were collected by the Agriculture, Fisheries and Conservation Department off the coast of Yeung Hau Temple in Tai O on Wednesday, and another was found yesterday.

The specimens collected early last week have been confirmed as H5N1 positive.

"This must clearly indicate some outbreak, I suspect not within Hong Kong," said Professor Malik Peiris of the Department of Microbiology at Hong Kong University.

"The carcasses are probably coming from the Pearl River Delta."

The full article can be found at: http://www.thestandard.com.hk/news_detail.asp?we_cat=4&art_id=77903&sid=22571533&con_type=1&d_str=20090206&fc=8

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EXPERTS WEIGH NEW H5N1 VACCINE STRATEGIES
By Lisa Schnirring
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
February 3, 2009

"Keiji Fukuda, MD, MPH, coordinator of the World Health Organization's (WHO's) global influenza program, told reporters that experts don't really know what virus will spark the next global pandemic, but given the persistent and lethal nature of the H5N1 virus, the WHO has received pledges from pharmaceutical manufacturers to develop a 150 million dose international vaccine stockpile. He said the stockpile is intended to stop or slow a pandemic if the outbreak is detected early enough.

The existence of individual-country H5N1 vaccine stockpiles and plans for a WHO global stockpile have raised complex questions about potential uses for the vaccine during the prepandemic period, Fukuda said.

Some countries are weighing what to do with the vaccines, especially since some doses are set to expire. Global health officials are considering other options, such as vaccinating people in high-risk countries such as China, Indonesia, or Vietnam or perhaps adding the antigen to seasonal flu vaccines as a priming strategy.

The United States, for example, has so far stockpiled about 26 million H5N1 vaccine doses, though some has already expired or is about to expire, according to a Sep 2008 report on US pandemic vaccine policy from the Congressional Budget Office (CBO). The HHS has launched studies to determine how long stockpiled vaccines remain safe and effective, but in the meanwhile it assumes a 2-year shelf life.

The United Kingdom has stockpiled 3 million doses of H5N1 vaccine. Several countries have announced stockpiling plans, including France, Ireland, Italy, and Austria, according to the CBO report. Other countries such as Japan are in the midst of clinical trials to produce their own H5N1 vaccines."

The full article can be found at: http://www.cidrap.umn.edu/cidrap/content/influenza/panflu/news/feb0309antigens-jw.html

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LIVE ATTENUATED INFLUENZA VIRUSES CONTAINING NS1 TRUNCATIONS AS VACCINE CANDIDATES AGAINST H5N1 HIGHLY PATHOGENIC AVIAN INFLUENZA
By John Steel, Anice C. Lowen, Lindomar Pena, Matthew Angel, Alicia Solórzano, Randy Albrecht, Daniel R. Perez, Adolfo García-Sastre, and Peter Pales
Journal of Virology
February 2009

"Using reverse genetics, a set of experimental live attenuated vaccine strains based on recombinant H5N1 influenza virus A/Viet Nam/1203/04 was generated. Each virus was attenuated through expression of a hemagglutinin protein in which the polybasic cleavage site had been removed. Viruses were generated which possessed a full-length NS1 or a C-terminally truncated NS1 protein of 73, 99, or 126 amino acids. Viruses with each NS genotype were combined with a PB2 polymerase gene which carried either a lysine or a glutamic acid at position 627. We predicted that glutamic acid at position 627 of PB2 would attenuate the virus in mammalian hosts, thus increasing the safety of the vaccine. All recombinant viruses grew to high titers in 10-day-old embryonated chicken eggs but were attenuated in mammalian cell culture. Induction of high levels of beta interferon by all viruses possessing truncations in the NS1 protein was demonstrated by interferon bioassay. The viruses were each found to be highly attenuated in a mouse model. Vaccination with a single dose of any virus conferred complete protection from death upon challenge with a mouse lethal virus expressing H5N1 hemagglutinin and neuraminidase proteins. In a chicken model, vaccination with a single dose of a selected virus encoding the NS1 1-99 protein completely protected chickens from lethal challenge with homologous HPAI virus A/Viet Nam/1203/04 (H5N1) and provided a high level of protection from a heterologous virus, A/egret/Egypt/01/06 (H5N1). Thus, recombinant influenza A/Viet Nam/1203/04 viruses attenuated through the introduction of mutations in the hemagglutinin, NS1, and PB2 coding regions display characteristics desirable for live attenuated vaccines and hold potential as vaccine candidates in poultry as well as in mammalian hosts."

The full article can be found at: http://jvi.asm.org/cgi/content/abstract/83/4/1742

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PLANT-DERIVED HEMAGGLUTININ PROTECTS FERRETS AGAINST CHALLENGE INFECTION WITH THE A/INDONESIA/05/05 STRAIN OF AVIAN INFLUENZA

By Yoko Shojia, Hong Bia, Konstantin Musiychuka, Amy Rheea, April Horseya, Gourgopal Roya, Brian Greena, Moneim Shamloula, Christine E. Farrancea, Barbara Taggartb, Nutan Mytleb, Natalia Ugulavaa, Shailaja Rabindrana, Vadim Metta, Jessica A. Chichestera and Vidadi Yusibov
Vaccine
February 11, 2009

"The global spread of highly pathogenic avian influenza virus (H5N1 subtype) has promoted efforts to develop human vaccines against potential pandemic outbreaks. However, current platforms for influenza vaccine production are cumbersome, limited in scalability and often require the handling of live infectious virus. We describe the production of hemagglutinin from the A/Indonesia/05/05 strain of H5N1 influenza virus by transient expression in plants, and demonstrate the immunogenicity and protective efficacy of the vaccine candidate in animal models. Immunization of mice and ferrets with plant-derived hemagglutinin elicited serum hemagglutinin-inhibiting antibodies and protected the ferrets against challenge infection with a homologous virus. This demonstrates that plant-derived H5 HA is immunogenic in mice and ferrets, and can induce protective immunity against infection with highly pathogenic avian influenza virus. Plants could therefore be suitable as a platform for the rapid, large-scale production of influenza vaccines in the face of a pandemic."

The full article can be found at: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4V7658R-1&_user=10&_coverDate=02%2F11%2F2009&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=842af86b87f7f301b02fd8749c0a116a

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BROAD CROSS-PROTECTION AGAINST H5N1 AVIAN INFLUENZA VIRUS INFECTION BY MEANS OF MONOCLONAL ANTIBODIES THAT MAP TO CONSERVED VIRAL EPITOPES

Immunotherapy Weekly
February 4, 2009

""Passive immunization with human H5 antisera or H5-specific monoclonal antibodies (MAbs) has potential as an effective treatment for acute H5N1 influenza virus infection, but its efficacy against antigenically diverse H5N1 viruses is unconfirmed. Cross-protection against antigenically diverse H5N1 strains with H5-specific MAbs, generated by successive immunization of antigenically distinct strains, was evaluated in mice."

"A panel of 52 broadly cross-reactive H5 specific MAbs were generated and characterized. One of these MAbs, 13D4, has been demonstrated to protect mice against lethal challenge by 4 H5N1 strains representing the current major genetic populations, clades 1, 2.1, 2.2, and 2.3, even at a stage of infection when H5N1 virus has disseminated beyond the pulmonary system. Complete neutralization of virus in lung tissue of infected animals was observed 24 h after treatment with 13D4. Mapping of this MAb with escape mutants showed it to bind to 2 conserved, possibly critical, sites of H5N1 hemagglutinin, 152 and 182. Generation of broadly cross-protective MAbs against H5N1 influenza virus may be optimized by selecting MAbs that target conserved sites in hemagglutinin."

"H5 MAbs such as 13D4 may prove to have therapeutic value in controlling infection due to current and future H5N1 variants."

The full article can be found at: (Y.X. Chen, et. al., "Broad Cross-Protection against H5N1 Avian Influenza Virus Infection by Means of Monoclonal Antibodies that Map to Conserved Viral Epitopes". Journal of Infectious Diseases, 2009;199(1):49-58). Link not available.

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