

21 July 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 #70**

- 1. FDA APPROVES VACCINE FOR 2009-2010 SEASONAL INFLUENZA:** *"The seasonal influenza vaccine will not protect against the 2009 H1N1 influenza virus that resulted in the declaration of a pandemic by the World Health Organization (WHO) on June 11, 2009."*
- 2. ISOLATION AND MOLECULAR CHARACTERIZATION OF EQUINE H3N8 INFLUENZA VIRUSES FROM PIGS IN CHINA:** *"This expansion of host range of equine H3N8 influenza viruses with mutations in the HA protein might raise the possibility of transmission of these viruses to humans."*
- 3. INFLUENZA A VIRUS LACKING M2 PROTEIN AS A LIVE ATTENUATED VACCINE:** *"Mice intranasally vaccinated with M2KO virus developed protective immune responses and survived a lethal challenge with the wild-type virus, suggesting that the M2KO virus has potential as a live attenuated vaccine."*
- 4. ACTIVATION OF TOLL-LIKE RECEPTOR SIGNALING PATHWAY FOR PROTECTION AGAINST INFLUENZA VIRUS INFECTION:** *"Taken together, these results do Support the potential role of TLR-3 and TLR-9 agonists such as Poly ICLC and LE Poly ICLC in protection against lethal seasonal and HPAI virus infection."*
- 5. GRANZYME A EXPRESSION REVEALS DISTINCT CYTOLYTIC CTL SUBSETS FOLLOWING INFLUENZA A VIRUS INFECTION:** *"Analysis of CTL grzA expression during influenza virus immunity has enabled a more detailed insight into the cytolytic mechanisms of virus elimination.."*
- 6. FIGHT FOR SWINE FLU VACCINE COULD GET UGLY:** *"Experts warn that during a global epidemic, which the world is in now, governments may be under tremendous pressure to protect their own citizens first before allowing companies to ship doses of vaccine out of the country."*
- 7. [UK] DOCTORS TO ISSUE 'FAST TRACK' DEATH CERTIFICATES FOR SWINE FLU:** *"Doctors are to be allowed to issue "fast-track" death certificates under Government plans to help the health system cope with the workload at the height of the swine flu pandemic."*
- 8. WHO SUSPENDS REPORTING OF H1N1 CASE COUNTS:** *"Citing the questionable usefulness of reporting pandemic H1N1 case counts and the burden it puts on countries experiencing widespread transmission, the World Health Organization (WHO) announced today it will no longer issue regular reports of confirmed global case totals."*
- 9. SCIENTISTS DISCOVER HOW FLU DAMAGES LUNG TISSUE:** *"A protein in influenza virus that helps it multiply also damages lung epithelial cells, causing fluid buildup in the lungs, according to new research from the University of Alabama at Birmingham (UAB) and Southern Research Institute."*
- 10. BAXTER HITS LIMIT ON SWINE FLU VACCINE ORDERS:** *"While at least 50 governments have placed orders or are negotiating with drug companies for supplies of flu vaccine against the fast spreading H1N1 strain, the lone U.S.-based maker has already taken on as much as it can handle."*
- 11. MUMBAI AIRPORT GETS TECHNOLOGY TO FIGHT SWINE FLU:** *"Airocide, technically, a photocatalytic conditioning system is capable of destroying microorganisms including anthrax and the swine flu virus."*
- 12. FAST RISE OF BROADLY CROSS-REACTIVE ANTIBODIES AFTER BOOSTING LONG-LIVED HUMAN MEMORY B CELLS PRIMED BY AN MF59 ADJUVANTED PREPANDEMIC VACCINE:** *"These results suggest that pre-pandemic vaccination strategies should be considered."*

**13. [UK] GUARDS TO PROTECT SWINE FLU DRUG DEPOTS:** "Security guards will be brought in to protect the swine flu medication when more than 100 new distribution centres are set up this week, amid fears it will be targeted by thieves."

## CB Daily Report

### Chem-Bio News

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#### **FDA APPROVES VACCINE FOR 2009-2010 SEASONAL INFLUENZA**

Infection Control Today Magazine  
July 20, 2009

"The U.S. Food and Drug Administration (FDA) today announced that it has approved a vaccine for 2009-2010 seasonal influenza in the United States. The seasonal influenza vaccine will not protect against the 2009 H1N1 influenza virus that resulted in the declaration of a pandemic by the World Health Organization (WHO) on June 11, 2009. The FDA continues to work with manufacturers, international partners and other government agencies to facilitate the availability of a safe and effective vaccine against the 2009 H1N1 influenza virus."

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"The vaccine for the 2009-2010 seasonal influenza contains:

an A/Brisbane/59/2007 (H1N1)-like virus

an A/Brisbane/10/2007 (H3N2)-like virus

a B/Brisbane/60/2008-like virus

The full article can be found at: <http://www.infectioncontrolday.com/hotnews/vaccine-for-seasonal-influenza-2009-2010.html>

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#### **ISOLATION AND MOLECULAR CHARACTERIZATION OF EQUINE H3N8 INFLUENZA VIRUSES FROM PIGS IN CHINA**

Biotech Law Weekly  
July 17, 2009

"During 2004-2006 swine influenza virus surveillance, two strains of H3N8 influenza viruses were isolated from pigs in central China. Sequence and phylogenetic analyses of eight gene segments revealed that the two swine isolates were of equine origin and most closely related to European equine H3N8 influenza viruses from the early 1990s."

"Comparison of hemagglutinin (HA) amino acid sequences showed several important substitutions. One substitution caused the loss of a potential glycosylation site, and two substitutions, located at the cleavage site and adjacent to the receptor-binding pocket, respectively, had been reported previously in canine H3N8."

"This expansion of host range of equine H3N8 influenza viruses with mutations in the HA protein might raise the possibility of transmission of these viruses to humans."

The full article can be found at: (J.G. Tu, et. al., "Isolation and molecular characterization of equine H3N8 influenza viruses from pigs in China". Archives of Virology, 2009;154(5):887-890). Link not

available.

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## **INFLUENZA A VIRUS LACKING M2 PROTEIN AS A LIVE ATTENUATED VACCINE**

Pharma Investments, Ventures & Law Weekly

July 19, 2009

"Here, we examined the potency of M2KO influenza virus as a live attenuated influenza vaccine. M2KO virus grew as efficiently as the wild-type virus in cells stably expressing the wild-type M2, indicating the feasibility of efficient vaccine production."

"Mice intranasally vaccinated with M2KO virus developed protective immune responses and survived a lethal challenge with the wild-type virus, suggesting that the M2KO virus has potential as a live attenuated vaccine."

The full article can be found at: (S. Watanabe, et. al., "Influenza A Virus Lacking M2 Protein as a Live Attenuated Vaccine". Journal of Virology, 2009;83(11):5947-5950). Link not available.

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## **ACTIVATION OF TOLL-LIKE RECEPTOR SIGNALING PATHWAY FOR PROTECTION AGAINST INFLUENZA VIRUS INFECTION**

Drug Week

July 17, 2009

"This study aims to evaluate the antiviral role Of nucleic acid-based agonists for the activation of toll-like receptor(TLR) signaling pathways, and its protective role in respiratory influenza A virus infections. TLR-3 is expressed on myeloid dendritic cells, respiratory epithelium, and macrophages, and appears to play a central role in mediating both the antiviral and inflammatory responses of the innate immunity in combating viral infections."

"Influenza viruses can effectively inhibit the host's ability to produce interferons, and thereby Suppress the immune system's antiviral defence mechanisms. Poly ICLC is a synthetic double stranded RNA comprising of polyriboinosinic-poly ribocytidylic acid (Poly IQ stabilized with L-lysine (L) and carboxymethylcellulose (C). Poly ICLC and liposome-encapsulated Poly ICLC (LE Poly ICLC) are TLR-3 agonists and are potent inducer of interferons and natural killer cells. Intranasal pre-treatment of mice with Poly ICLC and LE Poly ICLC provided high level of protection against lethal challenge with a highly lethal avian H5N1 influenza (HPAI) strain (A/H5N1/chicken/Henan clade 2), and against lethal seasonal influenza A/PR/8/34 [H1N1] and A/Aichi/2 [H3N2] Virus strains. The duration of protective antiviral immunity to multiple lethal doses of influenza virus A/PR/8/34 virus had been previously found to persist for up to 3 weeks in mice for LE Poly ICLC and 2 weeks for Poly ICLC. Similarly, pre-treatment of mice with CpG oligonucleotides (TLR-9 agonist) was also found to provide complete protection against influenza A/PR/8/34 infection in mice. RT-PCR analysis of lung tissues of mice treated with Poly ICLC and LE Poly ICLC revealed upregulation of TLR-3 mRNAs gene expression."

"Taken together, these results do Support the potential role of TLR-3 and TLR-9 agonists such as Poly ICLC and LE Poly ICLC in protection against lethal seasonal and HPAI virus infection."

The full article can be found at: (J.P. Wong, et. al., "Activation of toll-like receptor signaling pathway for protection against influenza virus infection". Vaccine, 2009;27(25-26 Sp.):3481-3483). Link not available.

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## **GRANZYME A EXPRESSION REVEALS DISTINCT CYTOLYTIC CTL SUBSETS FOLLOWING**

## **INFLUENZA A VIRUS INFECTION**

Immunotherapy Weekly  
July 22, 2009

“Here, we provide the first analysis of grzA protein expression by murine anti-viral CTL.”

"During the progression of influenza A virus infection, CTL expressed two divergent cytolytic phenotypes: grzA(-)B(+) and grzA(+)B(+). CTL lacked grzA expression during the initial rounds of antigen-driven division. High levels of grzA were expressed by influenza-specific CTL early post infection (day 6), particularly in tissues associated with the infected respiratory tract (bronchoalveolar lavage, lung). Following resolution of influenza infection, a small population of memory CTL expressed grzA. Interestingly, individual influenza A virus-derived epitope-specific CTL expressed different levels of grzA. The grzA expression hierarchy was determined to be K(b)PB1(703) = D(b)F2(62) = K(b)NS2(114) > (DNP366)-N-b = D(b)PA(224) and inversely correlated with CTL magnitude. Therefore following influenza infection, a CTL cytolytic hierarchy was established relating to the different profiles of antigen expression and relative immunodominance."

"Analysis of CTL grzA expression during influenza virus immunity has enabled a more detailed insight into the cytolytic mechanisms of virus elimination.."

The full article can be found at: (J.M. Moffat, et. al., "Granzyme A expression reveals distinct cytolytic CTL subsets following influenza A virus infection". European Journal of Immunology, 2009;39(5):1203-1210). Link not available.

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## **FIGHT FOR SWINE FLU VACCINE COULD GET UGLY**

By Maria Cheng  
Associated Press on Yahoo! News  
July 16, 2009

“An ugly scramble is brewing over the swine flu vaccine — and when it becomes available, Britain, the United States and other nations could find that the contracts they signed with pharmaceutical companies are easily broken.

Experts warn that during a global epidemic, which the world is in now, governments may be under tremendous pressure to protect their own citizens first before allowing companies to ship doses of vaccine out of the country.

That does not bode well for many countries, including the United States, which makes only 20 percent of the flu vaccines it uses, or Britain, where all of its flu vaccines are produced abroad.”

The full article can be found at:

[http://news.yahoo.com/s/ap/20090716/ap\\_on\\_he\\_me/eu\\_med\\_vaccine\\_fight](http://news.yahoo.com/s/ap/20090716/ap_on_he_me/eu_med_vaccine_fight)

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## **[UK] DOCTORS TO ISSUE 'FAST TRACK' DEATH CERTIFICATES FOR SWINE FLU**

By Philippe Naughton  
The Times Online (UK)  
July 15, 2009

“Doctors are to be allowed to issue "fast-track" death certificates under Government plans to help the health system cope with the workload at the height of the swine flu pandemic.

Sir Liam Donaldson, Chief Medical Officer for England, confirmed the planned move in an interview on

BBC's Newsnight.

"We want to try and reduce as much as possible the burden of work on doctors and we're considering all sorts of things which will help with that," he said. "It's one of a number of things that we hope at the height of the pandemic - which we may see in the autumn and winter - will reduce the burden of paperwork for doctors."

The full article can be found at:

[http://www.timesonline.co.uk/tol/life\\_and\\_style/health/article6714709.ece](http://www.timesonline.co.uk/tol/life_and_style/health/article6714709.ece)

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## **WHO SUSPENDS REPORTING OF H1N1 CASE COUNTS**

By Lisa Schnirring

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)

July 16, 2009

“Citing the questionable usefulness of reporting pandemic H1N1 case counts and the burden it puts on countries experiencing widespread transmission, the World Health Organization (WHO) announced today it will no longer issue regular reports of confirmed global case totals.

The WHO has issued 58 such reports since the start of the novel H1N1 outbreak, the last one on Jul 6.

In a statement today, the WHO said countries with sustained community transmission are having an extremely difficult time confirming cases through laboratory testing. In addition, counting individual cases isn't essential for monitoring the level or nature of risk posed by the virus or implementing response measures.

Detecting and confirming all possible cases is highly resource-intensive, the WHO said. "In some countries, this strategy is absorbing most national laboratory and resource capacity, leaving little capacity for the monitoring and investigation of severe cases and other exceptional events."

For these reasons, the WHO said it will no longer issue reports of confirmed cases. However, it said it will provide regular updates on the spread of pandemic flu in newly affected countries.

The focus of surveillance activities in countries where the virus is already established will shift to existing systems for monitoring seasonal flu, the WHO said. Countries are no longer required to submit regular reports of individual confirmed cases and deaths to the WHO.”

The full article can be found at:

<http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/jul1609cases-br.html>

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## **SCIENTISTS DISCOVER HOW FLU DAMAGES LUNG TISSUE**

Infection Control Today Magazine

July 17, 2009

“A protein in influenza virus that helps it multiply also damages lung epithelial cells, causing fluid buildup in the lungs, according to new research from the University of Alabama at Birmingham (UAB) and Southern Research Institute. Publishing online this week in the journal of the Federation of American Societies for Experimental Biology, the researchers say the findings give new insight into how flu attacks the lungs and provides targets for new treatments.

In severe cases of flu, fluid accumulates in the lungs, making it difficult to breathe and preventing oxygen from reaching the blood stream. The researchers report that M2, a protein in the flu virus,

damages a protein responsible for clearing fluid from the lungs by increasing the amount of oxidants, or free radicals, within the cells. Oxidants are necessary for proper cell function, but can become toxic if uncontrolled."

The full article can be found at: <http://www.infectioncontrolday.com/hotnews/how-flu-damages-lung-tissue.html>

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## **BAXTER HITS LIMIT ON SWINE FLU VACCINE ORDERS**

Reuters on ChicagoBusiness.com

July 16, 2009

"While at least 50 governments have placed orders or are negotiating with drug companies for supplies of flu vaccine against the fast spreading H1N1 strain, the lone U.S.-based maker has already taken on as much as it can handle.

Baxter International Inc. said on Thursday it has taken orders from five countries, including Britain, Ireland and New Zealand, for a total of 80 million doses of H1N1 vaccine and will not take any more.

"At this time we're not in a position to take additional orders," Baxter spokesman Chris Bona said.

However, Bona said the company has agreed to allocate a portion of its commercial production to the World Health Organization to address global public health issues."

The full article can be found at: <http://www.chicagobusiness.com/cgi-bin/news.pl?id=34785>

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## **MUMBAI AIRPORT GETS TECHNOLOGY TO FIGHT SWINE FLU**

By Aruna Ramesh

IBNLive.com

July 20, 2009

"Developed by NASA, this technology is the same as the one that purifies air in space stations.

Airocide, technically, a photocatalytic conditioning system is capable of destroying microorganisms including anthrax and the swine flu virus.

Air suctioned into the machine, Airocide is made to collide with hydroxyl radicals that are very reactive in the presence of UV light. The reaction mineralises and completely destroys not just microorganisms, but even gases, releasing pure air with traces of carbon dioxide and water vapour.

Director Great White Technology, Dharmesh Keswani says, "This technology is an FDA certified class II medical device."

The full article can be found at: <http://ibnlive.in.com/news/mumbai-airport-fitted-with-technology-to-fight-swine-flu/97528-17.html>

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## **FAST RISE OF BROADLY CROSS-REACTIVE ANTIBODIES AFTER BOOSTING LONG-LIVED HUMAN MEMORY B CELLS PRIMED BY AN MF59 ADJUVANTED PREPANDEMIC VACCINE**

Drug Week

July 24, 2009

"Proactive priming before the next pandemic could induce immune memory responses to novel influenza antigens. In an open-label study, we analyzed B cell memory and antibody responses of 54 adults who received 2 7.5-mu g doses of MF59-adjuvanted A/Vietnam/1194/2004 clade 1 (H5N1) vaccine."

"Twenty-four subjects had been previously primed with MF59-adjuvanted or plain clade 0-like A/duck/Singapore/1997 (H5N3) vaccine during 1999-2001. The prevaccination frequency of circulating memory B cells reactive to A/Vietnam/1194/2004 was low in both primed and unprimed individuals. However, at day 21 after boosting, MF59-adjuvanted primed subjects displayed a higher frequency of H5N1-specific memory B cells than plain-primed or unprimed subjects. The immune memory was rapidly mobilized by a single vaccine administration and resulted in high titers of neutralizing antibodies to antigenically diverse clade 0, 1, and 2 H5N1 viruses already at day 7. In general, postvaccination antibody titers were significantly higher in primed subjects than in unprimed subjects. primed with MF59-adjuvanted vaccine responded significantly better than those primed with plain vaccine, most notably in early induction and duration of cross-reacting antibody responses. After 6 months, high titers of cross-reactive antibody remained detectable among MF59-primed subjects. distant priming with clade 0-like H5N3 induces a pool of cross-reactive memory B cells that can be boosted rapidly years afterward by a mismatched MF59-adjuvanted vaccine to generate high titers of cross-reactive neutralizing antibodies rapidly."

"These results suggest that pre-pandemic vaccination strategies should be considered."

The full article can be found at: (G. Galli, et. al., "Fast rise of broadly cross-reactive antibodies after boosting long-lived human memory B cells primed by an MF59 adjuvanted prepandemic vaccine". Proceedings of the National Academy of Sciences of the United States of America, 2009;106(19):7962-7967). Link not available.

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## **[UK] GUARDS TO PROTECT SWINE FLU DRUG DEPOTS**

By Mark Blunden  
Metro.co.uk  
July 20, 2009

"Security guards will be brought in to protect the swine flu medication when more than 100 new distribution centres are set up this week, amid fears it will be targeted by thieves.

The location of collection points will be kept secret until they are ready to open and security experts have issued guidance to make sure staff and supplies are kept safe."

The full article can be found at: [http://www.metro.co.uk/news/article.html?Guards\\_to\\_protect\\_swine\\_flu\\_drug\\_depots&in\\_article\\_id=705817&in\\_page\\_id=34&ito=newsnow](http://www.metro.co.uk/news/article.html?Guards_to_protect_swine_flu_drug_depots&in_article_id=705817&in_page_id=34&ito=newsnow)

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