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 #57

1. MASS SPEC PINPOINTS FLU VIRUS TYPES: *"Researchers in Australia have shown that exquisitely accurate mass spectrometry can be used to distinguish between different sub-types of the influenza virus - a key issue for health agencies when monitoring outbreaks of the disease and the possible emergence of dangerous new mutants."*

2. COMPARISON OF THE TRIVALENT LIVE ATTENUATED VS. INACTIVATED INFLUENZA VACCINES AMONG U.S. MILITARY SERVICE MEMBERS: *"However, for Army and Air Force recruits, LAIV was found to provide significantly greater protection from influenza-like illnesses compared to TIV, with adjusted incidence rates of influenza-like illness 22–51% and 18–47% lower among LAIV compared to TIV recipients for the 2005–2006 and 2006–2007 influenza seasons, respectively."*

3. U.S. AIRPORT ENTRY SCREENING IN RESPONSE TO PANDEMIC INFLUENZA: MODELING AND ANALYSIS: *"In the first 100 days of a global pandemic, U.S. airport screening would evaluate over 17 M passengers with 800 K secondary screenings. 11,570 PI infected passengers (majority asymptomatic) would enter the U.S. undetected from all 18 airports."*

4. CANADA TO CHANGE FLU DRUGS IN PANDEMIC STOCKPILE: *"Canada will adjust the mix of antiviral drugs in an emergency pandemic stockpile this year, a response to concerns over the vulnerability of the main drug in the arsenal, Tamiflu, to the development of viral resistance."*

5. EXPRESSION OF MOUSE BETA-DEFENSIN-3 IN MDCK CELLS AND ITS ANTI-INFLUENZA-VIRUS ACTIVITY: *"The results demonstrated that mouse beta-defensins possess anti-influenza virus activity, suggesting that mouse beta-defensins might be used as agents to prevent and treat influenza."*

6. DESIGN AND SYNTHESIS OF 1,2-ANNULATED ADAMANTANE PIPERIDINES WITH ANTI-INFLUENZA VIRUS ACTIVITY: *"It is noteworthy that piperidine 23 displayed one of the highest selectivity indexes (SI >732) among aminoadamantanes or other cage structure amines tested till now."*

CB Daily Report

Chem-Bio News

MASS SPEC PINPOINTS FLU VIRUS TYPES
By Simon Hadlington
Chemistry World (Royal Society of Chemistry – UK)
April 16, 2009

"Researchers in Australia have shown that exquisitely accurate mass spectrometry can be used to distinguish between different sub-types of the influenza virus - a key issue for health agencies when monitoring outbreaks of the disease and the possible emergence of dangerous new mutants."

"Now, a group led by Kevin Downard of the University of Sydney has shown that it is possible to directly sub-type the proteins rather than rely on their genetic code by using a technique called Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry.

Here, the whole virus or the relevant antigenic protein is digested by an enzyme into peptide fragments. These fragments are then analysed by FT-ICR mass spectrometry. The technique has such a high resolution that it can unambiguously assign a peptide from mass alone, even when it is part of a highly complex mixture, such as a whole-virus digest. The resulting 'fingerprint' of peptides allows the virus to be typed and sub-typed, with different forms of the antigen yielding different fingerprints."

The full article can be found at: http://www.rsc.org/chemistryworld/News/2009/April/16040902.asp

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COMPARISON OF THE TRIVALENT LIVE ATTENUATED VS. INACTIVATED INFLUENZA VACCINES AMONG U.S. MILITARY SERVICE MEMBERS
By Angelia A. Eick, Zhong Wang, Hayley Hughes, Stephen M. Ford and Steven K. Tobler
Vaccine
April 19, 2009

"Limited effectiveness data are available comparing live attenuated influenza vaccine (LAIV) to inactivated influenza vaccine (TIV) among adults. To compare the incidence of influenza-like illness following immunization of adults with LAIV vs. TIV, we conducted a retrospective cohort analysis of active component U.S. military personnel for the 2005–2006 and 2006–2007 influenza seasons. Recruits experienced a much higher burden of disease compared to non-recruits, with crude incidence rates of influenza-like illness 2–16 times higher than non-recruits depending on the season and cohort. For both seasons, a slightly greater protection from influenza-like illness was found for non-recruits who received TIV compared to LAIV (adjusted incidence rate ratio, 1.17 (95% CI, 1.14–1.20) and 1.33 (95% CI, 1.30–1.36), 2005–2006 and 2006–2007 influenza seasons, respectively). However, for Army and Air Force recruits, LAIV was found to provide significantly greater protection from influenza-like illnesses compared to TIV, with adjusted incidence rates of influenza-like illness 22–51% and 18–47% lower among LAIV compared to TIV recipients for the 2005–2006 and 2006–2007 influenza seasons, respectively. Possible reasons for differences in recruit and non-recruit findings include differences in pre-existing influenza antibody levels, differing respiratory disease burden, and/or unmeasured confounding. Consideration of these findings should be made when developing influenza immunization policies."

The full article can be found at: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4W3NY2R-1&_user=616288&_coverDate=04%2F19%2F2009&_rdoc=1&_fmt=high&_orig=browse&_srch=doc-info(%23toc%235188%239999%23999999999%2399999%23FLA%23display%23Articles)&_cdi=5188&_sort=d&_docanchor=&_ct=154&_acct=C000032378&_version=1&_urlVersion=0&_userid=616288&md5=5a38699bd096a6c3e7551de8fd6d6d56

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U.S. AIRPORT ENTRY SCREENING IN RESPONSE TO PANDEMIC INFLUENZA: MODELING AND ANALYSIS
By John D. Malone, Robert Briganti, George A. Muller, Ashok Gadgil, Woody Delp, Benjamin H. McMahon, Russell Lee, Jim Kulesz and F. Matthew Mihelic
Travel Medicine and Infectious Disease
April 14, 2009

"In the first 100 days of a global pandemic, U.S. airport screening would evaluate over 17 M passengers with 800 K secondary screenings. 11,570 PI infected passengers (majority asymptomatic) would enter the U.S. undetected from all 18 airports. Foreign airport departure screening significantly decreased the false negative (infected/undetected) passengers. U.S. attack rates: no screening (26.9%–30.9%); screening (26.4%–30.6%); however airport screening results in 800 K–1.8 M less U.S. PI cases; 16 K–35 K less deaths (2% fatality rate). Antiviral medications for travel contact prophylaxis (10 contacts/PI passenger) were high – 8.8 M. False positives from all 18 airports: 100–200/day."

The full article can be found at: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B7578-4W2M6SG-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=f5a874ac507a066f7ab953b8cf093b99

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CANADA TO CHANGE FLU DRUGS IN PANDEMIC STOCKPILE
The Canadian Press
April 20, 2009

"Canada will adjust the mix of antiviral drugs in an emergency pandemic stockpile this year, a response to concerns over the vulnerability of the main drug in the arsenal, Tamiflu, to the development of viral resistance.

Supplies of the drug zanamivir - sold as Relenza by GlaxoSmithKline - will be beefed up in the national emergency stockpile, says Dr. Arlene King, the senior official responsible for pandemic influenza planning at the Public Health Agency of Canada.

As well, some stocks of an older flu drug, amantadine, will be added to the mix as an inexpensive extra. Scientists are studying whether using Tamiflu in combination with amantadine or a sister drug, rimantadine, will lower the likelihood flu strains will develop resistance to the few drugs currently marketed to treat influenza."

The full article can be found at: http://www.ctv.ca/servlet/ArticleNews/story/CTVNews/20090420/flu_drugs_090420/20090420?hub=Health

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EXPRESSION OF MOUSE BETA-DEFENSIN-3 IN MDCK CELLS AND ITS ANTI-INFLUENZA-VIRUS ACTIVITY
Preventive Medicine Week
April 26, 2009

"Mammalian beta-defensins (beta-defensins) are associated primarily with mucosal and skin innate immunity. Previous studies have demonstrated antimicrobial properties of a variety of defensin peptides. We have identified the presence of mouse beta-defensin 1, 2, and 3 genes (Mbd-1, 2, and 3) in trachea and lung tissues by RT-PCR before and after infection with influenza virus. We constructed a eukaryotic expression plasmid containing Mbd-3, pcDNA 3.1(+)/MBD-3, and the plasmid was introduced into Madin-Darby canine kidney (MDCK) cells by transfection. The expression of Mbd-3 in MDCK cells was verified by immunofluorescence test, RT-PCR, and Western blot. The pcDNA 3.1(+)/MBD-3 plasmid was injected into mice to observe its effect against influenza A virus (IAV) in vivo. Mouse beta-defensin genes could be expressed in trachea and lung tissues before IAV infection, but expression of Mbd-2 and Mbd-3 was increased significantly after IAV infection. The survival rate of mice with MBD-3 against IAV challenge was 71.43%, and MDCK cells with MBD-3 could clearly inhibit IAV replication."

"The results demonstrated that mouse beta-defensins possess anti-influenza virus activity, suggesting that mouse beta-defensins might be used as agents to prevent and treat influenza."

The full article can be found at: (Y. Jiang, et. al., "Expression of mouse beta-defensin-3 in MDCK cells and its anti-influenza-virus activity". Archives of Virology, 2009;154(4):639-47). Link not available.

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DESIGN AND SYNTHESIS OF 1,2-ANNULATED ADAMANTANE PIPERIDINES WITH ANTI-INFLUENZA VIRUS ACTIVITY
Drug Week
April 24, 2009

"1-2 Annulated adamantane piperidines 4, 6, 16, 17, 19, 23 and 25 were synthesized and evaluated for anti-influenza A virus activity."

"The stereoelectronic requirements for optimal antiviral potency were investigated. Piperidine 23 proved to be the most active of the compounds tested against influenza A virus, being 3.5-fold more active than amantadine, equipotent to rimantadine and 15-fold more potent than ribavirin."

"It is noteworthy that piperidine 23 displayed one of the highest selectivity indexes (SI >732) among aminoadamantanes or other cage structure amines tested till now."

The full article can be found at: (G. Zoidis, et. al., "Design and synthesis of 1,2-annulated adamantane piperidines with anti-influenza virus activity". Bioorganic & Medicinal Chemistry, 2009;17(4):1534-1541). Link not available.

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Steve Tesko: Steve.Tesko@anser.org

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