

19 August 2008

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 Supplement #24

1. MELBOURNE SCIENTIST WINS MAJOR AWARD FOR ANTI-INFLUENZA

RESEARCH: *"Professor Peter Colman and his colleagues discovered the drug zanamivir in 1989, a breakthrough that led to the development of life-saving anti-influenza medication."*

2. ANTIBODIES TO 1918 FLU PANDEMIC MAY PROVIDE MEANS TO TACKLE BIRD

FLU THREAT: *"Scientists in the United States have discovered that elderly survivors of the original 1918 flu pandemic, still have immunity to the virus."*

3. PRIORITIZATION OF INFLUENZA PANDEMIC VACCINATION TO MINIMIZE YEARS

OF LIFE LOST: *"Our findings shift the focus of pandemic vaccination strategies onto younger populations and illustrate the need for real-time surveillance of mortality patterns in a future pandemic."*

4. DEVIATION FROM THE RANDOM DISTRIBUTION PATTERN OF INFLUENZA A

VIRUS GENE SEGMENTS IN REASSORTANTS PRODUCED UNDER NON-SELECTIVE
CONDITIONS: *"The data demonstrate the previously unrecognized phenomenon of segment-specific deviation from the random distribution of parent genes in the reassortants."*

5. RAPID METHODS FOR DETECTING MYCOPLASMA CONTAMINATION IN THE

MANUFACTURE OF VACCINES, INCLUDING PANDEMIC INFLUENZA VACCINES, AND
OTHER BIOLOGICAL PRODUCTS: *This notice provides information on an upcoming open workshop on the topic being sponsored by the Center for Biologics Evaluation and Research of the US Food and Drug Administration.*

6. THE EVOLUTIONARY DYNAMICS OF HUMAN INFLUENZA B VIRUS: *"Additionally, we suggest that the interaction with influenza A virus may be central in shaping the evolutionary dynamics of influenza B virus, facilitating the shift of dominance between the Vic87 and the Yam88 lineages."*

7. ACTIVATION OF INVARIANT NKT [iNKT] CELLS ENHANCES THE INNATE IMMUNE RESPONSE AND IMPROVES THE DISEASE COURSE IN INFLUENZA A VIRUS

INFECTION: *"We conclude that activation of iNKT cells enhances early innate immune response in the lungs and contribute to antiviral immunity and improved disease course in influenza A virus infection."*

CB Daily Report

Chem-Bio News

MELBOURNE SCIENTIST WINS MAJOR AWARD FOR ANTI-INFLUENZA RESEARCH

ABC News

August 13, 2008

"Professor Peter Colman and his colleagues discovered the drug zanamivir in 1989, a breakthrough that led to the development of life-saving anti-influenza medication.

He will be presented with the \$50,000 Victoria Prize at a ceremony in Melbourne tonight."

"It took another 10 years in total of testing the drug in animals and then in people and then in large clinical trials to establish that this was a class of drugs that could indeed have an anti-viral effect in a patient," he said."

The full article can be found at: <http://www.abc.net.au/news/stories/2008/08/13/2334437.htm>

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ANTIBODIES TO 1918 FLU PANDEMIC MAY PROVIDE MEANS TO TACKLE BIRD FLU THREAT

News-Medical.net

August 18, 2008

"Scientists in the United States have discovered that elderly survivors of the original 1918 flu pandemic, still have immunity to the virus."

"In a study, led by Dr. James Crowe Junior, a professor of pediatrics and director of the Vanderbilt Program in Vaccine Sciences, researchers collected blood samples from 32 survivors age 91-101 years and found that all reacted to the 1918 virus, suggesting that they still possessed antibodies to the virus.

Samples of the virus used were collected by researchers from Mount Sinai and the Armed Forces Institute of Pathology in 2005 and were taken from the bodies of people killed in the outbreak whose bodies, and the virus, had been preserved in the permanently frozen soil of

Alaska."

The full article can be found at: <http://www.news-medical.net/?id=40760>

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PRIORITIZATION OF INFLUENZA PANDEMIC VACCINATION TO MINIMIZE YEARS OF LIFE LOST

Preventive Medicine Week

August 24, 2008

"Conventional vaccination strategies focus on those at highest risk for severe outcomes, including seniors, but do not consider (1) the signature pandemic pattern in which mortality risk is shifted to younger ages, (2) likely reduced vaccine response in seniors, and (3) differences in remaining years of life with age."

"We integrated these factors to project the age-specific years of life lost (YLL) and saved in a future pandemic, on the basis of mortality patterns from 3 historical pandemics, age-specific vaccine efficacy, and the 2000 US population structure. For a 1918-like scenario, the absolute mortality risk is highest in people <45 years old; in contrast, seniors (those >or=65 years old) have the highest mortality risk in the 1957 and 1968 scenarios. The greatest YLL savings would be achieved by targeting different age groups in each scenario; people <45 years old in the 1918 scenario, people 45-64 years old in the 1968 scenario, and people >45 years old in the 1957 scenario. Our findings shift the focus of pandemic vaccination strategies onto younger populations and illustrate the need for real-time surveillance of mortality patterns in a future pandemic."

The full article can be found in: (M.A. Miller, et. al., "Prioritization of influenza pandemic vaccination to minimize years of life lost". *Journal of Infectious Diseases*, 2008;198(3):305-11). Link not available.

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DEVIATION FROM THE RANDOM DISTRIBUTION PATTERN OF INFLUENZA A VIRUS GENE SEGMENTS IN REASSORTANTS PRODUCED UNDER NON-SELECTIVE CONDITIONS

Health Risk Factor Week

August 19, 2008

"High-frequency reassortment of gene segments is characteristic for influenza viruses, and it is considered to be of significance for the origin of pandemic influenza. In order to analyze whether the segregation of genes in the reassortants is random, or it deviates from the random pattern, we inoculated embryonated chicken eggs simultaneously with two influenza viruses, A/WSN/33 (H1N1) and A/Duck/ Czechoslovakia/56 (H4N6), at a high multiplicity of infection."

"The virus yield was used for plaque cloning, and the genetic content of plaque isolates was determined by analysis of the mobility of virus-induced proteins in polyacrylamide gel (for NP and NS genes), partial sequencing (for M gene) and polymerase chain reaction analysis with strain-specific primers for the other genes. Out of 37 isolates, 27 were reassortants. The majority of the reassortants contained the HA gene of A/WSN/33 (H1N1) virus and the NP gene of A/Duck/Czechoslovakia/56 (H4N6) virus. The data demonstrate the previously unrecognized phenomenon of segment-specific deviation from the random distribution of parent genes in the reassortants."

The full article can be found in: (N.L. Varich, et. al., "Deviation from the random distribution pattern of influenza A virus gene segments in reassortants produced under non-selective conditions". Archives of Virology, 2008;153(6):1149-1154). Link not available.

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RAPID METHODS FOR DETECTING MYCOPLASMA CONTAMINATION IN THE MANUFACTURE OF VACCINES, INCLUDING PANDEMIC INFLUENZA VACCINES, AND OTHER BIOLOGICAL PRODUCTS

US Food and Drug Administration News Release
July 21, 2008

"The purpose of the public workshop is to provide a forum on recent scientific and technical achievements in the development of rapid methods for mycoplasma testing during the manufacture of vaccines and other biological products. Such discussion may help to assess how these methods compare with currently used methods. Expedited manufacture may be of particular importance to public health during an influenza pandemic."

The full article can be found at: <http://www.fda.gov/cber/meetings/myco092208.htm>

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THE EVOLUTIONARY DYNAMICS OF HUMAN INFLUENZA B VIRUS

Virus Weekly
August 19, 2008

"Despite their close phylogenetic relationship, type A and B influenza viruses exhibit major epidemiological differences in humans, with the latter both less common and less often associated with severe disease. However, it is unclear what processes determine the evolutionary dynamics of influenza B virus, and how influenza viruses A and B interact at the evolutionary scale."

"To address these questions we inferred the phylogenetic history of human influenza B virus using complete genome sequences for which the date (day) of isolation was available. By comparing the phylogenetic patterns of all eight viral segments we determined the

occurrence of segment reassortment over a 30-year sampling period. An analysis of rates of nucleotide substitution and selection pressures revealed sporadic occurrences of adaptive evolution, most notably in the viral hemagglutinin and compatible with the action of antigenic drift, yet lower rates of overall and nonsynonymous nucleotide substitution compared to influenza A virus. Overall, these results led us to propose a model in which evolutionary changes within and between the antigenically distinct 'Yam88' and 'Vic87' lineages of influenza B virus are the result of changes in herd immunity, with reassortment continuously generating novel genetic variation."

"Additionally, we suggest that the interaction with influenza A virus may be central in shaping the evolutionary dynamics of influenza B virus, facilitating the shift of dominance between the Vic87 and the Yam88 lineages."

The full article can be found at: (R.B. Chen, et. al., "The evolutionary dynamics of human influenza B virus". *Journal of Molecular Evolution*, 2008;66(6):655-663). Link not available.

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ACTIVATION OF INVARIANT NKT [iNKT] CELLS ENHANCES THE INNATE IMMUNE RESPONSE AND IMPROVES THE DISEASE COURSE IN INFLUENZA A VIRUS INFECTION

Drug Week

August 22, 2008

"We show that activation of iNKT cells with alpha-galactosylceramide (alpha-GC) during influenza virus infection transiently enhanced early innate immune response without affecting T cell immunity, and reduced early viral titres in lungs of C57BL/6 mice. This is accompanied by a better disease course with improved weight loss profile. Temporal changes in iNKT cells in the liver, blood and lungs suggest activation and migration of iNKT cells from the liver to the lungs in mice that were administered alpha-GC. Improvement in viral titres appears dependent on activation of iNKT cells via the intraperitoneal route since intranasal administration of alpha-GC did not have the same effect."

"We conclude that activation of iNKT cells enhances early innate immune response in the lungs and contribute to antiviral immunity and improved disease course in influenza A virus infection."

The full article can be found at: (L.P. Ho, et. al., "Activation of invariant NKT cells enhances the innate immune response and improves the disease course in influenza A virus infection". *European Journal of Immunology*, 2008;38(7):1913-22). Link not available.

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