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Chem-Bio News– Pandemic Influenza Supplement # 35

1. WOULD AN INFLUENZA PANDEMIC QUALIFY AS A MAJOR DISASTER UNDER THE STAFFORD ACT?: *“In this case, interpreting a flu pandemic as either a natural or non-natural catastrophe is arguably reasonable.”*

2. UNIVERSAL ANTIBODIES AND THEIR APPLICATIONS TO THE QUANTITATIVE DETERMINATION OF VIRTUALLY ALL SUBTYPES OF THE INFLUENZA A VIRAL HEMAGGLUTININS: *“To our knowledge, this is the first report on the quantitative determination of virtually all influenza vaccines using a single universal antibody.”*

3. SHOULD INFLUENZA IMMUNISATION BE MANDATORY FOR HEALTHCARE WORKERS? YES: *“There is evidence that vaccinating long term care healthcare workers reduces mortality among long term care patients and that vaccinating hospital workers decreases the rate of nosocomial influenza in hospitalised patients.”*

4. SHOULD INFLUENZA IMMUNISATION BE MANDATORY FOR HEALTHCARE WORKERS? NO: *“Mandatory immunisation may alienate many staff and damage morale.”*

5. MEMORY T CELLS ESTABLISHED BY SEASONAL HUMAN INFLUENZA A INFECTION CROSS-REACT WITH AVIAN INFLUENZA A (H5N1) IN HEALTHY INDIVIDUALS: *“Thus, vaccine formulas inducing heterosubtypic T cell-mediated immunity may confer broad protection against avian and human influenza A viruses.”*

6. IMAGING AND CHARACTERIZING INFLUENZA A VIRUS mRNA TRANSPORT IN LIVING CELLS: *“These findings characterize influenza A virus mRNA transport in living cells and suggest that influenza A virus mRNA may be exported from the nucleus by the cellular TAP/p15 pathway with NS1 protein and RNAP-II participation.”*

7. SIZE-EXCLUSION CHROMATOGRAPHY AS A LINEAR TRANSFER SYSTEM: PURIFICATION OF HUMAN INFLUENZA VIRUS AS AN EXAMPLE: *“By application of the theory it is demonstrated how group separation operations can be optimized with respect to yield, purity, productivity and dilution of the product.”*

CB Daily Report

Chem-Bio News

WOULD AN INFLUENZA PANDEMIC QUALIFY AS A MAJOR DISASTER UNDER THE STAFFORD ACT?

By Edward C. Liu, Congressional Research Service
October 20, 2008

“The preceding analysis of the text and legislative history indicates that Congress did not directly address whether a flu pandemic is a natural catastrophe for purposes of the Stafford Act. Under the framework laid out by the Supreme Court in *Chevron*, the remaining question is whether a particular executive branch interpretation is “a reasonable choice within a gap left open by Congress.”⁵⁵ [*Chevron*, 467 U.S. at 866.]

In this case, interpreting a flu pandemic as either a natural or non-natural catastrophe is arguably reasonable. On the one hand, the manner in which a flu pandemic is likely to propagate does not require human intervention. Making flu pandemics eligible for major disasters makes the maximum amount of resources available to avert the loss of life, human suffering, and loss of income that is

likely to occur in the event of a flu pandemic. Some types of assistance that are only available in a major disaster declaration may be particularly useful in a flu pandemic. For instance, a flu pandemic is likely to result in a significantly reduced workforce as victims fall ill and others stay home to take care of them. The provision of unemployment assistance and emergency public transportation under the Stafford Act both may be an appropriate response, but are only available under a major disaster declaration.

On the other hand, a pandemic is substantially different than the climatic and geologic natural catastrophes listed by the Stafford Act, and many types of major disaster provisions, such as assistance to repair buildings or clear debris, are not likely to be necessary during a flu pandemic. Restricting flu pandemics to only emergency assistance arguably limits the burden on federal disaster relief funds. Additionally, other federal responses may be more appropriate to deal with a pandemic, such as the authority of the HHS Secretary to declare a public health emergency,⁵⁶ [For a more detailed discussion of authority and funding for public health emergencies, see CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by Sarah A. Lister, at 4-7, 16-18.] or impromptu legislation to provide assistance with respect to a particular incident.

Finally, it should be noted that the reasonableness of either interpretation is being evaluated under current law. Were Congress to conclude that flu pandemics categorically should or should not be eligible for major disaster assistance, it may amend the statute to explicitly say so. In that case, the clearly expressed intent of Congress would render any evaluation of an executive branch interpretation unnecessary, and Congress's intent would control."

The full article can be found at: <http://www.fas.org/sgp/crs/misc/RL34724.pdf>

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UNIVERSAL ANTIBODIES AND THEIR APPLICATIONS TO THE QUANTITATIVE DETERMINATION OF VIRTUALLY ALL SUBTYPES OF THE INFLUENZA A VIRAL HEMAGGLUTININS

By Stella Chun, Changgui Li, Gary Van Domselaar, Junzhi Wang, Aaron Farnsworth, Xiaoyu Cui, Harold Rode, Terry D. Cyr, Runtao He and Xuguang Li
Vaccine

November 5, 2008

"The fusion peptide is the only universally conserved sequence in the hemagglutinins of all 16 subtypes of influenza A and two genetic lineages of influenza B viruses. Here, peptides selected by bioinformatics approach were modified and conjugated to overcome serious technical hurdles such as the high hydrophobicity and weak immunogenicity of the viral fusion peptides. Antibodies generated against fusion peptides demonstrated remarkable specificity against the viral sequences and robustness of quantitatively analyzing the viral hemagglutinins even under stringent conditions. As quantitatively revealed by antibody-binding experiments, the fusion peptides of diverse hemagglutinins are exposed to the same degree upon unfolding at neutral pH to the physiologically fusogenic state. To our knowledge, this is the first report on the quantitative determination of virtually all influenza vaccines using a single universal antibody.

The full article can be found at: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4TVHKM5-2&_user=616288&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_version=1&_urlVersion=0&_userid=616288&md5=ebd651f8a3ed747d7828ffbeb3359ae1

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SHOULD INFLUENZA IMMUNISATION BE MANDATORY FOR HEALTHCARE WORKERS? YES

By Charles M Helms and Philip M Polgreen

British Medical Journal

October 28, 2008

"There is evidence that vaccinating long term care healthcare workers reduces mortality among long term care patients and that vaccinating hospital workers decreases the rate of nosocomial influenza in hospitalised patients. Moreover, an economic evaluation of immunisation of healthcare workers in the UK found that it is cost saving. In addition, further studies show that healthcare worker vaccination reduces absenteeism."

The full article can be found at: http://www.bmj.com/cgi/content/full/337/oct28_3/a2142

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SHOULD INFLUENZA IMMUNISATION BE MANDATORY FOR HEALTHCARE WORKERS? NO

David Isaacs and Julie Leask
British Medical Journal
October 28, 2008

"There is good evidence that patients are vulnerable to nosocomial influenza. Immunising healthcare workers who care for institutionalised elderly people protects the elderly against influenza and may even prevent deaths, although the benefit is greatest in elderly people who have not been immunised. However, there is virtually no published evidence that immunising healthcare workers protects other patient groups."

"Mandatory immunisation may alienate many staff and damage morale. Mandatory immunisation devalues staff by treating them as objects, not people. Furthermore, the message that healthcare workers have to be compelled to be immunised will galvanise and provide ammunition to opponents of immunisation. It risks polarising healthcare workers and producing a backlash with opposite consequences to those intended."

The full article can be found at: http://www.bmj.com/cgi/content/full/337/oct28_3/a2140

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MEMORY T CELLS ESTABLISHED BY SEASONAL HUMAN INFLUENZA A INFECTION CROSS-REACT WITH AVIAN INFLUENZA A (H5N1) IN HEALTHY INDIVIDUALS

TB & Outbreaks Week
November 11, 2008

"Current influenza vaccines stimulate antibody responses against the surface glycoproteins but are ineffective against strains that have undergone significant antigenic variation."

"An alternative approach is to stimulate pre-existing memory T cells established by seasonal human influenza A infection that could cross-react with H5N1 by targeting highly conserved internal proteins. To determine how common cross-reactive T cells are, we performed a comprehensive ex vivo analysis of cross-reactive CD4+ and CD8+ memory T cell responses to overlapping peptides spanning the full proteome of influenza A/Viet Nam/CL26/2005 (H5N1) and influenza A/New York/232/2004 (H3N2) in healthy individuals from the United Kingdom and Viet Nam. Memory CD4+ and CD8+ T cells isolated from the majority of participants exhibited human influenza-specific responses and showed cross-recognition of at least one H5N1 internal protein. Participant CD4+ and CD8+ T cells recognized multiple synthesized influenza peptides, including peptides from the H5N1 strain. Matrix protein 1 (M1) and nucleoprotein (NP) were the immunodominant targets of cross-recognition. In addition, cross-reactive CD4+ and CD8+ T cells recognized target cells infected with recombinant vaccinia viruses expressing either H5N1 M1 or NP."

"Thus, vaccine formulas inducing heterosubtypic T cell-mediated immunity may confer broad protection against avian and human influenza A viruses."

The full article can be found at: (L.Y. Lee, et. al., "Memory T cells established by seasonal human influenza A infection cross-react with avian influenza A (H5N1) in healthy individuals". Journal of Clinical Investigation, 2008; 118(10): 3478-90). Link not available.

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IMAGING AND CHARACTERIZING INFLUENZA A VIRUS mRNA TRANSPORT IN LIVING CELLS

Drug Week
November 14, 2008

"Here, we visualized the distribution and transport of influenza A virus mRNA in living cells using molecular beacon (MB) technology."

"Confocal-FRAP measurements determined that the transport of influenza A virus intronless mRNA, in both nucleus and cytoplasm, was energy dependent, being similar to that of Poly(A) RNA. Drug inhibition studies in living cells revealed that the export of influenza A virus mRNA is independent of the CRM1 pathway, while the function of RNA polymerase II (RNAP-II) may be needed. In addition, viral NS1 protein and cellular TAP protein were found associated with influenza A virus mRNA in the cell nucleus."

"These findings characterize influenza A virus mRNA transport in living cells and suggest that influenza A virus mRNA may be exported from the nucleus by the cellular TAP/p15 pathway with NS1 protein and RNAP-II participation."

The full article can be found at: (W. Wang, et. al., "Imaging and characterizing influenza A virus mRNA transport in living cells". Nucleic Acids Research, 2008;36(15):4913-4928). Link not available.

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SIZE-EXCLUSION CHROMATOGRAPHY AS A LINEAR TRANSFER SYSTEM: PURIFICATION OF HUMAN INFLUENZA VIRUS AS AN EXAMPLE

Medical Imaging Week

November 15, 2008

"Preparative size-exclusion chromatography suffers from low selectivity and productivity. Empirical optimization of operating conditions constitutes a laborious task due to many parameters."

"Here, a modeling framework based on linear systems theory is presented for predicting the influence of volume overloading. Impulse-responses characterizing system behavior are derived from experimental data by maximum entropy deconvolution. Theoretical derivations are validated experimentally by study of a model system and chromatography of human influenza virus."

"By application of the theory it is demonstrated how group separation operations can be optimized with respect to yield, purity, productivity and dilution of the product."

The full article can be found at: (B. Kalbfuss, et. al., "Size-exclusion chromatography as a linear transfer system: purification of human influenza virus as an example". Journal of Chromatography B, 2008;873(1):102-12). Link not available.

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