

2 September 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.

Should you wish to be removed from this S&T Supplement address group, just send an email to one of the people listed at the bottom of this message. This will not affect your continued receipt of the CB Daily.

Chem-Bio News – Pandemic Influenza Supplement #26

1. CRACKING DOWN ON COUNTERFEIT DRUGS: *“US scientists have developed a method for screening Tamiflu in an attempt to foil counterfeiters.”*

2. STRUCTURAL BASIS FOR SUPPRESSION OF A HOST ANTIVIRAL RESPONSE BY INFLUENZA A VIRUS: *“Here we report the 1.95-Å resolution X-ray crystal structure of the complex formed between the second and third zinc finger domain (F2F3) of CPSF30 and the C-terminal domain of the Ud NS1A protein.”*

3. SURGERY CANCELLED AS FLU HITS ROYAL: *“An outbreak of influenza in southern Tasmania has spread to the Royal Hobart Hospital.”*

4. [JA] HOSPITALS TO GET SPECIAL SUITS TO FIGHT FLU OUTBREAK: *“The Health, Labor and Welfare Ministry will purchase 40,000 phylactic suits for doctors and nurses to prepare for a future flu pandemic expected to be caused by a possible new strain of influenza.”*

5. ANTI-INFLUENZA VIRUS ACTIVITY OF EXTRACT OF JAPANESE WASABI LEAVES DISCARDED IN SUMMER: *“Therefore, such extracts are expected to be a promising source of a novel anti-influenza virus agent.”*

6. SUPERIOR IMMUNOGENICITY OF INACTIVATED WHOLE VIRUS H5N1 INFLUENZA VACCINE IS PRIMARILY CONTROLLED BY TOLL-LIKE RECEPTOR SIGNALLING: *“Our results show for a classic vaccine that the acquired immune response evoked by vaccination can be enhanced and steered by the innate immune system, which is triggered by interaction of an intrinsic vaccine component with a pattern recognition receptor (PRR).”*

7. NEW DECISION MODEL SEEKS TO AVERT FLU VACCINE MISMATCH OF 2007-2008 SEASON: *“It may be better to have some of the right vaccine than a lot of the wrong vaccine.”*

CB Daily Report

CRACKING DOWN ON COUNTERFEIT DRUGS

By Edward Morgan
Chemical Technology
August 28, 2008

"US scientists have developed a method for screening Tamiflu in an attempt to foil counterfeiters.

Counterfeiters have targeted Tamiflu, an antiviral flu drug effective against bird flu, due its high cost and demand. Scientists have found fake Tamiflu containing vitamin C instead of the active ingredient, oseltamivir.

Facundo Fernández and colleagues at Georgia Institute of Technology and the US Centers for Disease Control and Prevention, Atlanta, Georgia, used desorption electrospray ionisation mass spectrometry (DESI MS) to help authenticate Tamiflu capsules. They doped the electrospray solvent with crown ethers and studied the competitive complexation of the crown ethers with oseltamivir. They found that by using two different crown ethers with different binding affinities for oseltamivir, they could determine the amount of oseltamivir in the capsules without using an internal standard."

The full article can be found at: http://www.rsc.org/Publishing/ChemTech/Volume/2008/10/counterfeit_drugs.asp

The original article can be found at: Leonard Nyadong, Edward G. Hohenstein, Kristin Johnson, C. David Sherrill, Michael D. Green and Facundo M. Fernández, "Desorption electrospray ionization reactions between host crown ethers and the influenza neuraminidase inhibitor oseltamivir for the rapid screening of Tamiflu®", *Analyst*, 2008, DOI: 10.1039/b809471c. Link not available.

[Return to Top](#)

STRUCTURAL BASIS FOR SUPPRESSION OF A HOST ANTIVIRAL RESPONSE BY INFLUENZA A VIRUS

By Kalyan Das, Li-Chung Ma, Rong Xiao, Brian Radvansky, James Aramini, Li Zhao, Jesper Marklund, Rei-Lin Kuo, Karen Y. Twu, Eddy Arnold, Robert M. Krug, and Gaetano T. Montelione
Proceedings of the National Academy of Science
September 2008

"Here we report the 1.95-Å resolution X-ray crystal structure of the complex formed between the second and third zinc finger domain (F2F3) of CPSF30 and the C-terminal domain of the Ud NS1A protein. The complex is a tetramer, in which each of two F2F3 molecules wraps around two NS1A effector domains that interact with each other head-to-head. This structure identifies a CPSF30 binding pocket on NS1A comprised of amino acid

residues that are highly conserved among human influenza A viruses. Single amino acid changes within this binding pocket eliminate CPSF30 binding, and a recombinant Ud virus expressing an NS1A protein with such a substitution is attenuated and does not inhibit IFN- β pre-mRNA processing. This binding pocket is a potential target for antiviral drug development. The crystal structure also reveals that two amino acids outside of this pocket, F103 and M106, which are highly conserved (>99%) among influenza A viruses isolated from humans, participate in key hydrophobic interactions with F2F3 that stabilize the complex."

The full article can be found at: <http://www.pnas.org/content/early/2008/08/22/0805213105.abstract>

[Return to Top](#)

SURGERY CANCELLED AS FLU HITS ROYAL

ABC News

September 2, 2008

"An outbreak of influenza in southern Tasmania has spread to the Royal Hobart Hospital.

Queueing of ambulances with patients outside the emergency department and the cancellation of elective surgery is expected to continue today.

The hospital says with 29 staff off sick and growing influx of patients it has had no choice but to cancel elective surgeries."

The full article can be found at: <http://www.abc.net.au/news/stories/2008/09/02/2352626.htm>

[Return to Top](#)

[JA] HOSPITALS TO GET SPECIAL SUITS TO FIGHT FLU OUTBREAK

Daily Yomiuri Online

September 2, 2008

"The Health, Labor and Welfare Ministry will purchase 40,000 phylactic suits for doctors and nurses to prepare for a future flu pandemic expected to be caused by a possible new strain of influenza.

Drugs and medical supplies also will be stockpiled as part of the government's plan to enhance preparations to combat a flu pandemic.

The suits will be purchased in fiscal 2009 and 2010, ministry sources said.

The ministry has appropriated 3.1 billion yen for the protective suits, and special baby beds

and respirators, in its budget request for fiscal 2009."

The full article can be found at: <http://www.yomiuri.co.jp/dy/national/20080902TDY02309.htm>

[Return to Top](#)

ANTI-INFLUENZA VIRUS ACTIVITY OF EXTRACT OF JAPANESE WASABI LEAVES DISCARDED IN SUMMER

Life Science Weekly
September 2, 2008

"We investigated anti-influenza virus activity in these summer leaves as a new function. Seventy percent ethanol extracts of leaves harvested in July exhibited a high replication inhibition rate (98% or higher) in the type A strain (AH1N1, A/shimane/48/2002), its subtype (AH3N2, Alshimane/122/2002), and type B strain (B/shimane/2/2002). The extracts of summer leaves exhibited the same anti-influenza virus activity as winter leaves, and showed a stronger activity than stems, roots, and rhizomes. A potent anti-influenza virus activity was discovered in summer leaves of Japanese wasabi. The ethanol extracts inhibited influenza virus replication regardless of the hemagglutinin antigen type."

The full article can be found at: (K. Mochida, et. al., "Anti-influenza virus activity of extract of Japanese wasabi leaves discarded in summer". Journal of the Science of Food and Agriculture, 2008;88(10):1704-1708). Link not available.

[Return to Top](#)

SUPERIOR IMMUNOGENICITY OF INACTIVATED WHOLE VIRUS H5N1 INFLUENZA VACCINE IS PRIMARILY CONTROLLED BY TOLL-LIKE RECEPTOR SIGNALLING

By Felix Geeraedts, Nadege Goutagny, Veit Hornung, Martina Severa, Aalzen de Haan, Judith Pool, Jan Wilschut, Katherine A. Fitzgerald, Anke Huckriede
PLoS Pathogens
September 2, 2008

"In unprimed individuals, inactivated whole virus (WIV) vaccines are more immunogenic and induce protective antibody responses at a lower antigen dose than other formulations like split virus (SV) or subunit (SU) vaccines. The reason for this discrepancy in immunogenicity is a long-standing enigma. Here, we show that stimulation of Toll-like receptors (TLRs) of the innate immune system, in particular stimulation of TLR7, by H5N1 WIV vaccine is the prime determinant of the greater magnitude and Th1 polarization of the WIV-induced immune response, as compared to SV- or SU-induced responses. This TLR dependency largely explains the relative loss of immunogenicity in SV and SU vaccines. The natural pathogen-associated molecular pattern (PAMP) recognized by TLR7 is viral genomic ssRNA. Processing of whole virus particles into SV or SU vaccines destroys the integrity of the viral particle and leaves the viral RNA prone to degradation or involves its active removal. Our

results show for a classic vaccine that the acquired immune response evoked by vaccination can be enhanced and steered by the innate immune system, which is triggered by interaction of an intrinsic vaccine component with a pattern recognition receptor (PRR). The insights presented here may be used to further improve the immune-stimulatory and dose-sparing properties of classic influenza vaccine formulations such as WIV, and will facilitate the development of new, even more powerful vaccines to face the next influenza pandemic."

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000138>

[Return to Top](#)

NEW DECISION MODEL SEEKS TO AVERT FLU VACCINE MISMATCH OF 2007-2008 SEASON

Vaccine Weekly

September 3, 2008

"To avoid producing vaccines that treat the wrong strains during flu season, the FDA should consider deferring some of its selections as well as other changes to the vaccine composition, according to a study by two decision analysts published in a journal of the Institute for Operations Research and the Management Sciences (INFORMS®)."

"There are two key takeaways from this research," says Prof. Kornish. "First, that the FDA should be willing to consider deferring a decision about which strains to include if early, conclusive evidence isn't available. This would mean accepting the proposition that identifying the right strain is worth waiting for, even if the supply produced won't be sufficient. It may be better to have some of the right vaccine than a lot of the wrong vaccine."

"Second, the FDA should reexamine its commitment to the rigid structure of the vaccine, with exactly one strain from each of three categories. For example, if there's agreement on choosing two of the strains and disagreement about which strain to pick for the third, why not include four?"

"Repeated Commit-or-Defer Decisions with a Deadline: The Influenza Vaccine Composition" is by Laura J. Kornish of the University of Colorado and Ralph L. Keeney of Duke University. It appears in the current issue of Operations Research." [Link not available.](#)

[Return to Top](#)

END of CB Daily Report.

Send subscription requests, unsubscribing requests, questions and comments to:

Steve Tesko: Steve.Tesko@anser.org

Copyright 2008. *Analytic Services Inc.*

[Analytic Services Inc. DMCA Copyright Notice: http://www.homelandsecurity.org/bulletin/Draft_ANSER_DCMA_Copyright_Notice.htm](http://www.homelandsecurity.org/bulletin/Draft_ANSER_DCMA_Copyright_Notice.htm)

Use of these news articles does not reflect official endorsement.

In accordance with Title 17 (USC), Section 107, this material is distributed without profit or payment and is intended for nonprofit research and educational purposes only.

Reproduction for private use or gain is subject to original copyright restrictions.

PRIVACY POLICY

Content provided in the *CB Daily Report* does not reflect the viewpoint(s) of Analytic Services Inc. Analytic Services Inc. does not share, publish, or in any way redistribute subscriber email addresses or any other personal information.