

18 August 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 #74

1. IOM HEARS DIVERSE FINDINGS ON PPE FOR FLU: *"The IOM panel learned, for example, that N95 respirators—whether fit-tested or not—reduced respiratory illnesses in a recent multiple-hospital study in China, whereas surgical masks were not effective. But other studies, focusing on household transmission of flu, suggested that both surgical masks and N95-type respirators are valuable."*

2. AVIAN INFLUENZA STRAIN PRIMES BRAIN FOR PARKINSON'S DISEASE: *"At least one strain of the H5N1 avian influenza virus leaves survivors at significantly increased risk for Parkinson's disease and possibly other neurological problems later in life, according to new research from St. Jude Children's Research Hospital."*

3. EFFECTIVE EXPRESSION OF RECOMBINANT CYTOTOXIC PROTEIN VIA ITS ATTACHMENT TO A POLYGLUTAMINE DOMAIN: *"Collectively, covalent fusion with polyQ or other aggregate-forming domains presents a novel approach for industrial production of cytotoxic proteins and also holds promise for gene therapy applications.."*

4. DICLOFENAC ENHANCES PROINFLAMMATORY CYTOKINE-INDUCED NITRIC OXIDE PRODUCTION THROUGH NF-KAPPA B SIGNALING IN CULTURED ASTROCYTES: *"This study demonstrates that iNOS and NO are induced in astrocyte cultures by proinflammatory cytokines. Addition of DCF further augments NO production. This effect is mediated via NF-kappa B signaling and leads to cell damage. The enhancement of DCF on NO production may explain the significant increase in the mortality rate of influenza-associated encephalopathy in patients treated with DCF."*

5. OSTEOPOROSIS DRUGS EFFECTIVE IN KILLING FLU VIRUSES: *"Two existing drugs used to treat osteoporosis may be effective in killing influenza viruses, including the new H1N1 swine flu and the H5N1 bird flu viruses, researchers in Hong Kong have found."*

6. LINK BETWEEN SWINE FLU JAB AND DEADLY SYNDROME WILL BE PROBED: *"The Health Protection Agency (HPA) has asked doctors to check for increases in a brain disorder called Guillain-Barré syndrome (GBS) once the national vaccination programme begins."*

7. SECOND WAVE OF SWINE FLU COULD OVERWHELM RESOURCES IN EUROPE AND NORTH AMERICA SAY CANADIAN EXPERTS: *"A panel of experts in Canada has written an article in a leading medical journal suggesting that if the H1N1 pandemic swine flu follows the same disease pattern in the northern hemisphere this fall as it has in the southern hemisphere, then resources in North America and Europe could be overwhelmed. The experts say strong leadership will be needed to mobilize effective immunization and other campaigns and they also call for the appointment of national and local leaders and champions."*

CB Daily Report

Chem-Bio News

IOM HEARS DIVERSE FINDINGS ON PPE FOR FLU

By Robert Roos

“A task force of the Institute of Medicine (IOM), charged with making recommendations about how to protect healthcare workers against novel H1N1 influenza, today heard a variety of evidence that respirators and masks can shield healthcare workers (HCWs) and others from getting respiratory illnesses.

The IOM panel learned, for example, that N95 respirators—whether fit-tested or not—reduced respiratory illnesses in a recent multiple-hospital study in China, whereas surgical masks were not effective. But other studies, focusing on household transmission of flu, suggested that both surgical masks and N95-type respirators are valuable.

Still another study, involving students at the University of Michigan, suggested that the combination of surgical masks and hand sanitizers may reduce the risk of respiratory illness, but the results didn't achieve statistical significance.

The committee also heard about the problems that some HCWs have with face protection—including a concern among pregnant HCWs in Singapore that wearing an N95 may cause fetal hypoxia.

Evidence on the clinical effectiveness of personal protective equipment (PPE) has been notoriously fuzzy. In the face of the murky science, the IOM has been asked to provide a recommendation to the Centers for Disease Control and Prevention (CDC) and the Occupational Safety and Health Administration (OSHA) by Sep 1.

The CDC currently recommends that HCWs who enter the room of a patient in isolation for suspected or confirmed novel H1N1 flu should wear an N95 respirator or equivalent protection.”

The full article can be found at:

<http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/aug1209iom-jw.html>

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AVIAN INFLUENZA STRAIN PRIMES BRAIN FOR PARKINSON'S DISEASE

Infection Control Today Magazine

August 12, 2009

“At least one strain of the H5N1 avian influenza virus leaves survivors at significantly increased risk for Parkinson's disease and possibly other neurological problems later in life, according to new research from St. Jude Children's Research Hospital.

In the Aug. 10 online early edition of the Proceedings of the National Academy of Sciences, researchers reported that mice which survived infection with an H5N1 flu strain were more likely than uninfected mice to develop brain changes associated with neurological disorders like Parkinson's and Alzheimer's diseases. Parkinson's and Alzheimer's involve loss of brain cells crucial to a variety of tasks, including movement, memory and intellectual functioning. The study revealed the H5N1 flu strain caused a 17 percent loss of the same neurons lost in Parkinson's as well as accumulation in certain brain cells of a protein implicated in both diseases.

"This avian flu strain does not directly cause Parkinson's disease, but it does make you more susceptible," said Richard Smeyne, PhD, associate member in St. Jude Developmental Neurobiology. Smeyne is the paper's senior author. "Around age 40, people start to get a decline in brain cells. Most people die before they lose enough neurons to get Parkinson's. But we believe this H5N1 infection changes the curve. It makes the brain more sensitive to another hit, possibly involving other environmental toxins," Smeyne explained.

Smeyne noted the work involved a single strain of the H5N1 flu virus, the A/Vietnam/1203/04 strain.

The threat posed by other viruses, including the current H1N1 pandemic flu virus, is still being studied.

Early indications are that the H1N1 pandemic strain carries a low neurologic risk, said Richard Webby, Ph.D., director of the World Health Organization Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds, which is based at St. Jude. Webby, who is also an associate member of the St. Jude Department of Infectious Diseases, was not involved in the H5N1 study led by Smeyne.

This study also supports the theory that a hit-and-run mechanism is at work in Parkinson's disease. The investigators believe the H5N1 infection sparks an immune response that persists long after the initial threat is gone, setting patients up for further devastating losses from a second hit, possibly from another infection, drug or environmental toxin. In this case, researchers believe the flu virus is the first hit that sets up development of Parkinson's at a later time."

The full article can be found at: <http://www.infectioncontrolday.com/hotnews/avian-flu-parkinsons-disease-link.html>

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EFFECTIVE EXPRESSION OF RECOMBINANT CYTOTOXIC PROTEIN VIA ITS ATTACHMENT TO A POLYGLUTAMINE DOMAIN

Biotech Law Weekly
August 21, 2009

Inadvertent cytotoxicity may hinder the expression of many recombinant proteins that are of industrial or medicinal importance. Here, we show that covalent binding of the influenza A cytotoxic protein M2 to a polyglutamine domain (polyQ-M2; QM2) results in significant delay of its cytotoxic effects when compared to wildtype protein (M2wt)."

"We also show that while expression of recombinant M2wt from A/WSN/1933 strain could not be attained in vaccinia virus (VV), polyQ-M2 was successfully expressed in this system. Moreover, we demonstrate that in cell culture, the polyQ domain is cleaved off following 48 h of expression, thus releasing free and active M2. Similarly, we show the spontaneous cleavage and polyQ release from fusion with another distinct polypeptide, green fluorescent protein (GFP). Expression of M2 from QM2 construct was more prolonged than one based on M2wt-expressing construct, markedly exceeding it at the later time points. Therefore, cell death caused by a toxic polypeptide may be suppressed via genetic fusion with polyQ, resulting in its enhanced expression, followed by slow release of the free polypeptide from the fusion."

"Collectively, covalent fusion with polyQ or other aggregate-forming domains presents a novel approach for industrial production of cytotoxic proteins and also holds promise for gene therapy applications.."

The full article can be found at: (P.O. Ilyinskii, et. al., "Effective Expression of Recombinant Cytotoxic Protein via Its Attachment to a Polyglutamine Domain". Omics - a Journal of Integrative Biology, 2009;13(3):211-217). Link not available.

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DICLOFENAC ENHANCES PROINFLAMMATORY CYTOKINE-INDUCED NITRIC OXIDE PRODUCTION THROUGH NF-KAPPA B SIGNALING IN CULTURED ASTROCYTES

Drug Week
August 21, 2009

"Recently, the number of reports of encephalitis/encephalopathy associated with influenza virus has increased, In addition, the use of a non-steroidal anti-inflammatory drug, diclofenac sodium (DCF), is associated with a significant increase in the mortality rate of influenza-associated encephalopathy. Activated astrocytes are a source of nitric oxide (NO), which is largely produced by inducible NO synthase (iNOS) in response to proinflammatory cytokines."

"Therefore, we investigated whether DCF enhances nitric oxide production in astrocytes stimulated with proinflammatory cytokines. We stimulated cultured rat astrocytes with three cytokines, interleukin-1 beta, tumor necrosis factor-alpha and interferon-gamma, and then treated the astrocytes with DCF or acetaminophen (N-acetyl-p-aminophenol: APAP). iNOS and NO production in astrocyte Cultures were induced by proinflammatory cytokines. The addition of DCF augmented NO production, but the addition of APAP did not. NF-kappa B inhibitors SN50 and MG132 inhibited iNOS gene expression in cytokine-stimulated astrocytes with or without DCF. Similarly, NF-kappa B p65 Stealth small interfering RNA suppressed iNOS gene expression in cytokine-stimulated astrocytes with or without DCF. LDH activity and DAPI staining showed that DCF induces cell damage in cytokine-stimulated astrocytes. An iNOS inhibitor, L-NMMA, inhibited the cytokine- and DCF-induced cell damage."

"This study demonstrates that iNOS and NO are induced in astrocyte cultures by proinflammatory cytokines. Addition of DCF further augments NO production. This effect is mediated via NF-kappa B signaling and leads to cell damage. The enhancement of DCF on NO production may explain the significant increase in the mortality rate of influenza-associated encephalopathy in patients treated with DCF."

The full article can be found at: (H. Kakita, et. al., "Diclofenac enhances proinflammatory cytokine-induced nitric oxide production through NF-kappa B signaling in cultured astrocytes". Toxicology and Applied Pharmacology, 2009;238(1):56-63). Link not available.

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OSTEOPOROSIS DRUGS EFFECTIVE IN KILLING FLU VIRUSES

By Tan Ee Lyn

Reuters

August 14, 2009

"Two existing drugs used to treat osteoporosis may be effective in killing influenza viruses, including the new H1N1 swine flu and the H5N1 bird flu viruses, researchers in Hong Kong have found.

The two drugs are pamidronate and zoledronate, which are marketed by Novartis AG under the brand names Aredia and Reclast, respectively.

In their experiment, the researchers exposed human cells that had been infected with the influenza viruses to the two drugs.

They observed that the drugs triggered extra production of a type of white blood cell called yd-T cells, which went on to kill human cells that were infected with the flu viruses."

The full article can be found at: <http://www.reuters.com/article/healthNews/idUSTRE57D1SJ20090814>

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LINK BETWEEN SWINE FLU JAB AND DEADLY SYNDROME WILL BE PROBED

By Laura Donnelly

The Telegraph (UK)

August 16, 2009

"The Health Protection Agency (HPA) has asked doctors to check for increases in a brain disorder called Guillain-Barré syndrome (GBS) once the national vaccination programme begins.

Its letter refers to the use of a swine flu vaccine in the United States in 1976, when 25 people died from GBS, while just one died from swine flu.

The syndrome, which can be fatal, attacks the lining of the nerves, causing paralysis and inability to breathe. Concerns have already been raised that the new vaccine has not been sufficiently tested and that the effects, especially on children, are unknown.”

The full article can be found at: <http://www.telegraph.co.uk/health/swine-flu/6036326/Link-between-swine-flu-jab-and-deadly-syndrome-will-be-probed.html>
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SECOND WAVE OF SWINE FLU COULD OVERWHELM RESOURCES IN EUROPE AND NORTH AMERICA SAY CANADIAN EXPERTS

Medical News Today
August 18, 2009

“A panel of experts in Canada has written an article in a leading medical journal suggesting that if the H1N1 pandemic swine flu follows the same disease pattern in the northern hemisphere this fall as it has in the southern hemisphere, then resources in North America and Europe could be overwhelmed. The experts say strong leadership will be needed to mobilize effective immunization and other campaigns and they also call for the appointment of national and local leaders and champions.

The editorial article was written by Dr Paul Hébert, Editor-in-Chief of the Canadian Medical Association Journal (CMAJ), and colleagues, and appears in the 17 August issue of the journal.

Hébert and colleagues wrote that vaccination must be the top priority against H1N1 flu this fall if the anticipated second wave of the pandemic virus follows the same pattern of spread in the northern hemisphere as it has in the southern hemisphere.

Canada and much of the Western world does not have much experience in implementing time-sensitive mass vaccination campaigns, wrote the panel. We already struggle to get vulnerable groups vaccinated for seasonal flu, they added.”

The full article can be found at: <http://www.medicalnewstoday.com/articles/160981.php>
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