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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 #56

1. HEALTH WORKERS ON TRIAL FOR VACCINE SCAM IN POLAND: "Nine health workers went on trial in northern Poland Monday accused of having tested a vaccine against bird flu on nearly 200 patients without their knowledge, court officials said."

2. CONCERNS ARISE OVER SYMPTOMLESS EGYPT BIRD FLU CASES: "The World Health Organisation is concerned some Egyptians may carry the highly pathogenic bird flu virus without showing symptoms, which could give it more of a chance to mutate to a strain that spreads easily among humans."

3. STRUCTURAL BASIS FOR DSRNA RECOGNITION BY NS1 PROTEIN OF INFLUENZA A VIRUS: "Agrobacterium co-infiltration assay further supports that the unique Arg38 pair plays important roles in dsRNA binding in vivo."

4. REVERSE GENETICS-GENERATED ELASTASE-DEPENDENT SWINE INFLUENZA VIRUSES ARE ATTENUATED IN PIGS: "Thus, these mutants may have the potential to serve as live attenuated vaccines."

5. COMPARISON OF VIRAL ISOLATION AND MULTIPLEX REAL-TIME REVERSE TRANSCRIPTION-PCR FOR CONFIRMATION OF RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA VIRUS DETECTION BY ANTIGEN IMMUNOASSAYS: "In a clinical setting where viral isolation is performed to confirm rapid antigen immunoassay results for these common respiratory viruses, one-step real-time reverse transcriptase PCR testing can be a more sensitive and timely confirmatory method."

6. FUNCTIONALLY DIVERSE SUBSETS IN CD4 T CELL RESPONSES AGAINST INFLUENZA: "Using influenza as an example, we also discuss the merits of employing reductionist approaches to explore how unique subsets of CD4 T cells are generated, what mechanisms of protection they use, and where they stand on the axes of differentiation that define T cell subsets."

7. BLOCKING DEVELOPMENT OF A CD8(+) T CELL RESPONSE BY TARGETING LYMPHATIC RECRUITMENT OF APC: "These results reveal lymphatic entry as an important step that may be rate limiting in the development of immunity and reconfirm its potential as a target for localized immunotherapy in inflammation and tissue rejection."

CB Daily Report

Chem-Bio News

HEALTH WORKERS ON TRIAL FOR VACCINE SCAM IN POLAND

Agence France-Presse on Yahoo! News
April 6, 2009

"Nine health workers went on trial in northern Poland Monday accused of having tested a vaccine against bird flu on nearly 200 patients without their knowledge, court officials said."

“The medical personnel are charged with administering a vaccine banned in Poland against the deadly H5N1 strain of bird flu that can be transmitted to humans.

The patients were paid for the vaccines, Polish news agency PAP reported.

They allegedly led their patients, many of them poor and homeless, to believe they were being vaccinated against ordinary flu.”

The full article can be found at: http://news.yahoo.com/s/afp/20090406/hl_afp/polandhealthflujustice
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CONCERNS ARISE OVER SYMPTOMLESS EGYPT BIRD FLU CASES

By Cynthia Johnston

Reuters

April 8, 2009

“The World Health Organisation is concerned some Egyptians may carry the highly pathogenic bird flu virus without showing symptoms, which could give it more of a chance to mutate to a strain that spreads easily among humans.

Whether such cases exist still has to be put to the test and will be the focus of a planned Egyptian government study backed by the global health body, said John Jabbour, a Cairo-based emerging diseases specialist at WHO.

"This is a concern only, now. It is a question to be asked," Jabbour told Reuters. He said a change in the pattern of human bird flu infections this year in Egypt had raised concerns about the existence of so-called sub clinical cases.”

“Jabbour said the rise in infections in children without similar cases among adults had triggered questions as to whether adults were being infected with the virus but not falling ill.”

The full article can be found at: <http://af.reuters.com/article/egyptNews/idAFL746788620090408?feedType=RSS&feedName=egyptNews&sp=true>

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STRUCTURAL BASIS FOR DSRNA RECOGNITION BY NS1 PROTEIN OF INFLUENZA A VIRUS

Health Risk Factor Week

April 14, 2009

“Here, we report the crystal structure of NS1A RNA-binding domain (RBD) bound to a double-stranded RNA (dsRNA) at 1.7 angstrom. NS1A RBD forms a homodimer to recognize the major groove of A-form dsRNA in a length-independent mode by its conserved concave surface formed by dimeric anti-parallel alpha-helices. dsRNA is anchored by a pair of invariable arginines (Arg38) from both monomers by extensive hydrogen bonds. In accordance with the structural observation, isothermal titration calorimetry assay shows that the unique Arg38-Arg38 pair and two Arg35-Arg46 pairs are crucial for dsRNA binding, and that Ser42 and Thr49 are also important for dsRNA binding.”

"Agrobacterium co-infiltration assay further supports that the unique Arg38 pair plays important roles in dsRNA binding in vivo."

The full article can be found at: (A. Cheng, et. al., "Structural basis for dsRNA recognition by NS1 protein of influenza A virus". Cell Research, 2009;19(2):187-195). Link not available

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REVERSE GENETICS-GENERATED ELASTASE-DEPENDENT SWINE INFLUENZA VIRUSES ARE ATTENUATED IN PIGS

Vaccine Weekly
April 8, 2009

"It has been shown that conversion of the haemagglutinin (HA) cleavage site from a trypsin-sensitive motif to an elastase-sensitive motif resulted in attenuated viruses in mouse models. However, application of this attenuation approach in a natural host has not been achieved yet. Here, we report that using reverse genetics, we generated two mutant SIVs derived from strain A/SW/SK/18789/02 (H1N1). Mutant A/SW/SK-R345V carries a mutation from arginine to valine at aa 345 of HA. Similarly, mutant A/SW/SK-R345A encodes alanine instead of arginine at aa 345 of HA. Our data showed that both mutants are solely dependent on neutrophil elastase cleavage in tissue culture. These tissue culture-grown mutant SIVs showed similar growth properties in terms of plaque size and growth kinetics to the wild-type virus. In addition, SIV mutants were able to maintain their genetic information after multiple passaging on MDCK cells. Furthermore, mutant SIVs were highly attenuated in pigs."

"Thus, these mutants may have the potential to serve as live attenuated vaccines."

The full article can be found at: (A. Masic, et. al., "Reverse genetics-generated elastase-dependent swine influenza viruses are attenuated in pigs". Journal of General Virology, 2009;90(Part 2):375-385). Link not available.

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COMPARISON OF VIRAL ISOLATION AND MULTIPLEX REAL-TIME REVERSE TRANSCRIPTION-PCR FOR CONFIRMATION OF RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA VIRUS DETECTION BY ANTIGEN IMMUNOASSAYS

Virus Weekly
April 14, 2009

"We evaluated the Prodesse ProFlu-1 real-time reverse transcription-PCR multiplex assay with the Smart-Cycler instrument for the detection of human respiratory syncytial virus (RSV) and influenza A and B viruses in comparison to conventional cell culture and antigen immunoassays with the BD Directigen A + B and Binax NOW RSV assays over two successive respiratory virus seasons. Ninety-two percent of the 361 specimens tested were nasopharyngeal aspirates obtained from individual patients, of which 119 were positive for RSV and 59 were positive for influenza virus," scientists in Kingston, Canada report (see also Respiratory Syncytial Virus).

"The median age of the patients whose specimens were positive for RSV and influenza virus were 6.3 months and 42.4 years, respectively. The specificity of all of the methods tested was $\geq 99\%$, and the individual sensitivities of NOW RSV, RSV culture, Directigen A + B, influenza virus culture, and the Proflu-1 PCR for influenza/RSV were 82% (95% confidence interval [CI], 73 to 88), 57% (95% CI, 44 to 69), 59% (95% CI, 44 to 72), 54% (95% CI, 38 to 69), and 98% (95% CI, 93 to 100)/95% (95% CI, 85 to 99), respectively."

"In a clinical setting where viral isolation is performed to confirm rapid antigen immunoassay results for these common respiratory viruses, one-step real-time reverse transcriptase PCR testing can be a more sensitive and timely confirmatory method."

The full article can be found at: (R,S. Liao, et. al., "Comparison of Viral Isolation and Multiplex Real-Time Reverse Transcription-PCR for Confirmation of Respiratory Syncytial Virus and Influenza Virus Detection by Antigen Immunoassays". Journal of Clinical Microbiology, 2009;47(3):527-532). Link not available.

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FUNCTIONALLY DIVERSE SUBSETS IN CD4 T CELL RESPONSES AGAINST INFLUENZA

Biotech Week

April 8, 2009

"However, our studies suggest that current paradigms explaining how memory CD4 T cells provide protection are inadequate. This is likely due to both the paucity of and heterogeneity of memory CD4 T cells observed *in vivo*, which make analysis extremely difficult. Here, we discuss new findings that indicate there is extensive functional heterogeneity within effector and memory CD4 T cell populations both *in vivo* and *in vitro*."

"Using influenza as an example, we also discuss the merits of employing reductionist approaches to explore how unique subsets of CD4 T cells are generated, what mechanisms of protection they use, and where they stand on the axes of differentiation that define T cell subsets."

The full article can be found at: (T.M. Strutt, et. al., "Functionally diverse subsets in CD4 T cell responses against influenza". *Journal of Clinical Immunology*, 2009;29(2):145-50). Link not available.

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BLOCKING DEVELOPMENT OF A CD8(+) T CELL RESPONSE BY TARGETING LYMPHATIC RECRUITMENT OF APC

Immunotherapy Weekly

April 8, 2009

"Generating a protective immune response to viral infection is known to depend upon the priming and clonal expansion of virus-specific CD8(+) T cells by Ag-loaded dendritic cells (DC) within secondary lymphoid tissue. However, the actual initiation of the response involves critical upstream events that control the recruitment of mature Ag-charged DC from the periphery via afferent lymphatics, events that are still only partly understood."

"Recent evidence has revealed that transmigration of lymphatic endothelium by DC is regulated by the adhesion molecules ICAM-1 and VCAM-1 both *in vitro* and *in vivo*. These findings imply that lymphatic entry may be an important rate-limiting step in primary immunity and a possible target for immune intervention. In this study, we have explored such possibilities using an F-5 TCR-transgenic mouse model to assess the contribution of lymphatic cell adhesion molecules in the CD8(+) T cell response to influenza virus nucleoprotein (NP). We show for the first time that immunization with ICAM-1- and VCAM-1-blocking mAbs can impair the T cell response in lymph node-draining sites of dermally administered nucleoprotein vaccine (MVA.HIVA.NP) by targeting lymphatic uptake of Ag-loaded DC ahead of other cell adhesion molecule-dependent events. These results reveal lymphatic entry as an important step that may be rate limiting in the development of immunity and reconfirm its potential as a target for localized immunotherapy in inflammation and tissue rejection."

The full article can be found at: (D. Teoh, et. al., "Blocking Development of a CD8(+) T Cell Response by Targeting Lymphatic Recruitment of APC". *Journal of Immunology*, 2009;182(4):2425-2431). Link not available.

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