

1 April 2010

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 - S&T Edition

- 1. CONTROLLED RELEASE ANTIBIOTICS FOR DRY POWDER LUNG DELIVERY:** *"The potential for antibiotic therapy, and specifically CR antibiotic therapy using dry powder inhalers, provides a promising route for the treatment of pulmonary infection."*
- 2. STRONG ANTIBODY RESPONSES INDUCED BY PROTEIN ANTIGENS CONJUGATED ONTO THE SURFACE OF LECITHIN-BASED NANOPARTICLES:** *"Immunization of mice with the PA-conjugated nanoparticles elicited a quick, strong, and durable anti-PA antibody response that afforded protection of the mice against a lethal dose of anthrax lethal toxin challenge."*
- 3. THE smpB-ssrA MUTANT OF YERSINIA PESTIS FUNCTIONS AS A LIVE ATTENUATED VACCINE TO PROTECT MICE AGAINST PULMONARY PLAGUE INFECTION:** *"Taken together, our results indicate that the smpB-ssrA mutant of Y. pestis possesses the desired qualities for a live attenuated cell-based vaccine against pneumonic plague."*
- 4. YERSINIA PESTIS WITH REGULATED DELAYED ATTENUATION AS A VACCINE CANDIDATE TO INDUCE PROTECTIVE IMMUNITY AGAINST PLAGUE:** *"Our results demonstrate that arabinose-dependent regulated crp expression is an effective strategy to attenuate Y. pestis while retaining strong immunogenicity, leading to protection against the pneumonic and bubonic forms of plague."*
- 5. DOXYCYCLINE LOADED POLY(ETHYLENE GLYCOL) HYDROGELS FOR HEALING VESICANT-INDUCED OCULAR WOUNDS:** *"The current studies demonstrate that the doxycycline-PEG hydrogels accelerate corneal wound healing after vesicant injury offering a therapeutic option for ocular mustard injuries."*
- 6. DEOXYNIVALENOL AND NIVALENOL INHIBIT LIPOPOLYSACCHARIDE-INDUCED NITRIC OXIDE PRODUCTION BY MOUSE MACROPHAGE CELLS:** *"These results indicate that DON and NIV inhibit the LPS-induced NO and IFN-beta production, which both play an important role for host protection against invading pathogens, and suggests that the inhibition of these factors may be involved in the immunotoxic effects of these mycotoxins."*
- 7. MUCOSAL PARAINFLUENZA VIRUS-VECTORED VACCINE AGAINST EBOLA VIRUS REPLICATES IN THE RESPIRATORY TRACT OF VECTOR-IMMUNE MONKEYS AND IS IMMUNOGENIC:** *"These data suggest that HPIV3/EboGP will be immunogenic in adults as well as children."*
- 8. p-HEXAFLUOROISOPROPANOL PHENYL COVALENTLY FUNCTIONALIZED SINGLE-WALLED CARBON NANOTUBES FOR DETECTION OF NERVE AGENTS:** *"Excellent sensitivity and selectivity of the hybridized SWCNT-HFIPPH devices suggest that it has great capability of detecting explosives and chemical warfare agents."*
- 9. BETA-GLUCURONIDASE ACTIVITY IS A SENSITIVE BIOMARKER TO ASSESS LOW-LEVEL ORGANOPHOSPHORUS INSECTICIDE EXPOSURE:** *"It was concluded that plasma BG activity is more sensitive biomarker as well as urinary OP metabolites than BChE for low-level exposure in humans."*

CB Daily Report

Chem-Bio News

CONTROLLED RELEASE ANTIBIOTICS FOR DRY POWDER LUNG DELIVERY

Pharma Law Weekly

March 23, 2010

"Microparticles containing 90:10 ratio of polyvinyl alcohol (PVA) and single antibiotics or combinations were obtained via spray drying. The microparticles were evaluated in terms of particle size, morphology, thermal properties, aerosol performance, and in vitro release. Analysis of the micro-particle morphology indicated comparable size distributions (2.04 +/- 0.06, 2.15 +/- 0.01, and 2.21 +/- 0.01 μm for ciprofloxacin, doxycycline, and co-spray-dried antibiotic formulations, respectively). Thermal analysis of the microparticles suggested similar responses, which were dominated by the endothermic peaks observed for PVA alone. Analysis of the aerosol performance suggested that the individual antibiotic formulations had different aerosol profiles that were dependent on the antibiotic used. In comparison, the combination CR antibiotics had identical aerosol profiles, suggesting that the microparticles were homogeneous. The release of antibiotics from the CR microparticles showed that $\leq 50\%$ was released over a 6-hour period in comparison to $\geq 90\%$ being released in the first hour for microparticles containing no PVA."

"The potential for antibiotic therapy, and specifically CR antibiotic therapy using dry powder inhalers, provides a promising route for the treatment of pulmonary infection."

The full article can be found at: (H. Adi, et. al., "Controlled release antibiotics for dry powder lung delivery". Drug Development and Industrial Pharmacy, 2010;36(1):119-126). Link not available.

[Return to Top](#)

STRONG ANTIBODY RESPONSES INDUCED BY PROTEIN ANTIGENS CONJUGATED ONTO THE SURFACE OF LECITHIN-BASED NANOPARTICLES

Pharma Law Weekly

March 23, 2010

"An accumulation of research over the years has demonstrated the utility of nanoparticles as antigen carriers with adjuvant activity. Herein we defined the adjuvanticity of a novel lecithin-based nanoparticle engineered from emulsions."

"The nanoparticles were spheres of around 200 nm. Model protein antigens, bovine serum albumin (BSA) or Bacillus anthracis protective antigen (PA) protein, were covalently conjugated onto the nanoparticles. Mice immunized with the BSA-conjugated nanoparticles developed strong anti-BSA antibody responses comparable to that induced by BSA adjuvanted with incomplete Freund's adjuvant and 6.5-fold stronger than that induced by BSA adsorbed onto aluminum hydroxide. Immunization of mice with the PA-conjugated nanoparticles elicited a quick, strong, and durable anti-PA antibody response that afforded protection of the mice against a lethal dose of anthrax lethal toxin challenge. The potent adjuvanticity of the nanoparticles was likely due to their ability to move the antigens into local draining lymph nodes, to enhance the uptake of the antigens by antigen-presenting cells (APCs), and to activate APCs."

"This novel nanoparticle system has the potential to serve as a universal protein-based vaccine carrier capable of inducing strong immune responses."

The full article can be found at: (B.R.Sloat, et. al., "Strong antibody responses induced by protein antigens conjugated onto the surface of lecithin-based nanoparticles". Journal of Controlled Release, 2010;141(1):93-100). Link not available.

[Return to Top](#)

THE *smpB-ssrA* MUTANT OF YERSINIA PESTIS FUNCTIONS AS A LIVE ATTENUATED VACCINE TO PROTECT MICE AGAINST PULMONARY PLAGUE INFECTION

World Disease Weekly

March 23, 2010

"The bacterial SmpB-SsrA system is a highly conserved translational quality control mechanism that helps maintain the translational machinery at full capacity. Here we present evidence to demonstrate that the smpB-ssrA genes are required for pathogenesis of *Yersinia pestis*, the causative agent of plague."

"We found that disruption of the smpB-ssrA genes leads to reduction in secretion of the type III secretion-related proteins YopB, YopD, and LcrV, which are essential for virulence. Consistent with these observations, the smpB-ssrA mutant of *Y. pestis* was severely attenuated in a mouse model of infection via both the intranasal and intravenous routes. Most significantly, intranasal vaccination of mice with the smpB-ssrA mutant strain of *Y. pestis* induced a strong antibody response. The vaccinated animals were well protected against subsequent lethal intranasal challenges with virulent *Y. pestis*."

"Taken together, our results indicate that the smpB-ssrA mutant of *Y. pestis* possesses the desired qualities for a live attenuated cell-based vaccine against pneumonic plague."

The full article can be found at: (N.A. Okan, et. al., "The smpB-ssrA mutant of *Yersinia pestis* functions as a live attenuated vaccine to protect mice against pulmonary plague infection". *Infection and Immunity*, 2010;78(3):1284-93). Link not available.

[Return to Top](#)

YERSINIA PESTIS WITH REGULATED DELAYED ATTENUATION AS A VACCINE CANDIDATE TO INDUCE PROTECTIVE IMMUNITY AGAINST PLAGUE

Health Risk Factor Week

March 23, 2010

"Two mutant strains of *Yersinia pestis* KIM5+, a Deltacr_p mutant and a mutant with arabinose-dependent regulated delayed-shutoff crp expression (araC P(BAD) crp), were constructed, characterized in vitro, and evaluated for virulence, immunogenicity, and protective efficacy in mice. Both strains were highly attenuated by the subcutaneous (s.c.) route."

"The 50% lethal doses (LD₅₀.) of the Deltacr_p and araC P(BAD) crp mutants were approximately 1,000,000-fold and 10,000-fold higher than those of *Y. pestis* KIM5+, respectively, indicating that both strains were highly attenuated. Mice vaccinated s.c. with 3.8 x 10⁷ CFU of the Deltacr_p mutant developed high anti-*Y. pestis* and anti-LcrV serum IgG titers, both with a strong Th2 bias, and induced protective immunity against subcutaneous challenge with virulent *Y. pestis* (80% survival) but no protection against pulmonary challenge. Mice vaccinated with 3.0 x 10⁴ CFU of the araC P(BAD) crp mutant also developed high anti-*Y. pestis* and anti-LcrV serum IgG titers but with a more balanced Th1/Th2 response. This strain induced complete protection against s.c. challenge and partial protection (70% survival) against pulmonary challenge."

"Our results demonstrate that arabinose-dependent regulated crp expression is an effective strategy to attenuate *Y. pestis* while retaining strong immunogenicity, leading to protection against the pneumonic and bubonic forms of plague."

The full article can be found at: (W. Sun, et. al., "Yersinia pestis with regulated delayed attenuation as a vaccine candidate to induce protective immunity against plague". *Infection and Immunity*, 2010;78(3):1304-13). Link not available.

[Return to Top](#)

DOXYCYCLINE LOADED POLY(ETHYLENE GLYCOL) HYDROGELS FOR HEALING VESICANT-INDUCED OCULAR WOUNDS

Pharma Law Weekly

March 23, 2010

"Half mustard (CEES) and nitrogen mustard (NM) are commonly used surrogates and vesicant analogs of

the chemical warfare agent sulfur mustard. In the current study, in situ forming poly(ethylene glycol) (PEG)-based doxycycline hydrogels are developed and evaluated for their wound healing efficacy in CEES and NM-exposed rabbit corneas in organ culture."

"The hydrogels, characterized by UV-Vis spectrophotometry, rheometry, and swelling kinetics, showed that the hydrogels are optically transparent, have good mechanical strength and a relatively low degree of swelling (<7%). In vitro doxycycline release from the hydrogel disks (0.25% w/v) was found to be biphasic with release half times of similar to 12 and 72 h, respectively, with 80-100% released over a 7-day period. Permeation of doxycycline through vesicant wounded corneas was found to be 2.5 to 3.4 fold higher than non-wounded corneas. Histology and immunofluorescence studies showed a significant reduction of matrix metalloproteinase-9 (MMP-9) and improved healing of vesicant-exposed corneas by doxycycline hydrogels compared to a similar dose of doxycycline delivered in phosphate buffered saline (PBS, pH 7.4)."

"The current studies demonstrate that the doxycycline-PEG hydrogels accelerate corneal wound healing after vesicant injury offering a therapeutic option for ocular mustard injuries."

The full article can be found at: (S.S. Anumolu, et. al., "Doxycycline loaded poly(Ethylene glycol) hydrogels for healing vesicant-induced ocular wounds". Biomaterials, 2010;31(5):964-974). Link not available.

[Return to Top](#)

DEOXYNIVALENOL AND NIVALENOL INHIBIT LIPOPOLYSACCHARIDE-INDUCED NITRIC OXIDE PRODUCTION BY MOUSE MACROPHAGE CELLS

Drug Week

March 19, 2010

"Deoxynivalenol (DON) and nivalenol (NIV), trichothecene mycotoxins, are secondary metabolites produced by Fusarium fungi. Trichothecene mycotoxins cause immune dysfunction, thus leading to diverse responses to infection."

"The present study evaluated the effect of DON and NIV on nitric oxide (NO) production by RAW264 cells stimulated with lipopolysaccharide (LPS). LPS-induced NO production was reduced in the presence of these toxins. The transcriptional activation and expression of inducible NO synthase (iNOS) by LPS were also repressed by these toxins. DON or NIV inhibited LPS-induced expression of interferon-beta (IFN-beta), which plays an indispensable role in LPS-induced iNOS expression."

"These results indicate that DON and NIV inhibit the LPS-induced NO and IFN-beta production, which both play an important role for host protection against invading pathogens, and suggests that the inhibition of these factors may be involved in the immunotoxic effects of these mycotoxins."

The full article can be found at: (K. Sugiyama, et. al., "Deoxynivalenol and nivalenol inhibit lipopolysaccharide-induced nitric oxide production by mouse macrophage cells". Toxicology Letters, 2010;192(2):150-4). Link not available.

[Return to Top](#)

MUCOSAL PARAINFLUENZA VIRUS-VECTORED VACCINE AGAINST EBOLA VIRUS REPLICATES IN THE RESPIRATORY TRACT OF VECTOR-IMMUNE MONKEYS AND IS IMMUNOGENIC

Blood Weekly

April 1, 2010

"We previously used human parainfluenza virus type 3 (HPIV3) as a vector to express the Ebola virus (EBOV) GP glycoprotein. The resulting HPIV3/EboGP vaccine was immunogenic and protective against EBOV challenge in a non-human primate model."

"However, it remained unclear whether the vaccine would be effective in adults due to preexisting

immunity to HPIV3. Here, the immunogenicity of HPIV3/EboGP was compared in HPIV3-naive and HPIV3-immune Rhesus monkeys. After a single dose of HPIV3/EboGP, the titers of EBOV-specific serum ELISA or neutralization antibodies were substantially less in HPIV3-immune animals compared to HPIV3-naive animals. However, after two doses, which were previously determined to be required for complete protection against EBOV challenge, the antibody titers were indistinguishable between the two groups. The vaccine virus appeared to replicate, at a reduced level, in the respiratory tract despite the preexisting immunity. This may reflect the known ability of HPIV3 to re-infect and may also reflect the presence of EBOV GP in the vector virion, which confers resistance to neutralization in vitro by HPIV3-specific antibodies."

"These data suggest that HPIV3/EboGP will be immunogenic in adults as well as children."

The full article can be found at: (A.A. Bukreyev, et. al., "Mucosal parainfluenza virus-vectored vaccine against Ebola virus replicates in the respiratory tract of vector-immune monkeys and is immunogenic". *Virology*, 2010;399(2):290-8). Link not available.

[Return to Top](#)

p-HEXAFLUOROISOPROPANOL PHENYL COVALENTLY FUNCTIONALIZED SINGLE-WALLED CARBON NANOTUBES FOR DETECTION OF NERVE AGENTS

Journal of Technology & Science

April 4, 2010

"Novel p-hexafluoroisopropanol phenyl (HFIPPH) covalently functionalized single-walled carbon nanotubes (SWCNTs) have been prepared through in situ diazonium. reaction between SWCNTs and p-hexafluoroisopropanol aniline; moreover, the hybridized material can be characterized by ultraviolet vision near infrared spectroscopy, Raman spectroscopy, thermogravimetric analysis, X-ray photoelectron spectrometry field-emission scanning electron microscopy and high resolution transmission electron microscopy."

"that the one-dimensional electronic structures of the functionalized tubes could be basically maintained without damaging their electronic properties. Considered that strong hydrogen-bonding can be formed between hexafluoroisopropanol groups and dimethyl methylphosphonate (DMMP) (simulant of nerve agent sarin), the SWCNT-HFIPPH sensing devices have been fabricated and employed to detect DMMP."

"Excellent sensitivity and selectivity of the hybridized SWCNT-HFIPPH devices suggest that it has great capability of detecting explosives and chemical warfare agents."

The full article can be found at: (L.T. Kong, et. al., "p-Hexafluoroisopropanol phenyl covalently functionalized single-walled carbon nanotubes for detection of nerve agents". *Carbon*, 2010;48(4):1262-1270). Link not available.

[Return to Top](#)

BETA-GLUCURONIDASE ACTIVITY IS A SENSITIVE BIOMARKER TO ASSESS LOW-LEVEL ORGANOPHOSPHORUS INSECTICIDE EXPOSURE

Drug Week

March 19, 2010

"Acetylcholinesterase and butyrylcholinesterase (BChE) activities in blood are widely used as the biomarkers for organophosphorus insecticide (OP) exposure. In the present study, we conducted a cross-sectional study to evaluate plasma beta-glucuronidase (BG), a sensitive biomarker candidate for OP exposure, BChE activities and urinary dialkyl phosphates (DAPs), OP metabolites."

"We assessed the relationship between these biomarker levels in the following groups: 32 controls (control), 21 pest control operators and their co-workers who had not sprayed OPs within 3 days prior to sample collection (PCO1), and 21 pest control operators who sprayed OPs within those 3 days (PCO2). Logarithmically transformed age-adjusted means of DAPs were 3.88, 5.62 and 6.45 nmol/g creatinine for

control, PCO1 and PCO2, respectively ($p < 0.001$ for difference, $p < 0.001$ for trend). Logarithmically transformed age-adjusted means of BG were 1.40, 1.52 and 1.85 micromol/L/h for control, PCO1 and PCO2, respectively. BG activity, but not BChE, was increased according to their OP exposure level ($p = 0.038$ for difference, $p = 0.026$ for trend)."

"It was concluded that plasma BG activity is more sensitive biomarker as well as urinary OP metabolites than BChE for low-level exposure in humans."

The full article can be found at: (J. Ueyama, et. al., "Beta-glucuronidase activity is a sensitive biomarker to assess low-level organophosphorus insecticide exposure". *Toxicology Letters*, 2010;193(1):115-9). 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.