

10 December 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 – S&T Edition

1. CHANGING GENOTYPES OF CHOLERA TOXIN (CT) OF VIBRIO CHOLERAE O139 IN BANGLADESH AND DESCRIPTION OF THREE NEW CT GENOTYPES: *"This change and the impact that it causes to the epidemiology of cholera caused by O139 should be closely monitored."*

2. ANALYSIS OF THE FC GAMMA RECEPTOR-DEPENDENT COMPONENT OF NEUTRALIZATION MEASURED BY ANTHRAX TOXIN NEUTRALIZATION ASSAYS: *"These findings should be considered when interpreting anthrax toxin neutralization assay output."*

3. POLY-GAMMA-D-GLUTAMIC ACID AND PROTECTIVE ANTIGEN CONJUGATE VACCINES INDUCE FUNCTIONAL ANTIBODIES AGAINST THE PROTECTIVE ANTIGEN AND CAPSULE OF BACILLUS ANTHRACIS IN GUINEA-PIGS AND RABBITS: *"Our results demonstrate that PA-PGA conjugate vaccines are effective in the guinea-pig model, in addition to the previously reported mouse model."*

4. IDENTIFICATION OF BACILLUS ANTHRACIS BY USING MATRIX-ASSISTED LASER DESORPTION IONIZATION-TIME OF FLIGHT MASS SPECTROMETRY AND ARTIFICIAL NEURAL NETWORKS: *"For the identification of B. anthracis, independent validation of optimized ANN models yielded a diagnostic sensitivity of 100% and a specificity of 100%."*

5. POLYMERS MOP UP RADIOACTIVE ISOTOPES: *"Together with his colleague Sevilimendu Narasimhan from the Bhabha Atomic Research Center in Kalpakkam, India, the chemist PD Dr. Börje Sellergren from the Institute of Environmental Research at Technische Universität Dortmund has developed a new method to reduce the amount of this radioactive waste considerably. His approach: small beads consisting of a special polymer which "fishes" the radioactivity out of the water."*

6. DISINFECTING IN THE DARK: *"An efficient titania photocatalyst that continues to work when the lights go out gives continuous protection against bacteria, say scientists in the US."*

7. EXPANDING THE INFECTION RESEARCH KIT: *"Lindhorst and colleagues have created new in vitro tools that use plates coated with sugar mannose, mimicking a cell's surface, and two different methods of detecting adhered bacteria. The new methods are 'more like in real biology, with adhesion to surfaces [which can be compared with cells],' says Lindhorst."*

CB Daily Report

Chem-Bio News

CHANGING GENOTYPES OF CHOLERA TOXIN (CT) OF VIBRIO CHOLERAE O139 IN BANGLADESH AND DESCRIPTION OF THREE NEW CT GENOTYPES

Immunotherapy Weekly
December 2, 2009

"We determined the genotype of cholera toxin by amplifying and sequencing the B-subunit in a sequential collection of 90 strains of Vibrio cholerae O139 isolated over the past 13 years since its first

description in 1992. Representative strains isolated during 1993-1997 harboured ctxB of El Tor type (genotype 3)."

"Twenty-six strains isolated during 1999, 2001, 2005 and three strains isolated in 1998, 2000 and 2002 were identified to belong to new ctxB genotypes 4 and 5, respectively. Genotype 5 was similar to genotype 1 except at position 28 (D & rarr; A). The genotype 6 was similar to genotype 4 except at position 34 (H & rarr; P). The implication of switch in terms of function of the toxin and its impact on human disease is unclear. How this change has influenced their prevalence relative to that of V. cholerae O1 in human infection is also not clear. The other common virulence gene clusters including the Vibrio pathogenicity island-1, Vibrio seventh pandemic island (VSP)-I and VSP-II of V. cholerae O139 did not show any remarkable difference from that of the O1 El Tor strains. Overall, the majority of the O139 strains tested in this study were similar to the El Tor strains but had altered ctxB genotype."

"This change and the impact that it causes to the epidemiology of cholera caused by O139 should be closely monitored."

The full article can be found at: (N.A. Bhuiyan, et. al., "Changing genotypes of cholera toxin (CT) of Vibrio cholerae O139 in Bangladesh and description of three new CT genotypes". Fems Immunology and Medical Microbiology, 2009;57(2):136-141). Link not available.

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ANALYSIS OF THE FC GAMMA RECEPTOR-DEPENDENT COMPONENT OF NEUTRALIZATION MEASURED BY ANTHRAX TOXIN NEUTRALIZATION ASSAYS

Medical Letter on the CDC & FDA

November 29, 2009

"Anthrax toxin neutralization assays are used to measure functional antibody levels elicited by anthrax vaccines in both preclinical and clinical studies. In this study, we investigated the magnitude and molecular nature of Fc gamma (Fc gamma) receptor-dependent toxin neutralization observed in commonly used forms of the anthrax toxin neutralization assay."

"Significantly more Fc gamma receptor-dependent neutralization was observed in the J774A.1 cell-based assay than in the RAW 264.7 cell-based assay, a finding that could be due to the larger numbers of Fc gamma receptors that we found on J774A.1 cells by using flow cytometry. Thus, the extent to which Fc gamma receptor-dependent neutralization contributes to the total neutralization measured by the assay depends on the specific cell type utilized in the assay. Using Fc gamma receptor blocking monoclonal antibodies, we found that at least three murine Fc gamma receptor classes, IIB, III, and IV, can contribute to Fc gamma receptor-dependent neutralization. When antibodies elicited by immunization of rabbits with protective-antigen-based anthrax vaccines were analyzed, we found that the magnitude of Fc gamma receptor-dependent neutralization observed in the J774A.1 cell-based assay was dependent on the concentration of protective antigen utilized in the assay. Our results suggest that the characteristics of the antibodies analyzed in the assay (e. g., species of origin, isotype, and subclass), as well as the assay design (e. g., cell type and protective antigen concentration), could significantly influence the extent to which Fc gamma receptor-dependent neutralization contributes to the total neutralization measured by anthrax toxin neutralization assays."

"These findings should be considered when interpreting anthrax toxin neutralization assay output."

The full article can be found at: (A. Verma, et. al., "Analysis of the Fc Gamma Receptor-Dependent Component of Neutralization Measured by Anthrax Toxin Neutralization Assays". Clinical and Vaccine Immunology, 2009;16(10):1405-1412). Link not available.

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POLY-GAMMA-D-GLUTAMIC ACID AND PROTECTIVE ANTIGEN CONJUGATE VACCINES INDUCE FUNCTIONAL ANTIBODIES AGAINST THE PROTECTIVE ANTIGEN AND CAPSULE OF BACILLUS

ANTHRACIS IN GUINEA-PIGS AND RABBITS

Medical Letter on the CDC & FDA

December 6, 2009

"The three components of the exotoxin, protective antigen (PA), lethal factor and edema factor act in a binary combination, which results in massive edema and organ failure in the progress of anthrax disease. The antiphagocytic PGA capsule disguises the bacilli from immune surveillance and allows unimpeded growth of bacilli in the host. Because PA can elicit a protective immune response, it has been a target of the anthrax vaccine. In addition to PA, efforts have been made to include PGA as a component of the anthrax vaccine. In this study, we report that PA-PGA conjugates induce expressions of anti-PA, anti-PGA and toxin-neutralizing antibodies in guinea-pigs and completely protect guinea-pigs against a 50 x LD50 challenge with fully virulent B. anthracis spores. Polyclonal rabbit antisera produced against either PA or ovalbumin conjugated to a PGA-15mer offer a partial passive protection to guinea-pigs against B. anthracis infection, indicating that anti-PGA antibodies play a protective role."

"Our results demonstrate that PA-PGA conjugate vaccines are effective in the guinea-pig model, in addition to the previously reported mouse model."

The full article can be found at: (D.Y. Lee, et. al., "Poly-gamma-d-glutamic acid and protective antigen conjugate vaccines induce functional antibodies against the protective antigen and capsule of Bacillus anthracis in guinea-pigs and rabbits". Fems Immunology and Medical Microbiology, 2009;57(2):165-172). Link not available.

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IDENTIFICATION OF BACILLUS ANTHRACIS BY USING MATRIX-ASSISTED LASER DESORPTION IONIZATION-TIME OF FLIGHT MASS SPECTROMETRY AND ARTIFICIAL NEURAL NETWORKS

Medical Letter on the CDC & FDA

December 13, 2009

"This report demonstrates the applicability of a combination of matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (MS) and chemometrics for rapid and reliable identification of vegetative cells of the causative agent of anthrax, Bacillus anthracis. Bacillus cultures were prepared under standardized conditions and inactivated according to a recently developed MS-compatible inactivation protocol for highly pathogenic microorganisms."

"MALDI-TOF MS was then employed to collect spectra from the microbial samples and to build up a database of bacterial reference spectra. This database comprised mass peak profiles of 374 strains from Bacillus and related genera, among them 102 strains of B. anthracis and 121 strains of B. cereus. The information contained in the database was investigated by means of visual inspection of gel view representations, univariate t tests for biomarker identification, unsupervised hierarchical clustering, and artificial neural networks (ANNs). Analysis of gel views and independent t tests suggested B. anthracis- and B. cereus group-specific signals. For example, mass spectra of B. anthracis exhibited discriminating biomarkers at 4,606, 5,413, and 6,679 Da. A systematic search in proteomic databases allowed tentative assignment of some of the biomarkers to ribosomal protein or small acid-soluble proteins. Multivariate pattern analysis by unsupervised hierarchical cluster analysis further revealed a subproteome-based taxonomy of the genus Bacillus. Superior classification accuracy was achieved when supervised ANNs were employed."

"For the identification of B. anthracis, independent validation of optimized ANN models yielded a diagnostic sensitivity of 100% and a specificity of 100%."

The full article can be found at: (P. Lasch, et. al., "Identification of Bacillus anthracis by Using Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry and Artificial Neural Networks". Applied and Environmental Microbiology, 2009;75(22):7229-7242). Link not available.

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POLYMERS MOP UP RADIOACTIVE ISOTOPES

NanoTechwire.com
December 06, 2009

“Nuclear Power could solve our energy problems but it has rather nasty by-products: radioactive waste. And this does not only concern the old core rods whose disposal causes a lot of problems. Reactor operation also brings along extensive amounts of low-level waste, especially contaminated cooling water. This water also has to be costly disposed of in compliance with rigorous security restrictions. Together with his colleague Sevilimendu Narasimhan from the Bhabha Atomic Research Center in Kalpakkam, India, the chemist PD Dr. Börje Sellergren from the Institute of Environmental Research at Technische Universität Dortmund has developed a new method to reduce the amount of this radioactive waste considerably. His approach: small beads consisting of a special polymer which "fishes" the radioactivity out of the water.”

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“To overcome this problem, Sellergren and Narasimhan were looking for a material which binds cobalt while ignoring iron. They developed a special polymer which is made through a procedure called “molecular imprinting”. This polymer is made in an environment containing cobalt. Then the cobalt-ions are extracted with hydrochloric acid, meaning that they are virtually “washed out”. The resulting cobalt-sized holes – the imprinting – are able to trap cobalt – and just cobalt – in other environments. The result: a small amount of this polymer can mop up a large amount of radioactive isotopes.

The team is now forming the polymer into small beads that can pass through the cooling system of a nuclear-power station. They expect that it would be more economical and environment-friendly to concentrate radioactivity into such beads than to dispose of large amounts of low-level waste. There obviously is a demand. Some 40 new nuclear-power stations are being built around the world. And the International Atomic Energy Agency estimates that a further 70 will be built in the next 15 years.”

The full article can be found at: <http://nanotechwire.com/news.asp?nid=9087>
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DISINFECTING IN THE DARK

By Fay Nolan-Neylan
Highlights in Chemical Science
December 04, 2009

“An efficient titania photocatalyst that continues to work when the lights go out gives continuous protection against bacteria, say scientists in the US.

Photocatalysts create electron-hole pairs which generate free radicals able to undergo secondary reactions such as killing bacteria. Most current visible-light photocatalytic disinfection materials are based on anion-doped titanium oxide, explains Jian-Ku Shang at the University of Illinois at Urbana-Champaign. But they only operate in the light when electron and hole pairs are produced.

Shang and colleagues added palladium oxide PdO nanoparticles to nitrogen-doped titania. The nanoparticles act as a photoelectron trap and under visible light illumination, electrons flow from the titania to the PdO nanoparticles. When the light is switched off a catalytic memory effect makes the PdO nanoparticles release the electrons back slowly. The photocatalyst continues to operate in the dark, limiting the growth of bacteria for up to 24 hours.”

The full article can be found at:
http://www.rsc.org/Publishing/ChemScience/Volume/2010/01/Dark_disinfection.asp
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EXPANDING THE INFECTION RESEARCH KIT

Frances Galvin
Highlights in Chemical Biology
December 08, 2009

“Scientists in Germany and Denmark have developed two complementary techniques to examine how bacteria cause infections.”

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“Two common assays to investigate the bacteria's binding use either guinea pig blood or ELISA technology, where a series of antibodies and an enzyme detect binding. But these techniques are not ideal as the first does not allow testing of adhesion to surfaces and in the second different antibodies are needed for each different application and the binding cannot be directly detected, explains Thisbe Lindhorst at the Otto Diels Institute of Organic Chemistry, Kiel, Germany.

Lindhorst and colleagues have created new in vitro tools that use plates coated with sugar mannose, mimicking a cell's surface, and two different methods of detecting adhered bacteria. The new methods are 'more like in real biology, with adhesion to surfaces [which can be compared with cells],' says Lindhorst.

The first method uses the molecule biotin to label E. coli bacteria, which are allowed to bind to either the surface or inhibitor in solution. An oxidising enzyme linked to a protein with high affinity for biotin can then be added and the bacteria binding can be detected by the change in the light absorbance caused by enzyme oxidation of an added substrate. The second assay enables direct detection of the binding, by growing bacteria tagged with green fluorescent protein that can be detected directly by the fluorescence readout.”

The full article can be found at:

http://www.rsc.org/Publishing/Journals/cb/Volume/2010/01/infection_kit.asp

The original article can be found at: <http://www.rsc.org/Publishing/Journals/CC/article.asp?doi=b922525k>

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