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## **Chem-Bio News– S&T Edition**

### **1. BOTULINUM NEUROTOXIN DEVOID OF RECEPTOR BINDING DOMAIN**

**TRANSLOCATES ACTIVE PROTEASE:** *“These findings indicate that, in addition to its individual functions, each module [of the tri-modular protein] acts as a chaperone for the others, working in concert to achieve productive intoxication.”*

### **2. MUCOSAL IMMUNIZATION WITH ATTENUATED SALMONELLA ENTERICA SEROVAR TYPHI EXPRESSING PROTECTIVE ANTIGEN OF ANTHRAX TOXIN (PA83) PRIMES MONKEYS FOR ACCELERATED SERUM ANTIBODY RESPONSES TO**

**PARENTERAL PA83 VACCINE:** *“In nonhuman primates, the success of this anthrax vaccine strategy based on heterologous mucosal priming followed by a parenteral subunit vaccine booster paves the way for clinical trials.”*

**3. SELECTION TOOL FOR FOODBORNE NOROVIRUS OUTBREAKS:** *“Our study demonstrates the added value of a reporting system amalgamated across countries; the FBVE [Foodborne Viruses in Europe] dataset can form the basis of this tool, which may be a first step towards detection of diffuse outbreaks.”*

**4. TOWARDS QUORUM-QUENCHING CATALYTIC ANTIBODIES:** *“The development of a novel method to attenuate bacterial virulence is reported, which is based upon the use of designed transition-state analogues to select human catalytic antibodies capable of degrading bacterial quorum-sensing molecules.”*

### **5. MEASUREMENT OF NITROGEN MUSTARD DEGRADATION PRODUCTS BY POLY (DIMETHYLSILOXANE) MICROCHIP ELECTROPHORESIS WITH CONTACTLESS CONDUCTIVITY DETECTION:**

*“Compared to conventional analytical methods, this miniaturized system offers promise for on-site monitoring of degradation products of the nitrogen mustard class of chemical warfare agents, with advantages of cost-effective construction., simple operation, portability, and small required sample volumes.”*

# CB Daily Report

## Chem-Bio News

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### **BOTULINUM NEUROTOXIN DEVOID OF RECEPTOR BINDING DOMAIN TRANSLOCATES ACTIVE PROTEASE**

By Audrey Fischer, Darren J. Mushrush, D. Borden Lacy, Mauricio Montal  
PLoS Pathogens  
December, 2008

"Clostridium botulinum neurotoxin (BoNT) causes flaccid paralysis by disabling synaptic exocytosis. Intoxication requires the tri-modular protein to undergo conformational changes in response to pH and redox gradients across endosomes, leading to the formation of a protein-conducting channel. The ~50 kDa light chain (LC) protease is translocated into the cytosol by the ~100 kDa heavy chain (HC), which consists of two modules: the N-terminal translocation domain (TD) and the C-terminal Receptor Binding Domain (RBD). Here we exploited the BoNT modular design to identify the minimal requirements for channel activity and LC translocation in neurons. Using the combined detection of substrate proteolysis and single-channel currents, we showed that a di-modular protein consisting only of LC and TD was sufficient to translocate active protease into the cytosol of target cells. The RBD is dispensable for cell entry, channel activity, or LC translocation; however, it determined a pH threshold for channel formation. These findings indicate that, in addition to its individual functions, each module acts as a chaperone for the others, working in concert to achieve productive intoxication."

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000245;jsessionid=9B61DB46334122A4595B18309F07C56E>

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### **MUCOSAL IMMUNIZATION WITH ATTENUATED SALMONELLA ENTERICA SEROVAR TYPHI EXPRESSING PROTECTIVE ANTIGEN OF ANTHRAX TOXIN (PA83) PRIMES MONKEYS FOR ACCELERATED SERUM ANTIBODY RESPONSES TO PARENTERAL PA83 VACCINE**

By James E. Galen, Magaly Chinchilla, Marcela F. Pasetti, Jin Yuan Wang, Licheng Zhao, Ivonne Arciniega-Martinez, David J. Silverman, and Myron M. Levine  
The Journal of Infectious Diseases  
December 19, 2008

"Salmonella enterica serovar Typhi vaccine strain CVD 908-htrA was genetically engineered for stable plasmid-based expression of protective antigen of anthrax toxin (PA83) fused with the export protein ClyA (ClyA-PA83). The priming potential of CVD 908-htrA expressing ClyA-PA83 was assessed in 12 rhesus and 20 cynomolgus macaques that were immunized mucosally (i.e., intranasally) on days 0 and 14. A parenteral booster with purified PA83 plus alum was given to rhesus macaques on days 42 and 225; cynomolgus monkeys received a

booster with either PA or licensed anthrax vaccine (BioThrax; Emergent Biosolutions) only one time, 3 months after priming. Monkeys primed with *S. Typhi* expressing ClyA-PA83 developed high levels of serum toxin-neutralization activity (TNA) antibodies (50% effective dose [ED50], > ), 7 days after receipt of the booster, whereas unprimed controls lacked serum TNA (ED50, 0). In nonhuman primates, the success of this anthrax vaccine strategy based on heterologous mucosal priming followed by a parenteral subunit vaccine booster paves the way for clinical trials."

The full article can be found at: <http://www.journals.uchicago.edu/doi/abs/10.1086/596066>

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## **SELECTION TOOL FOR FOODBORNE NOROVIRUS OUTBREAKS**

By Linda P.B. Verhoef, Annelies Kroneman, Yvonne van Duynhoven, Hendriek Boshuizen, Wilfrid van Pelt, and Marion Koopmans

Journal of Emerging Infectious Diseases

January, 2009

"Globalization of the food industry, centralized production, and the wide geographic distribution of products support the need for increased international surveillance of foodborne viral outbreaks, which may occur in clusters in different countries. Because control of pathogens in the food chain requires hazard analysis critical control points and verification of measures taken, detection of the pathogen is an important step (1). However, viral contamination of food is less likely to be recognized than bacterial contamination due to the infrequency of testing for viruses (2). Moreover, foods acceptable by bacterial standards are not necessarily safe from viral contamination. For example, norovirus may be present in shellfish and it may still meet the European Union *Escherichia coli* standard for human consumption (3). Consequently, foodborne viral infections are common, despite successful measures to reduce bacterial contamination. Recognition of foodborne viral outbreaks with international consequences would benefit from a linked and consistent reporting network among countries."

"Because of the etiologic dominance of viruses, the network's primary focus is on norovirus infections (7) that have been more frequently reported in recent years after emergence of novel variant strains in the population (8,9). Kroneman et al. described strengths and limitations of the FBVE [Foodborne Viruses in Europe] data collection (6) but stated that outbreak reports need to be interpreted with caution; the number and content of these reports may vary considerably among countries because surveillance databases may be different. Most of these reports link outbreaks to person-to-person transmission; international interventions and follow-up are rare. In ~40% of the outbreaks, no suspected mode of transmission was reported. Therefore, epidemiologic or virologic criteria should be used during the early stages of an outbreak investigation to determine whether foodborne sources should be considered. Given that surveillance systems are overwhelmed during norovirus peak seasons, use of these criteria would assist in focusing follow-up activities.

Our objective was to retrospectively derive, from surveillance data, a predictive model that

could serve prospectively in the selection of norovirus outbreaks potentially related to food. Such a tool could be used to warn food safety authorities (FSAs) earlier, to improve the quality of outbreak report data, and to provide better estimates of the effects of viral foodborne disease. Our study demonstrates the added value of a reporting system amalgamated across countries; the FBVE dataset can form the basis of this tool, which may be a first step towards detection of diffuse outbreaks.”

The full article can be found at: <http://www.cdc.gov/eid/content/15/1/31.htm>

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## **TOWARDS QUORUM-QUENCHING CATALYTIC ANTIBODIES**

By Prashant B. Kapadnisa, Evan Hallb, Madeleine Ramstedta, Warren R. J. D. Gallowaya, Martin Welchb and David R. Spring  
Chemical Communications  
December 11, 2008

“The development of a novel method to attenuate bacterial virulence is reported, which is based upon the use of designed transition-state analogues to select human catalytic antibodies capable of degrading bacterial quorum-sensing molecules.

Antibiotic drugs have played an essential role in the global increase in life expectancy and quality of life that has occurred over the last century.<sup>1</sup> However, the emergence and increasing prevalence of multi-drug-resistant bacterial strains are eroding such gains.<sup>1,2</sup> Existing antibiotics generally inhibit bacterial cellular processes that are essential for microbial survival.<sup>2,3</sup> An inherent problem with this approach is that it creates a selection pressure for drug-resistant mutations.<sup>4,5</sup> Bacterial antivirulence therapies seek to avoid the development of treatment-induced resistance. In this context, bacterial quorum-sensing systems offer an attractive target.<sup>6</sup>

Quorum sensing is the intercellular signalling mechanism, mediated by small molecules, which many bacteria use to co-ordinate gene expression with population density.<sup>7</sup> Quorum sensing is used by many bacterial pathogens to regulate virulence; however, it is not essential for survival.<sup>8</sup> Thus, disruption of quorum sensing (so-called quorum quenching) should attenuate pathogenicity without imposing the same selection for resistance, compared to existing antibiotic treatments.<sup>9</sup>”

The full article can be found at: [http://www.rsc.org/delivery/\\_ArticleLinking/DisplayHTMLArticleforfree.cfm?JournalCode=CC&Year=2009&ManuscriptID=b819819e&Iss=Advance\\_Article](http://www.rsc.org/delivery/_ArticleLinking/DisplayHTMLArticleforfree.cfm?JournalCode=CC&Year=2009&ManuscriptID=b819819e&Iss=Advance_Article)

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**MEASUREMENT OF NITROGEN MUSTARD DEGRADATION PRODUCTS BY POLY (DIMETHYLSILOXANE) MICROCHIP ELECTROPHORESIS WITH CONTACTLESS**

## CONDUCTIVITY DETECTION

Electronics Newsweekly

December 31, 2008

"A poly(dimethylsiloxane) (PDMS) microfluidic device with contactless conductivity detection for the determination of nitrogen mustard degradation products is reported. Three alkyl ethanolamines: N-methyldiethanolamine (MDEA), N-ethyldiethanolamine (EDEA), and triethanolamine (TEA), (degradation/ precursor products of HN-1, HN-2 and HN-3 blister agents) were analyzed by microchip capillary electrophoresis (CE)."

"The original PDMS channel was coated by poly(ethyleneimine) (PEI) to improve the separation of three ethanolamines. Experimental conditions for the separation and detection processes have been optimized to yield well defined separation and high sensitivity. The response times for the three ethanolamines were less than 5 min., the detection limits were 2.0-4.0 mg L<sup>-1</sup> and the relative standard derivations for the migration times and peak heights were 1.6-2.3% and 4.1-5.7%, respectively The linearity of calibration for each of the compounds was as follows: MDEA,  $r(2) = 0.970$ ; EDEA,  $r(2) = 0.994$ ; TEA,  $r(2) = 0.988$ . Applicability of this method for natural (lake and tap) water samples was also demonstrated."

"Compared to conventional analytical methods, this miniaturized system offers promise for on-site monitoring of degradation products of the nitrogen mustard class of chemical warfare agents, with advantages of cost-effective construction., simple operation, portability, and small required sample volumes."

The full article can be found at: (Y.S. Ding, et. al., "Measurement of Nitrogen Mustard Degradation Products by Poly(Dimethylsiloxane") Microchip Electrophoresis with Contactless Conductivity Detection. *Electroanalysis*, 2008;20(20):2192-2198). Link not available.

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**Steve Tesko:** [Steve.Tesko@anser.org](mailto:Steve.Tesko@anser.org)

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