

12 March 2009

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## **Chem-Bio News – S&T Edition**

### **1. THE ADENYLATE CYCLASE TOXINS OF BACILLUS ANTHRACIS AND BORDETELLA PERTUSSIS PROMOTE TH2 CELL DEVELOPMENT BY SHAPING T CELL ANTIGEN RECEPTOR SIGNALING:**

*"These results demonstrate that, notwithstanding their differences in their intracellular localization, which result in focalized cAMP production, both toxins directly affect the Th1/Th2 balance by interfering with the same steps in TCR signaling, and suggest that their adjuvanticity is likely to result from their combined effects on APC and CD4+ T cells."*

### **2. CLINICAL AND IMMUNOLOGICAL RESPONSE TO ATTENUATED TISSUE-CULTURED SMALLPOX VACCINE LC16M8:**

*"Administration of an attenuated tissue-cultured smallpox vaccine (LC16m8) to healthy adults was associated with high levels of vaccine take and seroconversion in those who were vaccinia-naive and yielded an effective booster response in some previously vaccinated individuals."*

### **3. EXPANDING ROUTES FOR DRUG DELIVERY:**

*"The system, developed by Rein Ulijn from the University of Strathclyde, UK, and colleagues, consists of hydrogel particles with branched peptide structures called actuators embedded throughout."*

### **4. FIGHTING MRSA WITH IONIC LIQUIDS:**

*"Brendan Gilmore and co-workers at the Queen's University, Belfast, UK, have shown that the compounds are effective antibacterial agents that can be used to break down microbial biofilms, a cause of hospital acquired infections such as MRSA."*

### **5. (WO/2009/015478) BACTERIAL ISOLATE AND METHODS FOR DETOXIFICATION OF TRICHOHECENE MYCOTOXINS:**

*"Also provided are compositions comprising the bacteria and methods of preventing or treating food, foodstuffs, crops and harvested crops that are contaminated or susceptible to contamination with trichothecene mycotoxins."*

### **6. QUANTUM-CHEMICAL COMPREHENSIVE STUDY OF THE ORGANOPHOSPHORUS COMPOUNDS ADSORPTION ON ZINC OXIDE SURFACES:**

*"Therefore, it can be concluded that the decomposition of nerve agents and their simulants will be easier on CaO, whereas ZnO should make an efficient sensor for the detection of such compounds."*

## **7. ATTOMOLAR PROTEIN DETECTION IN COMPLEX SAMPLE MATRICES WITH SEMI-HOMOGENEOUS FLUIDIC FORCE DISCRIMINATION ASSAYS:**

*"We also show that SH assays are adaptable for extraction, preconcentration, and identification of analytes in complex sample matrices, including assays for SEB and ricin toxoid in serum and whole blood."*

# CB Daily Report

## ***Chem-Bio News***

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### **THE ADENYLATE CYCLASE TOXINS OF BACILLUS ANTHRACIS AND BORDETELLA PERTUSSIS PROMOTE TH2 CELL DEVELOPMENT BY SHAPING T CELL ANTIGEN RECEPTOR SIGNALING**

By Silvia Rossi Paccani, Marisa Benagiano, Nagaja Capitani, Irene Zornetta, Daniel Ladant, Cesare Montecucco, Mario M. D'Elisos, Cosima T. Baldari

PLoS Pathogens

March 10, 2009

"The adjuvanticity of bacterial adenylate cyclase toxins has been ascribed to their capacity, largely mediated by cAMP, to modulate APC activation, resulting in the expression of Th2-driving cytokines. On the other hand, cAMP has been demonstrated to induce a Th2 bias when present during T cell priming, suggesting that bacterial cAMP elevating toxins may directly affect the Th1/Th2 balance. Here we have investigated the effects on human CD4+ T cell differentiation of two adenylate cyclase toxins, Bacillus anthracis edema toxin (ET) and Bordetella pertussis CyaA, which differ in structure, mode of cell entry, and subcellular localization. We show that low concentrations of ET and CyaA, but not of their genetically detoxified adenylate cyclase defective counterparts, potently promote Th2 cell differentiation by inducing expression of the master Th2 transcription factors, c-maf and GATA-3. We also present evidence that the Th2-polarizing concentrations of ET and CyaA selectively inhibit TCR-dependent activation of Akt1, which is required for Th1 cell differentiation, while enhancing the activation of two TCR-signaling mediators, Vav1 and p38, implicated in Th2 cell differentiation. This is at variance from the immunosuppressive toxin concentrations, which interfere with the earliest step in TCR signaling, activation of the tyrosine kinase Lck, resulting in impaired CD3 $\zeta$  phosphorylation and inhibition of TCR coupling to ZAP-70 and Erk activation. These results demonstrate that, notwithstanding their differences in their intracellular localization, which result in focalized cAMP production, both toxins directly affect the Th1/Th2 balance by interfering with the same steps in TCR signaling, and suggest that their adjuvanticity is likely to result from their combined effects on APC and CD4+ T cells. Furthermore, our results strongly support the key role of cAMP in the adjuvanticity of these toxins."

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000325;jsessionid=10B902888EE2CA6EC628836623F71E06>

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## **CLINICAL AND IMMUNOLOGICAL RESPONSE TO ATTENUATED TISSUE-CULTURED SMALLPOX VACCINE LC16M8**

By Tomoya Saito, MD, PhD; Tatsuya Fujii, MD; Yasuhiro Kanatani, MD, PhD; Masayuki Saijo, MD, PhD; Shigeru Morikawa, DVM, PhD; Hiroyuki Yokote, MS; Tsutomu Takeuchi, MD, PhD; Noriyuki Kuwabara, MD, PhD

Journal of the American Medical Association (JAMA)

March 11, 2009

“Results The proportions of take in vaccinia-naive and previously vaccinated individuals were 1443 of 1529 (94.4% [95% confidence interval {CI}, 93.2%-95.9%]) and 1465 of 1692 (86.6% [95% CI, 85.0%-88.2%]), respectively. Seroconversion or an effective booster response among the individuals with take was elicited in 37 of 41 (90.2% [95% CI, 81.2%-99.3%]) vaccinia-naive participants and in 93 of 155 (60.0% [95% CI, 52.3%-67.7%]) previously vaccinated participants. One case of allergic dermatitis and another of erythema multiforme, both of which were mild and self-limited, were suspected to be caused by vaccination. No severe adverse events were observed.

Conclusion Administration of an attenuated tissue-cultured smallpox vaccine (LC16m8) to healthy adults was associated with high levels of vaccine take and seroconversion in those who were vaccinia-naive and yielded an effective booster response in some previously vaccinated individuals.”

The full article can be found at: <http://jama.ama-assn.org/cgi/content/full/301/10/1025>

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## **EXPANDING ROUTES FOR DRUG DELIVERY**

By Alexandra Haywood

Chemical Biology (UK Royal Society of Chemistry)

March 10, 2009

“Peptide-triggered particles that release cargos when they meet an enzyme could find use delivering drugs in the body.

The system, developed by Rein Ulijn from the University of Strathclyde, UK, and colleagues, consists of hydrogel particles with branched peptide structures called actuators embedded throughout. The particles can be loaded with a payload such as a drug molecule.

When Ulijn's hydrogel particles encounter a protease - an enzyme that hydrolyses peptide bonds - the attached peptide actuators are cleaved. The result is a switch in the actuators' charge balance, from neutral to positive, causing the particles to swell to reduce repulsion between the positive charges. The payload can then diffuse out of the particles through the polymer mesh.”

The full article can be found at: [http://www.rsc.org/Publishing/Journals/cb/Volume/2009/4/Expanding\\_routes\\_for\\_drug\\_delivery.asp](http://www.rsc.org/Publishing/Journals/cb/Volume/2009/4/Expanding_routes_for_drug_delivery.asp)

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## **FIGHTING MRSA WITH IONIC LIQUIDS**

By Russell Johnson

Chemical Science (UK Royal Society of Chemistry)

March 6, 2009

“Brendan Gilmore and co-workers at the Queen's University, Belfast, UK, have shown that the compounds are effective antibacterial agents that can be used to break down microbial biofilms, a cause of hospital acquired infections such as MRSA.”

“Gilmore tested the effects of 1-alkyl-3-methylimidazolium chloride ionic liquids on the bacterial biofilms of several pathogens including methicillin-resistant *Staphylococcus aureus* and *Escherichia coli*. The team found that antibiofilm potency increased with the length of the alkyl chain. Biofilms are bacterial communities that enclose themselves in a protective polymer. They are more resistant to antibiotics or other sterilisation methods than their free-swimming counterparts.”

The full article can be found at: [http://www.rsc.org/Publishing/ChemScience/Volume/2009/04/MRSA\\_ionic\\_liquids.asp](http://www.rsc.org/Publishing/ChemScience/Volume/2009/04/MRSA_ionic_liquids.asp)

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## **(WO/2009/015478) BACTERIAL ISOLATE AND METHODS FOR DETOXIFICATION OF TRICHOHECENE MYCOTOXINS**

By ZHOU, Ting; (CA). GONG, Jianhua; (CA). YU, Hai; (CA). YOUNG, James, Christopher; (CA). LI, Xiu-Zhen; (CA). ZHU, Honghui; (CA). CAO, Rong; (CA).

YANG, Raymond, Xiaolong

World Intellectual Property Organization (WIPO)

February 5, 2009

“The invention provides a bacterial isolate defined by accession number 180507-1 filed with the International Depository Authority of Canada. The bacteria are capable of degrading trichothecene mycotoxins. Also provided are compositions comprising the bacteria and methods of preventing or treating food, foodstuffs, crops and harvested crops that are contaminated or susceptible to contamination with trichothecene mycotoxins. Kits are also provided.”

The full report can be found at: <http://www.wipo.int/pctdb/en/ia.jsp?ia=CA2008/001402>

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## QUANTUM-CHEMICAL COMPREHENSIVE STUDY OF THE ORGANOPHOSPHORUS COMPOUNDS ADSORPTION ON ZINC OXIDE SURFACES

News of Science

March 15, 2009

"Ab initio calculations at the density functional theory and the second-order Moller-Plesset perturbation theory levels, and using the n-layered integrated molecular orbital and molecular mechanics (ONIOM) method, have been performed for the adsorption of dimethyl methylphosphonate (DMMP) and tabun (GA) on (ZnO)(n) (where n = 4, 18, or 24 molecular clusters of (10 (1) over bar0) and (0001) zinc oxide surfaces). Different adsorption sites and DMMP orientations were considered."

"Calculations include the evaluation of the optimized geometries, atomic charges, interaction energies, various methods applied, and different sizes and surface types of the ZnO fragments. On both surfaces, the molecular adsorption proceeds as chemisorption via the formation of a Zn center dot center dot center dot O chemical bond in the case of the DMMP adsorption complex and a P center dot center dot center dot O covalent bond or a Zn center dot center dot center dot N chemical bond for GA adsorption complexes. The type of surface greatly affected the strength of the intermolecular interactions and the interaction energies. The results indicate that the adsorption of DMMP and GA is energetically more preferable on the nonpolar (10 (1) over bar0) ZnO surface. GA was determined to be bound more tightly to the ZnO surface than DMMP, but the adsorption energies were approximately twice as low as the values revealed for the adsorption of GA and DMMP on the CaO surface."

"Therefore, it can be concluded that the decomposition of nerve agents and their simulants will be easier on CaO, whereas ZnO should make an efficient sensor for the detection of such compounds."

The full article can be found at: (Y. Paukku, et. al., "Quantum-Chemical Comprehensive Study of the Organophosphorus Compounds Adsorption on Zinc Oxide Surfaces". Journal of Physical Chemistry C, 2009; 113(4):1474-1485). Link not available.

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## ATTOMOLAR PROTEIN DETECTION IN COMPLEX SAMPLE MATRICES WITH SEMI-HOMOGENEOUS FLUIDIC FORCE DISCRIMINATION ASSAYS

Electronics Newsweekly

March 18, 2009

"We describe a semi-homogenous (SH) implementation of a fluidic force discrimination (TM) (FFD) assay using only two reagent mixtures and three assay steps that can be performed in as little as 10 min. Previously microbead labels and FFD have been combined to achieve multiplexed, femtomolar nucleic acid hybridization and immunoassays in a microarray format."

"In SH FFD assays, the microbeads and any required intermediate receptors (e.g., secondary antibodies) are first mixed directly with a sample, allowing target analytes to be

efficiently captured onto the beads. The target-loaded beads are then specifically captured onto a microarray surface, with nonspecifically bound beads removed by controlled, laminar fluidic forces. The remaining beads on each microarray capture spot are counted to determine the targets' identities and concentrations. SH target collection provides a 1000-fold improvement in the assay sensitivity, down to attomolar concentrations, as demonstrated by our detection of staphylococcal enterotoxin B (SEB) at 35 aM (1 fg/ml). We also show that SH assays are adaptable for extraction, preconcentration, and identification of analytes in complex sample matrices, including assays for SEB and ricin toxoid in serum and whole blood."

"Finally, we present a detailed model of the reaction kinetics that reveals how capturing the targets onto the beads in solution provides a significant kinetic advantage at low target concentrations where mass transport to a microarray surface is most limited."

The full article can be found at: (S.P. Mulvaney, et. al., "Attomolar protein detection in complex sample matrices with semi-homogeneous fluidic force discrimination assays". *Biosensors & Bioelectronics*, 2009;24(5 Sp. Iss.):1109-1115). Link not available.

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