

3 December 2009

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## **Chem-Bio News – S&T Edition**

### **1. NERVE AGENT ANALOGUES THAT PRODUCE AUTHENTIC SOMAN, SARIN, TABUN, AND CYCLOHEXYL METHYLPHOSPHONATE-MODIFIED HUMAN BUTYRYLCHOLINESTERASE:**

*"However, the soman and sarin thiomethyl compounds yielded two types of adducts, one of which was thiomethyl phosphonate, a modification not found after treatment with authentic soman and sarin."*

### **2. SIMULTANEOUS DETECTION OF FIVE BIOTHRREAT AGENTS IN POWDER SAMPLES BY A MULTIPLEXED SUSPENSION ARRAY:**

*"Compared to conventional ELISA method, the suspension array has a higher sensitive ability, and can detect five biotthreat agents simultaneously with high reproducibility."*

### **3. INDUCTION OF SUPPRESSORS OF CYTOKINE SIGNALING [SOCS] BY THE TRICHOHECENE DEOXYNIVALENOL IN THE MOUSE:**

*"Taken together, DON-induced cytokine upregulation corresponded to increased expression of several SOCS, and was associated with suppression of GH-inducible gene expression in the liver."*

### **4. CARBON NANOTUBE-SENSOR-INTEGRATED MICROFLUIDIC PLATFORM FOR REAL-TIME CHEMICAL CONCENTRATION DETECTION:**

*"These results indicate great potential of EG-CNT for advanced nanosensors with superior sensitivity, ultra-low power consumption, and less fabrication complexity."*

### **5. DEGRADATION OF SULFUR MUSTARD ON KF/AL<sub>2</sub>O<sub>3</sub> SUPPORTS: INSIGHTS INTO THE PRODUCTS AND THE REACTIONS MECHANISMS:**

*"Out [sic] study on the detoxification of this blister agent showed the formation of nontoxic substitution and less-toxic elimination products ( $t(1/2) = 3.5-355$  h) Interestingly, the reaction rates Were found to be affected by MAS conditions, i.e., by a centrifugation effect."*

### **6. DEVELOPMENT OF ELISAS FOR THE CLASS-SPECIFIC DETERMINATION OF ORGANOPHOSPHORUS PESTICIDES:**

*"Compared to ELISAs previously developed with the same objective, the current ELISA demonstrates better sensitivity based on much lower mean IC<sub>50</sub> values in addition to improved class-selective determination based on considerably lower % CV values as well as precise discrimination against other types of pesticides."*

**7. ACUTE MICROINSTILLATION INHALATION EXPOSURE TO SARIN INDUCES CHANGES IN RESPIRATORY DYNAMICS AND FUNCTIONS IN GUINEA PIGS:** *"These results indicate that inhalation exposure to sarin alters respiratory dynamics and function at 4 hours, with return to normal levels at 24 hours post exposure."*

## CB Daily Report

### Chem-Bio News

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#### **NERVE AGENT ANALOGUES THAT PRODUCE AUTHENTIC SOMAN, SARIN, TABUN, AND CYCLOHEXYL METHYLPHOSPHONATE-MODIFIED HUMAN BUTYRYLCHOLINESTERASE**

Proteomics Weekly  
December 7, 2009

"The goal was to test 14 nerve agent model compounds of soman, sarin, tabun, and cyclohexyl methylphosphonofluoridate (GF) for their suitability as substitutes for true nerve agents. We wanted to know whether the model compounds would form the identical covalent adduct with human butyrylcholinesterase that is produced by reaction with true nerve agents."

"Nerve agent model compounds containing thiocholine or thiomethyl in place of fluorine or cyanide were synthesized as Sp and Rp stereoisomers. Purified human butyrylcholinesterase was treated with a 45-fold molar excess of nerve agent analogue at pH 7.4 for 17 h at 21 degrees C. The protein was denatured by boiling and was digested with trypsin. Aged and nonaged active site peptide adducts were quantified by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry of the tryptic digest mixture. The active site peptides were isolated by HPLC and analyzed by MALDI-TOF-TOF mass spectrometry. Serine 198 of butyrylcholinesterase was covalently modified by all 14 compounds. Thiocholine was the leaving group in all compounds that had thiocholine in place of fluorine or cyanide. Thiomethyl was the leaving group in the GF thiomethyl compounds. However, sarin thiomethyl compounds released either thiomethyl or isopropyl, while soman thiomethyl compounds released either thiomethyl or pinacolyl. Thiocholine compounds reacted more rapidly with butyrylcholinesterase than thiomethyl compounds. Labeling with the model compounds resulted in aged adducts that had lost the O-alkyl group (O-ethyl for tabun, O-cyclohexyl for GF, isopropyl for sarin, and pinacolyl for soman) in addition to the thiocholine or thiomethyl group. The nerve agent model compounds containing thiocholine and the GF thiomethyl analogue were found to be suitable substitutes for true soman, sarin, tabun, and GF in terms of the adduct that they produced with human butyrylcholinesterase."

"However, the soman and sarin thiomethyl compounds yielded two types of adducts, one of which was thiomethyl phosphonate, a modification not found after treatment with authentic soman and sarin."

The full article can be found at: (C. Gilley, et. al., "Nerve Agent Analogues That Produce

Authentic Soman, Sarin, Tabun, and Cyclohexyl Methylphosphonate-Modified Human Butyrylcholinesterase". Chemical Research in Toxicology, 2009;22(10):1680-1688). Link not available.

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## **SIMULTANEOUS DETECTION OF FIVE BIOTHREAT AGENTS IN POWDER SAMPLES BY A MULTIPLEXED SUSPENSION ARRAY**

Drug Week

December 4, 2009

"A suspension array-based multiplexed immunoassay was developed for rapid, sensitive, specific, and simultaneous detection of multiple bioterror-associated agents in powder samples. The 5-plexed immunoassays using sets of 9-plexed coupled fluorescent beads were employed to simultaneously detect five representative bioterror agents, including *B. anthracis* spore, *Y. pestis*, SARS-CoV, staphylococcal enterotoxin B (SEB) and ricin from a single powder sample and the feasibility for field samples was demonstrated by both blinded and standard laboratory trials."

"The detection sensitivity and dynamic range for the five bioterror agents from different powders might be varied depending on the nature of the powder and the feature of the contaminating agent. The limit of detection for *Y. pestis*, *B. anthracis* spores, SEB, ricin, SARS-CoV N protein in milk powder was 20 cfu, 111 cfu, 110pg, 5.4 ng and 2 ng per test respectively."

"Compared to conventional ELISA method, the suspension array has a higher sensitive ability, and can detect five bioterror agents simultaneously with high reproducibility."

The full article can be found at: (J. Wang, et. al., "Simultaneous detection of five bioterror agents in powder samples by a multiplexed suspension array". Immunopharmacology and Immunotoxicology, 2009; 31(3): 417-427).

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## **INDUCTION OF SUPPRESSORS OF CYTOKINE SIGNALING [SOCS] BY THE TRICHOHECENE DEOXYNIVALENOL IN THE MOUSE**

Biotech Week

December 2, 2009

"Deoxynivalenol (DON), a trichothecene mycotoxin found in grains and cereal-based foods worldwide, impairs weight gain in experimental animals but the underlying mechanisms remain undetermined. Oral exposure to DON induces rapid and transient upregulation of proinflammatory cytokine expression in the mouse."

"The latter are known to induce several suppressors of cytokine signaling (SOCS), some of

which impair growth hormone (GH) signaling. We hypothesized that oral exposure to DON will induce SOCS expression in the mouse. Real-time PCR and cytokine bead array revealed that oral gavage, with DON rapidly (1 h) induced tumor necrosis factor-alpha and interleukin-6 mRNA and protein expression in several organs and plasma, respectively. Upregulation of mRNAs for four well-characterized SOCS (CIS [cytokine-inducible SH2 domain protein], SOCS1, SOCS2, and SOCS3) was either concurrent with (1 h) or subsequent to cytokine upregulation (2 h). Notably, DON-induced SOCS3 mRNAs in muscle, spleen and liver, with C1S1, SOCS1, and SOCS2 occurring to a lesser extent. Hepatic SOCS3 mRNA was a very sensitive indicator of DON exposure with SOCS3 protein being detectable in the liver well after the onset of cytokine decline (5 h). Furthermore, hepatic SOCS upregulation was associated with about 75% suppression of GH-inducible insulin-like growth factor acid labile subunit."

"Taken together, DON-induced cytokine upregulation corresponded to increased expression of several SOCS, and was associated with suppression of GH-inducible gene expression in the liver."

The full article can be found at: (C.J. Amuzie, et. al., "Induction of Suppressors of Cytokine Signaling by the Trichothecene Deoxynivalenol in the Mouse". *Toxicological Sciences*, 2009; 111(2):277-287). Link not available.

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## **CARBON NANOTUBE-SENSOR-INTEGRATED MICROFLUIDIC PLATFORM FOR REAL-TIME CHEMICAL CONCENTRATION DETECTION**

Science Letter

December 1, 2009

"This paper presents the development of a chemical sensor employing electronic-grade carbon nanotubes (EG-CNTs) as the active sensing element for sodium hypochlorite detection. The sensor, integrated in a PDMS-glass microfluidic chamber, was fabricated by bulk aligning of EG-CNTs between gold microelectrode pairs using dielectrophoretic technique."

"Upon exposure to sodium hypochlorite solution, the characteristics of the carbon nanotube chemical sensor were investigated at room temperature under constant current mode. The sensor exhibited responsivity, which fits a linear logarithmic dependence on concentration in the range of 1/32 to 8 ppm, a detection limit lower than 5 ppb, while saturating at 16 ppm. The typical response time of the sensor at room temperature is on the order of minutes and the recovery time is a few hours. In particular, the sensor showed an obvious sensitivity to the volume of detected solution. It was found that the activation power of the sensor was extremely low, i.e. in the range of nanowatts."

"These results indicate great potential of EG-CNT for advanced nanosensors with superior sensitivity, ultra-low power consumption, and less fabrication complexity."

The full article can be found at: (L. Yang, et. al., "Carbon nanotube-sensor-integrated

microfluidic platform for real-time chemical concentration detection". Electrophoresis, 2009; 30(18 Sp. Iss): 3198-3205). Link not available.

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## **DEGRADATION OF SULFUR MUSTARD ON KF/AL<sub>2</sub>O<sub>3</sub> SUPPORTS: INSIGHTS INTO THE PRODUCTS AND THE REACTIONS MECHANISMS**

Journal of Technology & Science

November 29, 2009

"The degradation of the warfare agent sulfur Mustard (HD) adsorbed onto KF/Al<sub>2</sub>O<sub>3</sub> sorbents is described."

"These processes were explored by MAS NMR. using C-13-labeled sulfur mustard (HD\*) and LC-MS techniques. Our study on the detoxification of this blister agent showed the formation of nontoxic substitution and less-toxic elimination products ( $t(1/2) = 3.5-355$  h). Interestingly, the reaction rates were found to be affected by MAS conditions, i.e., by a centrifugation effect."

The full article can be found at: (Y. Zafrani, et. al., "Degradation of Sulfur Mustard on KF/Al<sub>2</sub>O<sub>3</sub> Supports: Insights into the Products and the Reactions Mechanisms". Journal of Organic Chemistry, 2009; 74(21):8464-8471). Link not available.

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## **DEVELOPMENT OF ELISAS FOR THE CLASS-SPECIFIC DETERMINATION OF ORGANOPHOSPHORUS PESTICIDES**

Immunotherapy Weekly

December 2, 2009

"Enzyme-linked immunosorbent assays (ELISAs) for the class-specific determination of organophosphorus (OP) pesticides were developed from monoclonal antibodies raised against haptens with the functional group common to OP pesticides. To develop antigen-coated, indirect, competitive ELISAs, four haptens with different spacer arm structures were used to prepare antibodies, while eight haptens were tested for use as coating antigens. A total of 32 ELISAs were developed with one selected as the most suitable one based on average IC<sub>50</sub> and % CV values."

"The chosen ELISA showed class-selective response to O,O-diethyl phosphorothioate and phosphorodithioate OP pesticides with negligible cross-reactivity to other types of pesticides. Average IC<sub>50</sub> and % CV values of this ELISA for the 12 OP pesticides were 89 ng/mL and 96%, respectively."

"Compared to ELISAs previously developed with the same objective, the current ELISA demonstrates better sensitivity based on much lower mean IC<sub>50</sub> values in addition to

improved class-selective determination based on considerably lower % CV values as well as precise discrimination against other types of pesticides."

The full article can be found at: (Y.Z. Piao, et., al., "Development of ELISAs for the Class-Specific Determination of Organophosphorus Pesticides". Journal of Agricultural and Food Chemistry, 2009; 57(21): 10004-10013). Link not available.

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## **ACUTE MICROINSTILLATION INHALATION EXPOSURE TO SARIN INDUCES CHANGES IN RESPIRATORY DYNAMICS AND FUNCTIONS IN GUINEA PIGS**

Medical Letter on the CDC & FDA

December 6, 2009

"This study investigates the toxic effects of sarin on respiratory dynamics following microinstillation inhalation exposure in guinea pigs. Animals are exposed to sarin for 4 minutes, and respiratory functions are monitored at 4 hours and 24 hours by whole-body barometric plethysmography."

"Data show significant changes in respiratory dynamics and function following sarin exposure. An increase in respiratory frequency is observed at 4 hours post exposure compared with saline controls. Tidal volume and minute volume are also increased in sarin-exposed animals 4 hours after exposure. Peak inspiratory flow increases, whereas peak expiratory flow increases at 4 hours and is erratic following sarin exposure. Animals exposed to sarin show a significant decrease in expiratory time and inspiratory time. End-inspiratory pause is unchanged whereas end-expiratory pause is slightly decreased 24 hours after sarin exposure."

"These results indicate that inhalation exposure to sarin alters respiratory dynamics and function at 4 hours, with return to normal levels at 24 hours post exposure."

The full article can be found at: (M.L. Conti, et. al., "Acute Microinstillation Inhalation Exposure to Sarin Induces Changes in Respiratory Dynamics and Functions in Guinea Pigs". International Journal of Toxicology, 2009; 28(5): 436-447). Link not available.

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