

19 November 2009

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## **Chem-Bio News - S&T Edition**

**1. PALMTOP PCR:** *"Choi's system is made up of a loop of thin plastic on a polymer chip. Convection is used to move the reaction mixture through the different temperature zones in the loop, removing the need for an external pump."*

**2. TIME-COURSE CHANGES OF ACETYLCHOLINESTERASE ACTIVITY IN BLOOD AND SOME TISSUES IN RATS AFTER INTOXICATION BY RUSSIAN VX:** *"While AChE and BChE activities were reduced only about 20% and 15%, respectively, the decline in activity was rapid, occurring within 3 min."*

**3. ANTHRAX LETHAL TOXIN ENHANCES I KAPPA B KINASE ACTIVATION AND DIFFERENTIALLY REGULATES PRO-INFLAMMATORY GENES IN HUMAN ENDOTHELIUM:** *"Together, these findings provide new mechanistic insight on how LT may disrupt the host response to anthrax."*

**4. IDENTIFICATION OF LINEAR EPITOPES IN BACILLUS ANTHRACIS PROTECTIVE ANTIGEN BOUND BY NEUTRALIZING ANTIBODIES:** *"These results identify the first linear neutralizing epitopes of PA and show that peptides containing epitope sequences can elicit neutralizing antibody responses, a finding that could be exploited for vaccine design."*

**5. DEGRADATION OF SULFUR MUSTARD ON KF/AL2O3 SUPPORTS: INSIGHTS INTO THE PRODUCTS AND THE REACTIONS MECHANISMS:** *"These processes were explored by MAS NMR. using C-13-labeled sulfur mustard (HD\*) and LC-MS techniques."*

**6. APPLICATION OF CONVENTIONAL SOLID-PHASE EXTRACTION FOR MULTIMYCOTOXIN ANALYSIS IN BEERS BY ULTRAHIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY:** *"This methodology combines the simplicity of SPE using conventional cartridges and UHPLC-MS/MS, producing a rapid, sensitive, and reliable procedure."*

**7. CRITICAL TIMING, LOCATION AND DURATION OF GLUCOCORTICOID ADMINISTRATION RESCUE MICE FROM SUPERANTIGEN-INDUCED SHOCK AND ATTENUATE LUNG INJURY:** *"This optimal dosing and schedule of glucocorticoid treatment mitigated lung inflammation and resulted in 100% survival in this intranasal mouse model of*

# CB Daily Report

## Chem-Bio News

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### **PALMTOP PCR**

By Laura Howes

Highlights in Chemical Technology

November 12, 2009

"Choi's system is made up of a loop of thin plastic on a polymer chip. Convection is used to move the reaction mixture through the different temperature zones in the loop, removing the need for an external pump. The time taken for the mixture to flow around the loop can be controlled by varying the angle of the chip. This simplification makes the chip more robust, and easily disposable. Also it works faster than conventional PCR, giving results in 10 minutes compared to the 71 minutes that it takes a conventional machine, says Choi."

The full article can be found at: [http://www.rsc.org/Publishing/ChemTech/Volume/2009/12/palmtop\\_pcr.asp](http://www.rsc.org/Publishing/ChemTech/Volume/2009/12/palmtop_pcr.asp)

The original article can be found at: <http://www.rsc.org/Publishing/Journals/LC/article.asp?doi=b915022f>

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### **TIME-COURSE CHANGES OF ACETYLCHOLINESTERASE ACTIVITY IN BLOOD AND SOME TISSUES IN RATS AFTER INTOXICATION BY RUSSIAN VX**

Proteomics Weekly

November 23, 2009

"The toxic effect of organophosphates is attributed to irreversible inhibition of acetylcholinesterase (AChE; EC 3.1.1.7), the enzyme that hydrolyses the neurotransmitter acetylcholine. Inhibition potency in vivo of one of the most toxic nerve agents--Russian VX (RVX; N,N-diethyl-2-[methyl-(2-methylpropoxy)phosphoryl]sulfanyethanamine) (1 x LD(50) dose administered intramuscularly, i.m.) was studied in rats."

"AChE in blood was inhibited by 50%, 3 min after i.m. RVX. Butylcholinesterase (BChE; EC 3.1.1.8) in plasma was inhibited less rapidly and only by 10-20%, 20 min after RVX. AChE and BChE activities in diaphragm were reduced only 35% and 15% at 30 min. While AChE and BChE activities were reduced only about 20% and 15%, respectively, the decline in activity was rapid, occurring within 3 min."

"These findings indicate that RVX most potently inhibits ChE outside the central nervous system."

The full article can be found at: (J.Z. Karasova, et. al., "Time-course changes of acetylcholinesterase activity in blood and some tissues in rats after intoxication by Russian VX". Neurotoxicity Research, 2009;16(4):356-60). Link not available.

ANALYST NOTE: The author's contact information is given as: Faculty of Military Health Sciences, Dept. of Toxicology, Trebesska 1575, 500 01 Hradec Kralove, Czech Republic.

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## **ANTHRAX LETHAL TOXIN ENHANCES I KAPPA B KINASE ACTIVATION AND DIFFERENTIALLY REGULATES PRO-INFLAMMATORY GENES IN HUMAN ENDOTHELIUM**

Life Science Weekly  
November 10, 2009

"Anthrax lethal toxin (LT) was previously shown to enhance transcriptional activity of NF-kappa B in tumor necrosis factor-alpha-activated primary human endothelial cells. Here we show that this LT-mediated increase in NF-kappa B activation is associated with the enhanced degradation of the inhibitory proteins I kappa B alpha and I kappa B beta but not I kappa B epsilon."

"Moreover, this was accompanied by enhanced activation of the I kappa B kinase complex (IKK), which is responsible for targeting I kappa B proteins for degradation. Importantly, LT enhancement of I kappa B alpha degradation was completely blocked by a selective IKK beta inhibitor, whereas I kappa B beta degradation was attenuated, suggesting a mechanistic link. Consistent with the above data, LT-cotreated cells show elevated phosphorylation of two IKK substrates, I kappa B alpha and p65, both of which were blocked by incubation with the IKK beta inhibitor. Consistent with NF-kappa B activation, LT increased transcription of the NF-kappa B regulated gene CD40. Conversely, LT inhibited transcription of another NF-kappa B-regulated gene, CCL2. This inhibition was linked to the LT-mediated suppression of another CCL2-regulating transcription factor, AP-1 (activator protein-1). These data suggest that LT-mediated enhancement of NF-kappa B is IKK-dependent, but importantly, the net effect of LT on the transcription of proinflammatory genes is driven by the cumulative effect of LT on the particular set of transcription factors that regulate a given promoter."

"Together, these findings provide new mechanistic insight on how LT may disrupt the host response to anthrax."

The full article can be found at: (J.M. Warfel, et. al., "Anthrax Lethal Toxin Enhances I kappa B Kinase Activation and Differentially Regulates Pro-inflammatory Genes in Human Endothelium". Journal of Biological Chemistry, 2009;284(38):25761-25771). Link not available.

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## **IDENTIFICATION OF LINEAR EPITOPES IN BACILLUS ANTHRACIS PROTECTIVE ANTIGEN BOUND BY NEUTRALIZING ANTIBODIES**

Medical Letter on the CDC & FDA

November 15, 2009

"To identify linear neutralizing epitopes of PA, 145 overlapping peptides covering the entire sequence of the protein were synthesized."

"Six monoclonal antibodies (mAbs) and antisera from mice specific for PA were tested for their reactivity to the peptides by enzyme-linked immunosorbent assays. Three major linear immunodominant B-cell epitopes were mapped to residues Leu(156) to Ser(170), Val(196) to Ile(210), and Ser(312) to Asn(326) of the PA protein. Two mAbs with toxin-neutralizing activity recognized two different epitopes in close proximity to the furin cleavage site in domain 1. The three-dimensional complex structure of PA and its neutralizing mAbs 7.5G and 19D9 were modeled using the molecular docking method providing models for the interacting epitope and paratope residues. For both mAbs, LeTx neutralization was associated with interference with furin cleavage, but they differed in effectiveness depending on whether they bound on the N- or C-terminal aspect of the cleaved products. The two peptides containing these epitopes that include amino acids Leu(156)-Ser(170) and Val(196)-Ile(210) were immunogenic and elicited neutralizing antibody responses to PA."

"These results identify the first linear neutralizing epitopes of PA and show that peptides containing epitope sequences can elicit neutralizing antibody responses, a finding that could be exploited for vaccine design."

The full article can be found at: (N. Abboud, et. al., "Identification of Linear Epitopes in Bacillus anthracis Protective Antigen Bound by Neutralizing Antibodies". Journal of Biological Chemistry, 2009; 284(37):25077-25086). 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**

Chemical & Chemistry

November 27, 2009

"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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## **APPLICATION OF CONVENTIONAL SOLID-PHASE EXTRACTION FOR MULTIMYCOTOXIN ANALYSIS IN BEERS BY ULTRAHIGH-PERFORMANCE LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY**

Medical Devices & Surgical Technology Week  
November 22, 2009

"A new analytical method has been developed and validated for the simultaneous analysis of mycotoxins (aflatoxins B1, B2, G1, G2, and M1, fumonisins B1 and B2, deoxynivalenol, ochratoxin A, HT-2 and T-2 toxins, and zearalenone) in beers. Mycotoxins were extracted by solid-phase extraction (SPE) using C18 as the cartridge."

"Several parameters such as type of sorbent, elution solvent, and dilution of the sample were evaluated. The separation and determination were carried out by ultrahigh performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS). The method was validated, and mean recoveries ranging from 70 to 106% were obtained. Repeatability and intermediate precision, expressed as relative standard deviations, were lower than 21% for all mycotoxins and levels assayed. The limits of quantification were lower than 0.5  $\mu$ g/L. The developed method has been applied for the analysis of several types of beers with different alcoholic content (nonalcoholic, normal, and special), and T2, HT-2 toxins, aflatoxin B1, and fumonisin B2 were detected."

"This methodology combines the simplicity of SPE using conventional cartridges and UHPLC-MS/MS, producing a rapid, sensitive, and reliable procedure."

The full article can be found at: (R. Romerogonzalez, et. al., "Application of Conventional Solid-Phase Extraction for Multimycotoxin Analysis in Beers by Ultrahigh-Performance Liquid Chromatography-Tandem Mass Spectrometry". Journal of Agricultural and Food Chemistry, 2009; 57(20): 9385-9392). Link not available.

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## **CRITICAL TIMING, LOCATION AND DURATION OF GLUCOCORTICOID ADMINISTRATION RESCUE MICE FROM SUPERANTIGEN-INDUCED SHOCK AND ATTENUATE LUNG INJURY**

Preventive Medicine Week  
November 22, 2009

"In this study we investigated the efficacy of glucocorticoid therapy in preventing SEB-induced lethal shock initiated through the respiratory route in mice. Dexamethasone, a potent anti-inflammatory steroid, administered intranasally on the first day, followed by intraperitoneal doses on the subsequent 4 days, was effective in attenuating SEB-induced hypothermia, and reduction in systemic and pulmonary proinflammatory mediator release."

"This optimal dosing and schedule of glucocorticoid treatment mitigated lung inflammation and resulted in 100% survival in this intranasal mouse model of SEB-mediated shock. ."

The full article can be found at: (T. Krakauer, et. al., "Critical timing, location and duration of glucocorticoid administration rescue mice from superantigen-induced shock and attenuate lung injury". *International Immunopharmacology*, 2009;9(10):1168-1174). Link not available.

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

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