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Chem-Bio News – S&T Edition

1. NONRANDOM DISTRIBUTION OF VECTOR TICKS (DERMACENTOR VARIABILIS) INFECTED BY FRANCISELLA TULARENSIS: *"We present evidence, for the first time, that the agent of tularemia persists in microfoci for at least four years."*

2. EXPOSURES RECORDED FOR PARTICIPANTS IN THE UK CHEMICAL WARFARE AGENT HUMAN RESEARCH PROGRAMME, 1941-1989: *"These categorizations have been used to assign veterans to exposure groups for epidemiological analysis."*

3. DEGRADATION OF CHEMICAL WARFARE AGENTS BY REACTIVE POLYMERS: *"The efficiency, ease of synthesis, and nontoxic nature of the PANOX and PHA polymers make them attractive materials in decontamination and as components of reactive barriers."*

4. BOTULINUM TOXIN DETECTION USING ALGAN/GAN HIGH ELECTRON MOBILITY TRANSISTORS: *"These results clearly demonstrate the promise of field-deployable electronic biological sensors based on AlGaN/GaN HEMTs for botulinum toxin detection."*

5. STRUCTURAL BASIS FOR ANTAGONISM OF HUMAN INTERLEUKIN 18 BY POXVIRUS INTERLEUKIN 18-BINDING PROTEIN:

6. A CAPACITIVE BIOSENSOR FOR DETECTION OF STAPHYLOCOCCAL ENTEROTOXIN B: *"The newly developed sensor has the benefits of simplicity, high sensitivity, and multiple use capability."*

CB Daily Report

Chem-Bio News

NONRANDOM DISTRIBUTION OF VECTOR TICKS (DERMACENTOR VARIABILIS) INFECTED BY FRANCISELLA TULARENSIS

By Heidi K. Goethert, Sam R. Telford, III

"We present evidence, for the first time, that the agent of tularemia persists in microfoci for at least four years. The existing literature alludes to the natural nidality of this bacterium and the importance thereof in its long-term survival in nature, but "natural foci" that have been described to date have been very nebulously defined, poorly analyzed, and at a scale much larger than what we describe. In addition, we demonstrate such a focus by using modern GIS methods as well as by genetic cluster analysis of bacterial DNA. The work, therefore, contributes to our understanding of how the agent of tularemia perpetuates over the long term. Furthermore, this paper serves as a paradigm for analyzing the ecology of other vector-borne infections and, in particular, demonstrating the mode of their long-term persistence in the environment."

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000319;jsessionid=BDA4BC87A52A9E0DE0996FBB8A823FAA>

[Return to Top](#)

EXPOSURES RECORDED FOR PARTICIPANTS IN THE UK CHEMICAL WARFARE AGENT HUMAN RESEARCH PROGRAMME, 1941-1989

Medical Letter on the CDC & FDA

March 15, 2009

"This study describes exposures to military veterans who participated between 1941 and 1989 in British research at Porton Down on the effects of exposure to chemical warfare agents and to defences against those agents. The study is part of a programme of epidemiological research initiated in response to service veterans' concerns about possible long-term health effects of their participation," investigators in Oxford, the United Kingdom report (see also Chemical Warfare).

"All entries in 97 books held in the Porton Down historical experimental archive covering the years 1939-1989 were reviewed. For tests between April 1941 and December 1989, data were abstracted on chemicals used, with additional detail abstracted for tests involving vesicants and nerve agents. For tests recorded during 1939-1941, similar data were abstracted for a representative sample of tests. Historical data were abstracted for 17 303 veterans included in the cohort study of 18 276 servicemen who took part in tests at Porton Down between 1941 and 1989. The median number of days per veteran on which tests were carried out was 2 days. The median difference between the last and first day of testing was 4 days. A large number of chemicals were tested over this period (n = 492). The type of chemical tested varied over time. Exposures were often modified by respirator use or use of protective clothing or protective equipment. It was possible to assign a quantitative measure of cumulative exposure to 73% of veterans exposed to the vesicant sulphur mustard-025EF3491 (34%) of exposed veterans had cumulative exposures ≥ 10.63 mg and for 70% of veterans exposed to the nerve agent sarin-025EF658 (29%) of exposed veterans had cumulative exposures ≥ 15.0 mg min m(-3). Ninety-three per cent of veterans exposed to sulphur mustard were classified to a semi-quantitative scale of dermal effect-

025EF3771 (37%) had a vesicle or necrosed area, and 69% of veterans exposed to sarin could be categorized by change in blood cholinesterase activity-025EF1033 (31%) had a depression in cholinesterase activity of $\geq 30\%$. The experimental archive at Porton Down has proved to be a rich source of data on tests conducted between 1941 and 1989. It has been possible to categorize most veterans according to date of test, chemical group, chemical, type of protection and, for certain chemicals, level of exposure and/or degree of acute toxicity."

"These categorizations have been used to assign veterans to exposure groups for epidemiological analysis."

The full article can be found at: (T.J. Keegan, et. al., "Exposures Recorded for Participants in the UK Chemical Warfare Agent Human Research Programme, 1941-1989". *Annals of Occupational Hygiene*, 2009;53(1):83-97). Link not available.

[Return to Top](#)

DEGRADATION OF CHEMICAL WARFARE AGENTS BY REACTIVE POLYMERS

Journal of Engineering

March 11, 2009

"Nucleophilic hydrolysis of chemical warfare agents (CWA), S-2-(diisopropylamino)ethyl O-ethyl methylphosphonothioate (VX), O-pinacolyl methylphosphonofluoridate (soman, or GD), and isopropyl methylphosphonofluoridate (sarin, or GB) by polyacrylamidoxime (PANOX) and poly(N-hydroxyacrylamide) (PHA) has been demonstrated. The reactive PANOX and PHA were obtained by one-step oximation of polyacrylonitrile and polyacrylamide, respectively."

"The polymers were converted to their respective oximate salts at pH values greater than the $pK(a)$ of oximate or amidoximate groups of 7.5 and 10.8, respectively. Although the PANOX and PHA exhibited spontaneous hydrolysis at ambient temperature and humidity, the conversion of the hydroxamate into the unreactive carboxylic groups was insignificant even at prolonged storage, so that the polymers maintained reactivity at ambient conditions. When exposed to ambient air or 100% humidity, the polymers imbibed up to 65 wt % water, which dramatically enhanced the polymer reactivity toward the CWA under study. The half-lives of VX in heterogeneous hydrolysis, which appeared to be pseudo-first-order in the polymer dispersions, were measured to be from 0.093 to 4.3 and 7.7 h in the presence of PANOX and PHA, respectively. The rates of hydrolytic activity of PANOX for VX exhibited a strong dependency on the degree of conversion of the amidoxime to amidoximate groups. The half-life of GB was less than 3 min. Only a minor presence of the toxic VX degradation product, S-[2-(diisopropylamino)ethyl]methylphosphonothioate (EA-2192), was detected in the course of degradation by the reactive polymers."

"The efficiency, ease of synthesis, and nontoxic nature of the PANOX and PHA polymers make them attractive materials in decontamination and as components of reactive barriers."

The full article can be found at: (L. Bromberg, et. al., "Degradation of Chemical Warfare Agents by Reactive Polymers". *Industrial & Engineering Chemistry Research*, 2009; 48

(3):1650-1659). Link not available.

[Return to Top](#)

BOTULINUM TOXIN DETECTION USING ALGAN/GAN HIGH ELECTRON MOBILITY TRANSISTORS

Journal of Technology & Science
March 1, 2009

"Antibody-functionalized, Au-gated AlGa_N/Ga_N high electron mobility transistors (HEMTs) were used to detect botulinum toxin. The antibody was anchored to the gate area through immobilized thioglycolic acid."

"The AlGa_N/Ga_N HEMT drain-source current showed a rapid response of less than 5 s when the target toxin in a buffer was added to the antibody-immobilized surface. We could detect a range of concentrations from 1 to 10 ng/ml."

"These results clearly demonstrate the promise of field-deployable electronic biological sensors based on AlGa_N/Ga_N HEMTs for botulinum toxin detection."

The full article can be found at: (Y.L. Wang, et. al., "Botulinum toxin detection using AlGa_N/Ga_N high electron mobility transistors". Applied Physics Letters, 2008; 93(26):62101). Link not available.

[Return to Top](#)

STRUCTURAL BASIS FOR ANTAGONISM OF HUMAN INTERLEUKIN 18 BY POXVIRUS INTERLEUKIN 18-BINDING PROTEIN

Preventive Medicine Week
March 8, 2009

"Functional homologs of human IL-18BP are encoded by all orthopoxviruses, including variola virus, the causative agent of smallpox. They contribute to virulence by suppressing IL-18-mediated immune responses. Here, we describe the 2.0-angstrom resolution crystal structure of an orthopoxvirus IL-18BP, ectromelia virus IL-18BP (ectvIL-18BP), in complex with hIL-18. The hIL-18 structure in the complex shows significant conformational change at the binding interface compared with the structure of ligand-free hIL-18, indicating that the binding is mediated by an induced-fit mechanism. EctvIL-18BP adopts a canonical Ig fold and interacts via one edge of its beta-sandwich with 3 cavities on the hIL-18 surface through extensive hydrophobic and hydrogen bonding interactions. Most of the ectvIL-18BP residues that participate in these interactions are conserved in both human and viral homologs, explaining their functional equivalence despite limited sequence homology. EctvIL-18BP blocks a putative receptor-binding site on IL-18, thus preventing IL-18 from engaging its receptor. Our structure provides insights into how IL-18BPs modulate hIL-18 activity."

"The revealed binding interface provides the basis for rational design of inhibitors against orthopoxvirus IL-18BP (for treating orthopoxvirus infection) or hIL-18 (for treating certain inflammatory and autoimmune diseases)."

The full article can be found at: (B. Krumm, et. al., "Structural basis for antagonism of human interleukin 18 by poxvirus interleukin 18-binding protein". Proceedings of the National Academy of Sciences of the United States of America, 2008;105(52):20711-20715). Link not available.

[Return to Top](#)

A CAPACITIVE BIOSENSOR FOR DETECTION OF STAPHYLOCOCCAL ENTEROTOXIN B

Proteomics Weekly

March 9, 2009

"A sensitive method for the detection of staphylococcal enterotoxin B (SEB) using a flow-injection capacitive biosensor is presented. SEB was purified from a crude culture filtrate of *Staphylococcus aureus* through three chromatographic steps."

"The first two steps were based on ion-exchange chromatography, and the last step was carried out on a gel filtration column. The SEB recovery values after the purification stages were 88%, 74%, and 12%, respectively. A horseradish peroxidase labeled antistaphylococcal enterotoxin B was prepared by the periodate method and was further employed in a sandwich-enzyme-linked immunosorbent assay (ELISA) for the determination of SEB concentrations in different samples obtained during the processing of the crude filtrate. The capacitive biosensor could detect SEB concentrations as low as 0.3 pg ml⁻¹ with a linearity ranging from 2.8 pg ml⁻¹ to 2.8 ng ml⁻¹ under optimized conditions. The response time was about 10 min. A good agreement was achieved between the developed capacitive biosensor system and ELISA as a reference method for detection of SEB levels in different purification samples."

"The newly developed sensor has the benefits of simplicity, high sensitivity, and multiple use capability."

The full article can be found at: (M. Labib, et. al., "A capacitive biosensor for detection of staphylococcal enterotoxin B". Analytical and Bioanalytical Chemistry, 2009;393(5):1539-44). Link not available.

[Return to Top](#)

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