

16 July 2009

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Chem-Bio News – S&T Edition

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IN IRANIAN VETERANS: *"The purpose of this study was to document the delayed toxic effects of sulphur mustard in Iranian veterans, focussing on head and neck complications."*

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5. NEW TARGET FOR CUSTOM ANTIBIOTICS DISCOVERED:

"Researchers at the Technische Universität München (TUM) in Munich, Germany have now cast light on a metabolic step that appears in many aggressive microorganisms like tuberculosis or malaria pathogens and that may provide a promising target for a new class of antibiotics."

6. STERILE SURFACES IN A FLASH: *"European scientists have created light-activated antimicrobial surfaces by modifying a material used in medical devices with tiny amounts of commonly used dyes."*

7. NERVE AGENTS ASSAY USING CHOLINESTERASE BASED BIOSENSOR:

"The biosensor was found long term stable at low as well its laboratory temperature."

8. (ALPHA(5)BETA(1)-INTEGRIN CONTROLS EBOLAVIRUS ENTRY BY REGULATING

ENDOSOMAL CATHEPSINS: *"These results provide further support for the requirement for endosomal cathepsins for ebolavirus infection, identify the DC forms of these cathepsins as previously unrecognized factors that contribute to cell tropism of this virus, and reveal a previously undescribed role for integrins during viral entry as regulators of endosomal cathepsins, which are required to prime the entry proteins of ebolavirus and other pathogenic viruses."*

CB Daily Report

Chem-Bio News

DELAYED HEAD AND NECK COMPLICATIONS OF SULPHUR MUSTARD POISONING IN IRANIAN VETERANS

By Zojaji R, Balali-Mood M, Mirzadeh M, Saffari A, Maleki M.

The Journal of Laryngology & Otology

July 2009

Objective: Sulphur mustard is a chemical warfare agent which was used against Iranian combatants and civilians between 1983 and 1988. The purpose of this study was to document the delayed toxic effects of sulphur mustard in Iranian veterans, focussing on head and neck complications.

Patients and methods: This was a two-year, prospective, descriptive study of 43 male Iranian veterans aged 34 to 48 years (mean 41.8 years) who were moderately disabled or worse due to sulphur mustard poisoning. Investigations were performed with consent, including haematological, biochemical and immunological tests, spirometry, chest X-ray, high resolution computed tomography of the lungs, and skin biopsies. Further investigations and interventions were performed as clinically indicated.

Results: The most affected sites were the lungs (95 per cent), peripheral nerves (77 per cent), skin (73 per cent), eyes (68 per cent), and head and neck (16.2 per cent). Of seven patients with mostly head and neck complications, four had a skin disorder (hyperpigmentation in all four, an erythematous, papular rash in two, and dry skin in one). Two patients had thyroid cancer (undifferentiated thyroid carcinoma in one and papillary carcinoma of a thyroglossal cyst in the other, 12 and 14 years after sulphur mustard exposure, respectively). One patient had nasopharyngeal carcinoma, 12 years after sulphur mustard exposure.

Conclusion:

Carcinomas of the thyroid and nasopharynx in three patients with sulphur mustard exposure are reported for the first time."

The full article can be found at: <http://www.ncbi.nlm.nih.gov/pubmed/19573255?dopt=Abstract>

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CONSTRUCTION OF A RECOMBINANT INTERGENUS MULTIDOMAIN CHIMERIC PROTEIN FOR SIMULTANEOUS EXPRESSION OF HAEMOLYSIN BL OF BACILLUS CEREUS, LISTERIOLYSIN O OF LISTERIA MONOCYTOGENES AND ENTEROTOXIN B OF STAPHYLOCOCCUS AUREUS

Medical Device Law Weekly
July 19, 2009

"The fusion gene (r-hle) comprising the conserved regions of hblD and the hly and entB genes was codon-optimized for expression in Escherichia coli and encoded a 50 kDa recombinant multidomain chimeric protein (r-HLE). Hyperimmune antiserum raised against r-HLE specifically reacted with the L, (38 kDa) component of the HBL complex of B. cereus, LLO (58 kDa) of L. monocytogenes and SEB (28 kDa) of S. aureus during Western blot analysis when tested on standard strains. During testing on isolates, the antiserum again identified the appropriate toxin molecules and was highly specific to the relevant bacterial species. The antigenicity of the SEB component of the r-HLE protein was also confirmed using a commercially available TECRA kit."

"The described procedure of creating a single antigenic molecule carrying components of three different toxins whilst still retaining the original antigenic determinants of individual toxins will be highly advantageous in the development of rapid, reliable and cost-effective immunoassays.."

The full article can be found at: (T.D.K. Kumar, et. al., "Construction of a recombinant intergenus multidomain chimeric protein for simultaneous expression of haemolysin BL of Bacillus cereus, listeriolysin O of Listeria monocytogenes and enterotoxin B of Staphylococcus aureus". Journal of Medical Microbiology, 2009;58(5):577-583). Link not available.

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A SINGLE COMPONENT TWO-VALENT LCRV-F1 VACCINE PROTECTS NON-HUMAN PRIMATES AGAINST PNEUMONIC PLAGUE

Health Risk Factor Week
July 14, 2009

"Vaccines against plague containing both the Fraction 1 (F1) and V antigens of Y. pestis have shown promise in protecting animal models against pneumonic plague, the deadliest form of the disease. Here we report on a plague vaccine consisting of the F1 and LcrV antigens fused to a single carrier molecule, the thermostable enzyme lichenase from Clostridium thermocellum, and expressed in and purified from Nicotiana benthamiana plants. When administered to Cynomolgus Macaques this purified plant-produced vaccine induced high titers of serum IgG, mainly of the IgG1 isotype, against both F1 and LcrV."

"These immunized animals were subsequently challenged and the LcrV-F1 plant-produced

vaccine conferred complete protection against aerosolized *Y. pestis*."

The full article can be found at: (J.A. Chichester, et. al., "A single component two-valent LcrV-F1 vaccine protects non-human primates against pneumonic plague". *Vaccine*, 2009; 27 (25-26 Sp.): 3471-3474). Link not available.

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OXIDATIVE DEGRADATION OF ORGANOPHOSPHOROUS PESTICIDES BY N-HALAMINE FABRICS

Science Letter
July 14, 2009

"Cotton and cotton/polyester fabrics containing halamine structures were able to react with certain organophosphorus pesticides upon contact."

"The reaction occurred at thione group in methyl parathion and malathion, and reaction products were oxon compounds. The fabric containing imide and amide halamine structures were able to oxidize 90% of methyl parathion in less than 2 h of contact time under room temperature, while the amine halamine structure needed longer time to reach the same level of oxidation."

"The reaction was endothermic, and the oxidation rate was in first order to the concentrations of the pesticides.."

The full article can be found at: (X. Fei, et. al., "Oxidative Degradation of Organophosphorous Pesticides by N-Halamine Fabrics". *Industrial & Engineering Chemistry Research*, 2009; 48(12):5604-5609). Link not available.

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NEW TARGET FOR CUSTOM ANTIBIOTICS DISCOVERED

Infection Control Today Magazine
July 14, 2009

"More and more bacterial stems are developing resistance to previously life-saving antibiotics. Physicians have been warning that fatality rates from infections could increase dramatically in the very near future. Researchers at the Technische Universität München (TUM) in Munich, Germany have now cast light on a metabolic step that appears in many aggressive microorganisms like tuberculosis or malaria pathogens and that may provide a promising target for a new class of antibiotics. The researchers present the results of their work in the current issue of the chemistry journal *Angewandte Chemie*."

Antibiotics hinder the production of essential compounds in microorganisms and can thus hold harmful pathogens in check. However, ever more bacterial stems are developing

multiple antibiotic resistances, thereby rendering previously life-saving medications ineffective. That is why researchers around the world are desperately searching for new reaction steps that are vital to microorganisms but play no relevant role in humans. Professor Michael Groll, Dr. Jörg Eppinger and Dr. Tobias Gräwert, biochemists at the Technische Universität München, and their team of researchers have described in detail the structural basis for just such a reaction step.

The cells of virtually all life forms synthesize essential natural substances belonging to the class of terpenes and steroids from the small isoprene building blocks dimethylallyl pyrophosphate (DMAPP) and isopentenyl pyrophosphate (IPP). Mammals and a large number of other organisms generate these essential metabolites via the so-called mevalonate pathway. But most human pathogens, including *Plasmodium falciparum*, have developed an alternate mechanism for producing these important substances. Now, this special pathway may spell doom for those bacteria. The TUM researchers have unraveled the structural basis of the terminal step in bacterial isoprene synthesis. The crucial enzyme has a most unusual structure, similar to a three-leaf clover, and may open a forceful line of attack for custom-tailored antibiotics."

The full article can be found at: <http://www.infectioncontrolday.com/hotnews/new-target-custom-antibiotics.html>

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STERILE SURFACES IN A FLASH

By Amaya Camara-Campos

Chemical Technology

July 10, 2009

"European scientists have created light-activated antimicrobial surfaces by modifying a material used in medical devices with tiny amounts of commonly used dyes.

Silicone is used in medical equipment, such as catheters. But bacteria can colonise its surface so that infections associated with catheter use are very common. Ivan Parkin, Mike Wilson, at University College London, and their colleagues in the UK and Spain have modified the polymer so that it kills bacteria when it is irradiated with a laser or visible light.

The researchers covalently bound organic dye molecules, methylene blue or toluidine blue O, to silicone surfaces. The process involves dipping a modified silicone in a solution of the dye for 24h, washing and drying it. It uses only small amounts of the dyes (picograms per mm²) but is very effective. After a few minutes' exposure to a low power laser, levels of viable *Escherichia coli* and *Staphylococcus epidermidis* on the polymeric surfaces dramatically drop: up to 99.999 per cent in the case of *S. epidermidis*.

The dyes work by generating reactive oxygen species under light irradiation and it is these that are toxic to the bacteria. The dyes have been incorporated into silicone before, but not covalently so they could potentially leach from the polymer."

The full article can be found at: <http://www.rsc.org/Publishing/ChemTech/Volume/2009/09/sterile-surfaces.asp>

The original article can be found at: <http://www.rsc.org/Publishing/Journals/JM/article.asp?doi=b905495b>

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NERVE AGENTS ASSAY USING CHOLINESTERASE BASED BIOSENSOR

Journal of Technology & Science

July 12, 2009

"Electrochemical biosensor based on electric eel acetylcholinesterase (ACME) (EC 3.1.1.7) was performed for assay of nerve agents - tabun, sarin, soman, cyclosarin, and VX. The biosensor used AChE as biorecognition element."

"The presence of nerve agents was accompanied by it strong inhibition of AChE activity. Enzyme activity is easily measurable by electrochemical oxidation of thiocholine created front acetylthiocholine (ATChCl) by AChE-catalyzed hydrolysis. The tested nerve agents were successfully assayed. The best limits of detection were achieved for sarin (5.88×10^{-10} M) and VX (8.51×10^{-10} M) after one-minute assay."

"The biosensor was found long term stable at low as well its laboratory temperature."

The full article can be found at: (M. Pohanka, et. al., "Nerve Agents Assay Using Cholinesterase Based Biosensor". *Electroanalysis*, 2009; 21(10):1177-1182). Link not available.

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(ALPHA(5)BETA(1)-INTEGRIN CONTROLS EBOLAVIRUS ENTRY BY REGULATING ENDOSOMAL CATHEPSINS

Gene Therapy Weekly

July 23, 2009

"Integrins are involved in the binding and internalization of both enveloped and nonenveloped viruses. By using 3 distinct cell systems-CHO cells lacking expression of alpha(5)beta(1)-integrin, HeLa cells treated with siRNA to alpha(5)-integrin, and mouse beta(1)-integrin knockout fibroblasts, we show that alpha(5)beta(1)-integrin is required for efficient infection by pseudovirions bearing the ebolavirus glycoprotein (GP)."

"These integrins are necessary for viral entry but not for binding or internalization. Given the

need for endosomal cathepsins B and L (CatB and CatL) to prime GPs for fusion, we investigated the status of CatB and CatL in integrin-positive and integrin-negative cell lines. alpha(5)beta(1)-Integrin-deficient cells lacked the double-chain (DC) forms of CatB and CatL, and this correlated with decreased CatL activity in integrin-negative CHO cells. These data indicate that alpha(5)beta(1)-integrin-negative cells may be refractory to infection by GP pseudovirions because they lack the necessary priming machinery (the double-chain forms of CatB and CatL). In support of this model, we show that GP pseudovirions that have been preprimed in vitro to generate the 19-kDa form of GP overcome the requirement for alpha(5)beta(1)-integrin for infection."

"These results provide further support for the requirement for endosomal cathepsins for ebolavirus infection, identify the DC forms of these cathepsins as previously unrecognized factors that contribute to cell tropism of this virus, and reveal a previously undescribed role for integrins during viral entry as regulators of endosomal cathepsins, which are required to prime the entry proteins of ebolavirus and other pathogenic viruses."

The full article can be found at: (K.L. Schornberg, et. al., "alpha(5)beta(1)-Integrin controls ebolavirus entry by regulating endosomal cathepsins". Proceedings of the National Academy of Sciences of the United States of America, 2009; 106(19):8003-8008). Link not available.

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