

26 February 2009

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

### **1. A SHORT COURSE OF ANTIBIOTIC TREATMENT IS EFFECTIVE IN PREVENTING DEATH FROM EXPERIMENTAL INHALATIONAL ANTHRAX AFTER DISCONTINUING ANTIBIOTICS:**

*"In the treatment of inhalational anthrax, the prolonged course of antibiotics required to achieve prophylaxis may not be necessary to prevent anthrax that results from the germination of retained spores after the discontinuation of antibiotics."*

### **2. HOUSEPLANT PEST GIVES CLUE TO POTENTIAL NEW ANTHRAX TREATMENT:**

*"Researchers at the University of Warwick have found how a citric acid-based Achilles heel used by a pathogen that attacks the popular African Violet house plant could be exploited not just to save African Violets but also to provide a potentially effective treatment for Anthrax."*

### **3. ANALYSIS OF THE DIFFERENTIAL HOST CELL NUCLEAR PROTEOME INDUCED BY ATTENUATED AND VIRULENT HEMORRHAGIC ARENAVIRUS INFECTION:**

*"This study provides a number of differentially expressed targets for further research and suggests that key events in pathogenesis may be established early in infection."*

**4. NANO-REGULATION CREEPS CLOSER:** *"On both sides of the Atlantic, government bodies responsible for the control of potentially hazardous materials have been widely criticised for a too-slow response to the burgeoning nanotechnology industry, failing even to collect the necessary nanoparticle safety data needed to guide policy."*

**5. THE MEDICAL POWER OF ATTRACTION:** *"US scientists have made a microfluidic device that cleanses blood of toxic pathogens."*

### **6. COADMINISTRATION OF CIDOFOVIR AND SMALLPOX VACCINE REDUCED VACCINATION SIDE EFFECTS BUT INTERFERED WITH VACCINE-ELICITED IMMUNE RESPONSES AND IMMUNITY TO MONKEYPOX:**

*"Thus, the single-dose coadministration of cidofovir and Dryvax effectively controlled vaccination side effects but significantly compromised vaccine-elicited immune responses and vaccine-induced immunity to monkeypox."*

### **7. REGULATORY T CELLS MODULATE STAPHYLOCOCCAL ENTEROTOXIN B [SEB]-**

**INDUCED EFFECTOR T-CELL ACTIVATION AND ACCELERATION OF COLITIS:** *"This suggests that Treg cells prevent SEB-induced mucosal inflammation through modulation of SEB-induced T-cell activation."*

**8. CHOLERA TOXIN INHIBITORS STUDIED WITH HIGH-PERFORMANCE LIQUID AFFINITY CHROMATOGRAPHY: A ROBUST METHOD TO EVALUATE RECEPTOR-LIGAND INTERACTIONS:** *"It offers multiple advantages, such as a low sample consumption, high reproducibility and short analysis time, which are often not observed in other methods of analysis."*

## CB Daily Report

### Chem-Bio News

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#### **A SHORT COURSE OF ANTIBIOTIC TREATMENT IS EFFECTIVE IN PREVENTING DEATH FROM EXPERIMENTAL INHALATIONAL ANTHRAX AFTER DISCONTINUING ANTIBIOTICS**

Preventive Medicine Week  
March 1, 2009

"Postexposure prophylaxis of inhalational anthrax requires prolonged antibiotic therapy or antibiotics and vaccination. The duration of treatment for established anthrax is controversial, because retained spores may germinate and cause disease after antibiotics are discontinued."

"Using rhesus macaques, we determined whether a short course of antibiotic treatment, as opposed to prophylaxis, could effectively treat inhalational anthrax and prevent disease caused by the germination of spores after discontinuation of antibiotics. Two groups of 10 rhesus macaques were exposed to an aerosol dose of *Bacillus anthracis* spores. Animals in group 1 received ciprofloxacin prophylaxis beginning 1-2 h after exposure. Those in group 2 began receiving ciprofloxacin after becoming bacteremic, and treatment was continued for 10 days. When each group 2 animal completed 10 days of therapy, the prophylactic antibiotic was discontinued in the paired group 1 animal. In group 1 (prophylaxis), no deaths occurred during antibiotic treatment, but only 2 (20%) of 10 animals survived after antibiotics were discontinued. In contrast, in group 2 (treatment), 3 deaths occurred during antibiotic treatment, but all 7 animals (100%) alive after 10 days of therapy survived when antibiotics were discontinued."

"In the treatment of inhalational anthrax, the prolonged course of antibiotics required to achieve prophylaxis may not be necessary to prevent anthrax that results from the germination of retained spores after the discontinuation of antibiotics."

The full article can be found at: (N.J. Vietri, et. al., "A Short Course of Antibiotic Treatment Is Effective in Preventing Death from Experimental Inhalational Anthrax after Discontinuing Antibiotics". *Journal of Infectious Diseases*, 2009; 199(3): 336-341). Link not available.

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## **HOUSEPLANT PEST GIVES CLUE TO POTENTIAL NEW ANTHRAX TREATMENT**

Physorg.com

February 24, 2009

“Researchers at the University of Warwick have found how a citric acid-based Achilles heel used by a pathogen that attacks the popular African Violet house plant could be exploited not just to save African Violets but also to provide a potentially effective treatment for Anthrax.”

“Like many bacteria *Pectobacterium chrysanthemi* competes with its host for iron. Without a supply of this essential nutrient the bacterium cannot grow. The University of Warwick researchers Dr Nadia Kadi, Dr Daniel Oves-Costales, Dr Lijiang Song and Professor Gregory Challis worked with colleagues at St Andrews University to examine how a "siderophore", one of the key tools the bacterium uses to harvest iron is assembled. They discovered how an enzyme catalyst in the assembly of this particular siderophore - called achromobactin - binds citric acid, a vital iron-binding component of the structure. Their findings show that this chemical pathway could be blocked or inhibited to prevent the bacterium from harvesting iron, essentially starving it.”

“A second piece of research conducted by three of the University of Warwick researchers (Dr Daniel Oves-Costales, Dr Lijiang Song and Professor Gregory L. Challis ) found that the deadly pathogen which causes Anthrax in humans uses an enzyme to incorporate citric acid into another siderophore that is very similar to the one used by the African Violet pathogen. The researchers showed that both enzymes recognise citric acid in the same way. This means a common strategy could be used to block both the Anthrax and African Violet pathogen siderophore synthesis pathways.”

The full article can be found at: <http://www.physorg.com/news154681012.html>

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## **ANALYSIS OF THE DIFFERENTIAL HOST CELL NUCLEAR PROTEOME INDUCED BY ATTENUATED AND VIRULENT HEMORRHAGIC ARENAVIRUS INFECTION**

Medical Letter on the CDC & FDA

March 8, 2009

"Despite continuing research, little is known about the molecular basis of pathogenesis, and this has hindered the design of novel antiviral therapeutics. Modulation of the host response is a potential strategy for the treatment of infectious diseases. We have previously investigated the global host response to attenuated and lethal arenavirus infections by using high-throughput immunoblotting and kinomics approaches. In this report, we describe the differential nuclear proteomes of a murine cell line induced by mock infection and infection with attenuated and lethal variants of PICV, investigated by using two-dimensional gel

electrophoresis. Spot identification using tandem mass spectrometry revealed the involvement of a number of proteins that regulate inflammation via potential modulation of NF-kappa B activity and of several heterogeneous nuclear ribonuclear proteins. Pathway analysis revealed a potential role for transcription factor XBP-1, a transcription factor involved in major histocompatibility complex II (MHC-II) expression; differential DNA-binding activity was revealed by electrophoretic mobility shift assay, and differences in surface MHC-II expression were seen following PICV infection. These data are consistent with the results of several previous studies and highlight potential differences between transcriptional and translational regulation."

"This study provides a number of differentially expressed targets for further research and suggests that key events in pathogenesis may be established early in infection."

The full article can be found at: (G.C. Bowick, et. al., "Analysis of the Differential Host Cell Nuclear Proteome Induced by Attenuated and Virulent Hemorrhagic Arenavirus Infection". Journal of Virology, 2009; 83(2): 687-700). Link not available.

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## **NANO-REGULATION CREEPS CLOSER**

By Victoria Gill

Chemistry World (UK Royal Society of Chemistry)

February 25, 2009

"Canada has introduced a mandatory safety reporting scheme for companies producing nanomaterials, becoming the first country in the world to do so. However, regulators in the US and Europe continue to dither over the issue - despite scientists' concern that there are too many gaps in the basic knowledge of nanoparticles' properties to support the development of informed regulation.

On both sides of the Atlantic, government bodies responsible for the control of potentially hazardous materials have been widely criticised for a too-slow response to the burgeoning nanotechnology industry, failing even to collect the necessary nanoparticle safety data needed to guide policy."

"In Europe, the recently introduced Reach (Registration, evaluation, authorisation and restriction of chemicals) regulations already apply to nanoparticles, and regulators are reviewing the legislation to clarify how it deals with nanomaterials.

However, as Reach currently stands, the quantities produced are often too small to be considered. 'The regulatory trigger for Reach is one tonne per year,' explains Qasim Chaudhry, senior scientist at the UK's Central Science Laboratory, who has led regulatory reviews on nanotechnology for Defra. 'But if someone is producing 999kg, that regulation won't cover it. And that amount is a huge number of nanoparticles. The threshold limits should be revisited.'

The full article can be found at: <http://www.rsc.org/chemistryworld/News/2009/>

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## **THE MEDICAL POWER OF ATTRACTION**

By Emma Shiells

Chemical Technology (UK Royal Society of Chemistry)

February 25, 2009

"US scientists have made a microfluidic device that cleanses blood of toxic pathogens."

"Ingber's device consists of four vertically stacked channels filled with flowing fungi-contaminated blood. He added magnetic microbeads coated with antibodies to the blood, which bound to the fungi. A magnetic field gradient generated across the channels continuously separated the fungi-bound beads from the blood. Ingber showed the device can clear 80 per cent of the fungi, 1000 times faster than other blood cleansing prototypes."

The full article can be found at: [http://www.rsc.org/Publishing/ChemTech/Volume/2009/04/medical\\_power\\_attraction.asp](http://www.rsc.org/Publishing/ChemTech/Volume/2009/04/medical_power_attraction.asp)

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## **COADMINISTRATION OF CIDOFOVIR AND SMALLPOX VACCINE REDUCED VACCINATION SIDE EFFECTS BUT INTERFERED WITH VACCINE-ELICITED IMMUNE RESPONSES AND IMMUNITY TO MONKEYPOX**

Drug Week

March 6, 2009

"While the smallpox vaccine, Dryvax or Dryvax-derived ACAM2000, holds potential for public immunization against the spread of smallpox by bioterror, there is serious concern about Dryvax-mediated side effects. Here, we report that a single-dose vaccination regimen comprised of Dryvax and an antiviral agent, cidofovir, could reduce vaccinia viral loads after vaccination and significantly control Dryvax vaccination side effects."

"However, coadministration of cidofovir and Dryvax also reduced vaccine-elicited immune responses of antibody and T effector cells despite the fact that the reduced priming could be boosted as a recall response after monkeypox virus challenge. Evaluations of four different aspects of vaccine efficacy showed that coadministration of cidofovir and Dryvax compromised the Dryvax-induced immunity against monkeypox, although the covaccinated monkeys exhibited measurable protection against monkeypox compared to that of naive controls."

"Thus, the single-dose coadministration of cidofovir and Dryvax effectively controlled vaccination side effects but significantly compromised vaccine-elicited immune responses and vaccine-induced immunity to monkeypox."

The full article can be found at: (H.Y. Wei, et. al., "Coadministration of Cidofovir and Smallpox Vaccine Reduced Vaccination Side Effects but Interfered with Vaccine-Elicited Immune Responses and Immunity to Monkeypox". Journal of Virology, 2009;83(2): 1115-1125). Link not available.

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## **REGULATORY T CELLS MODULATE STAPHYLOCOCCAL ENTEROTOXIN B [SEB]-INDUCED EFFECTOR T-CELL ACTIVATION AND ACCELERATION OF COLITIS**

Biotech Week

February 25, 2009

"SCID mice were fed SEB 3 and 7 days after reconstitution with CD4(+) CD45RB(high) or CD4(+) CD45RB(high) plus CD4(+) CD45RB(low) T cells. Mice were sacrificed at different time points to examine changes in tissue damage and in T-cell phenotypes. Feeding SEB failed to produce any clinical effect on SCID mice reconstituted with CD4(+) CD45RB(high) and CD4(+) CD45RB(low) T cells, but feeding SEB accelerated the development of colitis in SCID mice reconstituted with CD4(+) CD45RB(high) T cells alone. The latter was associated with an increase in the number of CD4(+) Vbeta8(+) T cells expressing CD69 and a significantly lower number of CD4(+) CD25(+) Foxp3(+) T cells. These changes were not observed in SCID mice reconstituted with both CD45RB(high) and CD45RB(low) T cells. In addition, SEB impaired the development of Treg cells in the SCID mice reconstituted with CD4(+) CD45RB(high) T cells alone but had no direct effect on Treg cells. In the absence of Treg cells, feeding SEB induced activation of mucosal T cells and accelerated the development of colitis."

"This suggests that Treg cells prevent SEB-induced mucosal inflammation through modulation of SEB-induced T-cell activation."

The full article can be found at: (A. Heriazon, et. al., "Regulatory T cells modulate staphylococcal enterotoxin B-induced effector T-cell activation and acceleration of colitis". Infection and Immunity, 2009;77(2):707-13). Link not available.

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## **CHOLERA TOXIN INHIBITORS STUDIED WITH HIGH-PERFORMANCE LIQUID AFFINITY CHROMATOGRAPHY: A ROBUST METHOD TO EVALUATE RECEPTOR-LIGAND INTERACTIONS**

Medical Imaging Week

February 21, 2009

"In this report, we demonstrate a high-performance liquid affinity chromatography approach called weak affinity chromatography to evaluate cholera toxin inhibitors. The cholera toxin B-subunit was covalently coupled to porous silica and a (weak) affinity column was produced.

The K-D values of galactose and meta-nitrophenyl alpha-d-galactoside were determined with weak affinity chromatography to be 52 and 1 mm, respectively, which agree well with IC50 values previously reported. To increase inhibition potency multivalent inhibitors have been developed and the interaction with multivalent glycopolypeptides was also evaluated. The affinity of these compounds was found to correlate with the galactoside content but K-D values were not obtained because of the inhomogeneous response and slow off-rate from multivalent interactions. Despite the limitations in obtaining direct K-D values of the multivalent galactopolypeptides, weak affinity chromatography represents an additional and valuable tool in the evaluation of monovalent as well as multivalent cholera toxin inhibitors."

"It offers multiple advantages, such as a low sample consumption, high reproducibility and short analysis time, which are often not observed in other methods of analysis."

The full article can be found at: (M. Bergstrom, et. al., "Cholera Toxin Inhibitors Studied with High-Performance Liquid Affinity Chromatography: A Robust Method to Evaluate Receptor-Ligand Interactions. *Chemical Biology & Drug Design*", 2009; 73(1):132-141). Link not available.

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