27 August 2009

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Chem-Bio News - S&T Edition

1. FDA APPROVES MILITARY FLU TESTING ON PORTABLE LAB: *"Military doctors can use a portable polymerase chain reaction (PCR) testing device to diagnose novel H1N1 flu infections in troops overseas, the FDA announced."*

2. SINGLE-INJECTION VACCINE PROTECTS NONHUMAN PRIMATES AGAINST INFECTION WITH MARBURG VIRUS AND THREE SPECIES OF EBOLA VIRUS: *"We developed an immunization scheme based on a single-injection vaccine that protects nonhuman primates against lethal challenge with representative strains of all human pathogenic filovirus species.."*

3. ANTI-TERROR ANTIBODIES: *"European scientists have developed a method to detect potential biological warfare agents in food."*

4. DEVELOPMENT AND CHARACTERIZATION OF A MOUSE MODEL FOR MARBURG HEMORRHAGIC FEVER: *"This mouse-adapted MARV strain can now be used to develop and evaluate novel vaccines and therapeutics and may also help to provide a better understanding of the virulence factors associated with MARV.."*

5. 'CHEMICAL NOSE' SENSOR SNIFFS BLOOD PROTEIN PROFILE: *"US scientists have developed a sensor system for profiling the protein content of human blood serum without needing individual receptors for each separate protein. The technique could be used to provide cheap preliminary disease diagnosis information, saving time and money by reducing unnecessary testing."*

6. TRANSCRIPTIONAL PROFILING OF SACCHAROMYCES CEREVISIAE UPON EXPOSURE TO SAXITOXIN: *"The molecular target of saxitoxin in higher eukaryotes is the voltage-gated sodium channel; however, its target in lower eukaryotic organisms remains unknown."*

7. EBOLAVIRUS VP35 INTERACTS WITH THE CYTOPLASMIC DYNEIN LIGHT CHAIN 8: *"Given that VP35 from various EBOV species interacts with DLC8, this interaction may have a role in regulating the EBOV life cycle.."*

CB Daily Report

Chem-Bio News

FDA APPROVES MILITARY FLU TESTING ON PORTABLE LAB
By John Gever
MedPage Today
August 26, 2009

“Military doctors can use a portable polymerase chain reaction (PCR) testing device to diagnose novel H1N1 flu infections in troops overseas, the FDA announced.

The emergency authorization was approved "to better protect our troops," said FDA Commissioner Margaret A. Hamburg, MD, in a statement.

The device, called JBAIDS (Joint Biological Agent Identification and Diagnostic System), is a rugged, suitcase-sized instrument that can run PCR-based molecular diagnostic tests. It has been under development for several years by a consortium of military health research centers, the CDC, and academic medical laboratories.”

The full article can be found at: http://www.medpagetoday.com/InfectiousDisease/URItheFlu/15699

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SINGLE-INJECTION VACCINE PROTECTS NONHUMAN PRIMATES AGAINST INFECTION WITH MARBURG VIRUS AND THREE SPECIES OF EBOLA VIRUS
Medical Letter on the CDC & FDA
August 30, 2009

“Among the most promising filovirus vaccines under development is a system based on recombinant vesicular stomatitis virus (VSV) that expresses a single filovirus glycoprotein (GP) in place of the VSV glycoprotein (G).”

"Here, we performed a proof-of-concept study in order to determine the potential of having one single-injection vaccine capable of protecting nonhuman primates against Sudan ebolavirus (SEBOV), Zaire ebolavirus (ZEBOV), Cote d'Ivoire ebolavirus (CIEBOV), and Marburgvirus (MARV). In this study, 11 cynomolgus monkeys were vaccinated with a blended vaccine consisting of equal parts of the vaccine vectors VSV Delta G/SEBOVGP, VSV Delta G/ZEBOVGP, and VSV Delta G/MARVGP. Four weeks later, three of these animals were challenged with MARV, three with CIEBOV, three with ZEBOV, and two with SEBOV. Three control animals were vaccinated with VSV vectors encoding a nonfilovirus GP and challenged with SEBOV, ZEBOV, and MARV, respectively, and five unvaccinated control animals were challenged with CIEBOV. Importantly, none of the macaques vaccinated with the blended vaccine succumbed to a filovirus challenge. As expected, an experimental control animal

vaccinated with VSV Delta G/ZEBOVGP and challenged with SEBOV succumbed, as did the positive controls challenged with SEBOV, ZEBOV, and MARV, respectively. All five control animals challenged with CIEBOV became severely ill, and three of the animals succumbed on days 12, 12, and 14, respectively. The two animals that survived CIEBOV infection were protected from subsequent challenge with either SEBOV or ZEBOV, suggesting that immunity to CIEBOV may be protective against other species of Ebola virus."

"We developed an immunization scheme based on a single-injection vaccine that protects nonhuman primates against lethal challenge with representative strains of all human pathogenic filovirus species.."

The full article can be found at: (T.W. Geisbert, et. al., "Single-Injection Vaccine Protects Nonhuman Primates against Infection with Marburg Virus and Three Species of Ebola Virus". Journal of Virology, 2009;83(14):7296-7304). Link not available.

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ANTI-TERROR ANTIBODIES
By Victoria Steven
Highlights in Chemical Biology
August 26, 2009

"European scientists have developed a method to detect potential biological warfare agents in food.

A possible scenario for a bioterrorism attack could involve food contamination with protein toxins, such as ricin and botulinum neurotoxins, says Brigitte Dorner, researcher into microbial toxins, of the Robert Koch Institute in Berlin. However, until now detecting toxins in such complex samples has been difficult. Dorner and colleagues in Germany and Switzerland have devised a highly sensitive system that can detect trace amounts of the toxins in foods such as milk, baby food and yoghurt.

Protein toxins are detected most effectively using immunological techniques, since antibodies bind to their targets with very high affinity. However, current methods for raising antibodies against toxins without causing animal poisoning are time consuming and labour intensive. Dorner and coworkers have used an alternative technique, immobilising the toxins on microbeads to reduce their toxicity, allowing the team to generate antibodies quickly in vivo.

The researchers then modified a commercially available system to analyse complex food samples using the antibodies. In Luminex xMAP technology antibodies are covalently coupled to beads embedded with dyes that generate signals in response to different targets - in this case the toxins. Dorner explains: 'We further developed the Luminex xMAP technology to incorporate magnetic beads to allow us to analyse complex matrices.' The magnetic property means that the beads can be easily removed from food samples and can undergo automated washings. This makes toxin detection in foods possible where many

other technologies have failed due to interference of sample components with binding agents or technical equipment.

Using the bead array, the researchers simultaneously detected trace amounts of five toxins, including ricin and botulinum neurotoxins, in food at lower concentrations than commercially available systems. Dorner says the technique has very good sensitivity. 'We are able to detect toxins down to a level of picograms per millilitre which, as far as I know, is superior to any limit published for other multiplex detection systems,' she says."

The full article can be found at: http://www.rsc.org/Publishing/Journals/cb/Volume/2009/10/Antiterror_antibodies.asp

The original article can be found at: http://www.rsc.org/Publishing/Journals/AN/article.asp?doi=b911525k

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DEVELOPMENT AND CHARACTERIZATION OF A MOUSE MODEL FOR MARBURG HEMORRHAGIC FEVER
Drug Week
August 28, 2009

"The lack of a mouse model has hampered an understanding of the pathogenesis and immunity of Marburg hemorrhagic fever (MHF), the disease caused by marburgvirus (MARV), and has created a bottleneck in the development of antiviral therapeutics. Primary isolates of the filoviruses, i.e., ebolavirus (EBOV) and MARV, are not lethal to immunocompetent adult mice."

"Previously, pathological, virologic, and immunologic evaluation of a mouse-adapted EBOV, developed by sequential passages in suckling mice, identified many similarities between this model and EBOV infections in nonhuman primates. We recently demonstrated that serially passaging virus recovered from the liver homogenates of MARV-infected immunodeficient (SCID) mice was highly successful in reducing the time to death in these mice from 50 to 70 days to 7 to 10 days after challenge with the isolate MARV-Ci67, -Musoke, or -Ravn. In this study, we extended our findings to show that further sequential passages of MARV-Ravn in immunocompetent mice caused the MARV to kill BALB/c mice. Serial sampling studies to characterize the pathology of mouse-adapted MARV-Ravn revealed that this model is similar to the guinea pig and nonhuman primate MHF models. Infection of BALB/c mice with mouse-adapted MARV-Ravn caused uncontrolled viremia and high viral titers in the liver, spleen, lymph node, and other organs; profound lymphopenia; destruction of lymphocytes within the spleen and lymph nodes; and marked liver damage and thrombocytopenia. Sequencing the mouse-adapted MARV-Ravn strain revealed differences in 16 predicted amino acids from the progenitor virus, although the exact changes required for adaptation are unclear at this time."

"This mouse-adapted MARV strain can now be used to develop and evaluate novel vaccines and therapeutics and may also help to provide a better understanding of the virulence

factors associated with MARV.."

The full article can be found at: (K.L. Warfield, et. al., “Development and Characterization of a Mouse Model for Marburg Hemorrhagic Fever”. Journal of Virology, 2009;83(13):6404-6415). Link not available.

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'CHEMICAL NOSE' SENSOR SNIFFS BLOOD PROTEIN PROFILE
By Phillip Broadwith
Chemistry World
August 24, 2009

“US scientists have developed a sensor system for profiling the protein content of human blood serum without needing individual receptors for each separate protein. The technique could be used to provide cheap preliminary disease diagnosis information, saving time and money by reducing unnecessary testing.

There is a direct link between levels of protein in human serum and disease, making protein levels an attractive target for sensors and diagnostics. However, with over 20,000 proteins present in human serum at a range of different concentrations, developing an effective sensor has been a challenging task.”

.....

“Techniques to detect specific proteins can be expensive because they generally use individual antibodies or complex mass spectrometry techniques and are limited to detecting only their target protein. Rotello explains that they needed a more general receptor system. The team used gold nanoparticles coated with short polymer chains that can be altered to tune the surface chemistry of the particles to favour binding to different types of proteins.

'That's the recognition part,' says Rotello, 'but you also need to generate a signal, and for that we used Green Fluorescent Protein (GFP).' The GFP sticks to the nanoparticles, which quenches its fluorescence, explains Rotello. 'When it's kicked off the particles by a competing protein, it lights up,' he adds. Different proteins will compete more or less strongly with GFP to bind nanoparticles with different surface chemistry, so the way a serum sample interacts with several different nanoparticles gives a fluorescence profile that reflects the concentrations of the proteins.

Using GFP as the reporter molecule will really help the technique be accepted by other researchers, says Eric Anslyn from the University of Texas, Austin. 'GFP is a really standard biochemical tool [as recognised by the Nobel prize for Chemistry in 2008], so molecular biologists will feel very comfortable using it.'

The full article can be found at: http://www.rsc.org/chemistryworld/News/2009/August/24080901.asp

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TRANSCRIPTIONAL PROFILING OF SACCHAROMYCES CEREVISIAE UPON EXPOSURE TO SAXITOXIN
Energy & Ecology
September 4, 2009

"Saxitoxin is a potent neurotoxin produced by several species of dinoflagellates and cyanobacteria. The molecular target of saxitoxin in higher eukaryotes is the voltage-gated sodium channel; however, its target in lower eukaryotic organisms remains unknown."

"The goal of this study was to obtain the transcriptional fingerprint of the model lower eukaryote Saccharomyces cerevisiae upon exposure to saxitoxin to identify potential genes suitable for biomarker development Microarray analyses identified multiple genes associated with copper and iron homeostasis and sulfur metabolism as significantly differentially expressed upon exposure to saxitoxin; these results were verified with quantitative reverse-transcriptase PCR (qRT-PCR). Additionally, the qRT-PCR assays were used to generate expression profiles in a subset of the differentially regulated genes across multiple exposure times and concentrations, the results of which demonstrated that overall, genes tended to respond in a consistent manner to the toxin. In general, the genes encoding the metallothioneins CUP1 and CRS5 were induced following exposure to saxitoxin, while those encoding the ferric/cupric reductase FRE1 and the copper uptake transporter CTR1 were repressed."

"The gene encoding the multicopper ferroxidase FET3, part of the high-affinity iron uptake system, was also induced in all treatments, along with the STR3 gene, which codes for the cystathionine beta-lyase found in the methionine biosynthetic pathway.."

The full article can be found at: (K.D. Cusick, et. al., "Transcriptional Profiling of Saccharomyces cerevisiae Upon Exposure to Saxitoxin". Environmental Science & Technology, 2009;43(15):6039-6045). Link not available.

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EBOLAVIRUS VP35 INTERACTS WITH THE CYTOPLASMIC DYNEIN LIGHT CHAIN 8
Blood Weekly
August 27, 2009

"The viral protein VP35 of ebolavirus (EBOV) is implicated to have diverse roles in the viral life cycle. We employed a yeast two-hybrid screen to search for VP35 binding partners and identified the cytoplasmic dynein light chain (DLC8) as a protein that interacts with VP35."

"Mapping analysis unraveled a consensus motif, SQTQT, within VP35 through which VP35 binds to DLC8. The disruption of DLC8 binding does not affect the ability of VP35 to inhibit

type I IFN production."

"Given that VP35 from various EBOV species interacts with DLC8, this interaction may have a role in regulating the EBOV life cycle.."

The full article can be found at: (T. Kubota, et. al., "Ebolavirus VP35 Interacts with the Cytoplasmic Dynein Light Chain 8". Journal of Virology, 2009;83(13):6952-6956). Link not available.

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