

4 March 2010

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## **Chem-Bio News – S&T Edition**

- 1. IMMOBILIZATION OF ENZYMES WITHIN HYDROGEL MICROPARTICLES TO CREATE OPTICAL BIOSENSORS FOR THE DETECTION OF ORGANOPHOSPHORUS COMPOUNDS:** *"These results indicate that AChE-SNAFL conjugates could be encapsulated within PEG hydrogel microparticles without a significant loss of the enzyme activity and that these microparticles could potentially be used as optical biosensors for the detection of organophosphorus compounds."*
- 2. LIQUID CHROMATOGRAPHIC POST-COLUMN OXIDATION METHOD FOR ANALYSIS OF PARALYTIC SHELLFISH TOXINS IN MUSSELS, CLAMS, SCALLOPS, AND OYSTERS: SINGLE-LABORATORY VALIDATION:** *"The instrumental technique was developed for the analysis of PST in shellfish as an alternative to the precolumn oxidation method, AOAC Official Method 2005.06, and a replacement for the current AOAC biological method 959.08."*
- 3. GAMMA IRRADIATION AS A BIOLOGICAL DECONTAMINANT AND ITS EFFECT ON COMMON FINGERMARK DETECTION TECHNIQUES AND DNA PROFILING:** *"The results demonstrated the successful recovery of latent marks and DNA establishing gamma irradiation as a viable decontamination option."*
- 4. COMPARISON OF ELISA AND SPR BIOSENSOR TECHNOLOGY FOR THE DETECTION OF PARALYTIC SHELLFISH POISONING TOXINS:** *"The reduced manual labor and simplicity of operation of the SPR biosensor compared to ELISA, ease of sample extraction and superior real time semi-quantitative analysis are key features that could make this technology applicable in a high-throughput monitoring unit."*
- 5. CHRONIC INHIBITION OF CYCLOOXYGENASE-2 ATTENUATES ANTIBODY RESPONSES AGAINST VACCINIA INFECTION:** *"These new findings support an essential role for Cox-2 in regulating humoral immunity."*
- 6. VACCINIA PROTEIN F12 HAS STRUCTURAL SIMILARITY TO KINESIN LIGHT CHAIN AND CONTAINS A MOTOR BINDING MOTIF REQUIRED FOR VIRION EXPORT:** *"Data presented demonstrate that F12 is critical for recruitment of kinesin-1 to virions and that a conserved tryptophan and aspartic acid (WD) motif, which is conserved in the kinesin-1-binding sequence (KBS) of the neuronal protein calyntenin/alcadein and several other cellular kinesin-1 binding proteins, is essential for kinesin-1 recruitment and virion transport."*
- 7. THE COMPLETE GENOME ANALYSIS OF CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUS ISOLATED IN TURKEY:** *"Based on the analysis of S, M, and L segments, CCHFV Turkey-Kelkit06 clustered in Group V, which represents the Europe/Turkey geographic lineage."*
- 8. GUIDANCE FOR INDUSTRY: CHARACTERIZATION AND QUALIFICATION OF CELL SUBSTRATES AND OTHER BIOLOGICAL MATERIALS USED IN THE PRODUCTION OF VIRAL VACCINES FOR INFECTIOUS DISEASE INDICATIONS:** *"This guidance applies to the development of viral vaccines for the prevention and treatment of infectious diseases that are regulated by the Office of Vaccines Research and Review (OVR) of the Center for Biologics Evaluation and Research (CBER) under section 351 of the Public Health Service (PHS) Act (42 U.S.C. 262)."*
- 9. TRANSIT THROUGH THE FLEA VECTOR INDUCES A PRETRANSMISSION INNATE IMMUNITY RESISTANCE PHENOTYPE IN YERSINIA PESTIS:** *"Y. pestis from infected fleas were more resistant to phagocytosis by macrophages than in vitro-grown bacteria, in part attributable to a cluster of insecticidal-like toxin genes that were highly expressed only in the flea."*
- 10. PREPARING A COMMUNITY HOSPITAL TO MANAGE WORK-RELATED EXPOSURES TO**

**INFECTIOUS AGENTS IN BIOSAFETY LEVEL 3 AND 4 LABORATORIES:** *"We developed a training program for HCWs [health care workers] that emphasized the optimal use of barrier precautions and used pathogen-specific modules and simulations with mannequins and fluorescent liquids that represented infectious body fluids. The facility and training led to increased willingness among HCWs to care for patients with all types of communicable diseases."*

**11. 'PAINLESS' VACCINE NEEDLE INVENTED IN JAPAN:** *"By penetrating just 0.5 millimetres before the needles dissolve and administer the vaccine, the patient feels no discomfort and there is no bleeding, said Professor Takada, of Kyoto Pharmaceutical University."*

## CB Daily Report

### Chem-Bio News

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#### **IMMOBILIZATION OF ENZYMES WITHIN HYDROGEL MICROPARTICLES TO CREATE OPTICAL BIOSENSORS FOR THE DETECTION OF ORGANOPHOSPHORUS COMPOUNDS**

Physics Week  
February 16, 2010

"As a first step in the development of an optical biosensor for the detection of organophosphorus compounds, we describe the immobilization of conjugates of enzyme (AChE) and pH-sensitive fluorophore (SNAFL-1) within the PEG hydrogel microparticles via a dispersion photopolymerization. The fluorescent response of the PEG microparticles containing AChE-SNAFL conjugates showed that AChE-SNAFL conjugates were successfully encapsulated within the microparticles and that AChE was still active after the encapsulation procedure."

"Using a quantitative analysis of enzyme activity, we found that 70% of AChE activity was maintained after conjugation and encapsulation. A leaching test showed that there was no significant AChE leaching into the surrounding media."

"These results indicate that AChE-SNAFL conjugates could be encapsulated within PEG hydrogel microparticles without a significant loss of the enzyme activity and that these microparticles could potentially be used as optical biosensors for the detection of organophosphorus compounds."

The full article can be found at: (B. Kim, et. al., "Immobilization of enzymes within hydrogel microparticles to create optical biosensors for the detection of organophosphorus compounds". Current Applied Physics, 2009;9(4 Suppl. 1):E225-E228). Link not available.

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#### **LIQUID CHROMATOGRAPHIC POST-COLUMN OXIDATION METHOD FOR ANALYSIS OF PARALYTIC SHELLFISH TOXINS IN MUSSELS, CLAMS, SCALLOPS, AND OYSTERS: SINGLE-LABORATORY VALIDATION**

Science Letter  
February 16, 2010

"A single-laboratory validation study was conducted for the LC post-column oxidation analysis of paralytic shellfish toxins (PST): saxitoxin (STX); neosaxitoxin (NEO); gonyautoxins (GTX)1-5; decarbamoyl gonyautoxins (dcGTX) 2 and 3; decarbamoyl saxitoxin (dcSTX); and N-sulfocarbamoyl-gonyautoxin-2 and 3 (C1 and C2) in mussels (*Mytilus edulis*), soft shell clams (*Mya arenaria*), scallops (*Placopectin magellanicus*), and oysters (*Crassostrea virginicus*). The instrumental technique was developed for the analysis of PST in shellfish as an alternative to the precolumn oxidation method, AOAC Official Method 2005.06, and a replacement for the current AOAC biological method 959.08."

"The method used reversed-phase LC with post-column oxidation and fluorescence detection. Test materials for method recovery were prepared by fortification of blank material with a cocktail of PST. used to determine method repeatability and intermediate precision were prepared by blending blank material with naturally incurred material. The target total toxicity levels evaluated in the study were 0.40, 0.80, and 1.60 mg STX center dot diHCl equivalents per kilogram [(eq/kg) 1/2, 1, and 2 times the regulatory limit]. Linearity, recovery, and within-laboratory precision parameters of the method were evaluated. Correlation coefficients of the calibration curves for all toxins studied were >0.99. Total toxin recovery ranged from 94 to 106% at the three levels of interest. Repeatability and intermediate precision RSD ranged from 2 to 7% and 2 to 8%, respectively. The method LOD and LOQ (assuming the presence of all toxins) were determined to be equivalent to 0.18 and 0.39 mg STX center dot diHCl eq/kg."

The full article can be found at: (J.M. Vanderiet, et. al., "Liquid Chromatographic Post-Column Oxidation Method for Analysis of Paralytic Shellfish Toxins in Mussels, Clams, Scallops, and Oysters: Single-Laboratory Validation". Journal of Aoac International, 2009;92(6):1690-1704). Link not available.

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### **GAMMA IRRADIATION AS A BIOLOGICAL DECONTAMINANT AND ITS EFFECT ON COMMON FINGERMARK DETECTION TECHNIQUES AND DNA PROFILING**

Health Risk Factor Week

February 23, 2010

"The use of disease-causing organisms and their toxins against the civilian population has defined bioterrorism and opened forensic science up to the challenges of processing contaminated evidence. This study sought to determine the use of gamma irradiation as an effective biological decontaminant and its effect on the recovery of latent fingerprints from both porous and nonporous items."

"Test items were contaminated with viable spores marked with latent prints and then decontaminated using a cobalt 60 gamma irradiator. Fingerprint detection was the focus with standard methods including 1,2-indanedione, ninhydrin, diazafluoren-9-one, and physical developer used during this study. DNA recovery using 20% Chelex extraction and quantitative real-time polymerase chain reaction was also explored. Gamma irradiation proved effective as a bacterial decontaminant with D-values ranging from 458 to 500 Gy for nonporous items and 797-808 Gy for porous ones."

"The results demonstrated the successful recovery of latent marks and DNA establishing gamma irradiation as a viable decontamination option."

The full article can be found at: R. Hoile, et. al., "Gamma Irradiation as a Biological Decontaminant and Its Effect on Common Fingerprint Detection Techniques and DNA Profiling". Journal of Forensic Sciences, 2010;55(1):171-177). Link not available.

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### **COMPARISON OF ELISA AND SPR BIOSENSOR TECHNOLOGY FOR THE DETECTION OF PARALYTIC SHELLFISH POISONING TOXINS**

Pharma Law Weekly

February 16, 2010

"An enzyme labeled immunosorbent assay (ELISA) and surface plasmon resonance (SPR) biosensor assay for the detection of paralytic shellfish poisoning (PSP) toxins were developed and a comparative evaluation was performed. A polyclonal antibody (BC67) used in both assay formats was raised to saxitoxin-jeffamine-BSA in New Zealand white rabbits."

"Each assay format was designed as an inhibition assay. Shellfish samples (n = 54) were evaluated by each method using two simple rapid extraction procedures and compared to the AOAC high

performance liquid chromatography (HPLC) and the mouse bioassay (MBA). The results of each assay format were comparable with the HPLC and MBA methods and demonstrate that an antibody with high sensitivity and broad specificity to PSP toxins can be applied to different immunological techniques. The method of choice will depend on the end-users needs."

"The reduced manual labor and simplicity of operation of the SPR biosensor compared to ELISA, ease of sample extraction and superior real time semi-quantitative analysis are key features that could make this technology applicable in a high-throughput monitoring unit."

The full article can be found at: (K. Campbell, et. al., "Comparison of ELISA and SPR biosensor technology for the detection of paralytic shellfish poisoning toxins". *Journal of Chromatography B - Analytical Technologies in the Biomedical and Life Sciences*, 2009;877(32):4079-4089). Link not available.

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## **CHRONIC INHIBITION OF CYCLOOXYGENASE-2 ATTENUATES ANTIBODY RESPONSES AGAINST VACCINIA INFECTION**

Health Risk Factor Week

February 23, 2010

"Generation of optimal humoral immunity to vaccination is essential to protect against devastating infectious agents such as the variola virus that causes smallpox. Vaccinia virus (VV), employed as a vaccine against smallpox, provides an important model of infection."

"Herein, we evaluated the importance cyclooxygenase-2 (Cox-2) in immunity to VV using Cox-2 deficient mice and Cox-2 selective inhibitory drugs. The effects of Cox-2 inhibition on antibody responses to live viruses such as vaccinia have not been previously described. Here, we used VV infection in Cox-2 deficient mice and in mice chronically treated with Cox-2 selective inhibitors and show that the frequency of VV-specific B cells was reduced, as well as the production of neutralizing IgG. VV titers were approximately 70 times higher in mice treated with a Cox-2 selective inhibitor. Interestingly, Cox-2 inhibition also reduced the frequency of IFN-gamma producing CD4(+) T helper cells, important for class switching. The significance of these results is that the chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), and other drugs that inhibit Cox-2 activity or expression, blunt the ability of B cells to produce anti-viral antibodies, thereby making vaccines less effective and possibly increasing susceptibility to viral infection."

"These new findings support an essential role for Cox-2 in regulating humoral immunity."

The full article can be found at: (M.P. Bernard, et. al., "Chronic inhibition of cyclooxygenase-2 attenuates antibody responses against vaccinia infection". *Vaccine*, 2010;28(5):1363-72). Link not available.

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## **VACCINIA PROTEIN F12 HAS STRUCTURAL SIMILARITY TO KINESIN LIGHT CHAIN AND CONTAINS A MOTOR BINDING MOTIF REQUIRED FOR VIRION EXPORT**

By Gareth W. Morgan, Michael Hollinshead, Brian J. Ferguson, Brendan J. Murphy, David C. J. Carpentier, Geoffrey L. Smith

*PLoS Pathogens*

February 26, 2010

“Abstract

Vaccinia virus (VACV) uses microtubules for export of virions to the cell surface and this process requires the viral protein F12. Here we show that F12 has structural similarity to kinesin light chain (KLC), a subunit of the kinesin-1 motor that binds cargo. F12 and KLC share similar size, pI,

hydropathy and cargo-binding tetratricopeptide repeats (TPRs). Moreover, molecular modeling of F12 TPRs upon the crystal structure of KLC2 TPRs showed a striking conservation of structure. We also identified multiple TPRs in VACV proteins E2 and A36. Data presented demonstrate that F12 is critical for recruitment of kinesin-1 to virions and that a conserved tryptophan and aspartic acid (WD) motif, which is conserved in the kinesin-1-binding sequence (KBS) of the neuronal protein calyculin/alcadein and several other cellular kinesin-1 binding proteins, is essential for kinesin-1 recruitment and virion transport. In contrast, mutation of WD motifs in protein A36 revealed they were not required for kinesin-1 recruitment or IEV transport. This report of a viral KLC-like protein containing a KBS that is conserved in several cellular proteins advances our understanding of how VACV recruits the kinesin motor to virions, and exemplifies how viruses use molecular mimicry of cellular components to their advantage.

#### Author Summary

Vaccinia virus (VACV), the vaccine used to eradicate smallpox, exploits the host cell motor kinesin-1 to export virus particles to the cell surface. We demonstrate that the VACV F12 protein has structural similarity with kinesin light chain (KLC) and facilitates viral transport using a kinesin binding sequence (KBS) that is conserved in several neuronal proteins. Dysfunction of some of these neuronal proteins can contribute to diseases, such as Alzheimer's. Mutation of the KBS in protein F12 showed it is essential for kinesin recruitment to virions and for virion transport to the cell surface. These findings enhance our understanding of how viruses hijack the host cell transport system, demonstrate conservation of a kinesin binding motif in cellular and viral proteins and identify targets for drug development."

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000785;jsessionid=0F78D04D25BFAA1935621DEB502D9820>

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### **THE COMPLETE GENOME ANALYSIS OF CRIMEAN-CONGO HEMORRHAGIC FEVER VIRUS ISOLATED IN TURKEY**

World Disease Weekly  
February 23, 2010

"It was first recognized in Turkey in 2002, with an increasing number of cases reported between 2002 and 2009. Recent analysis of complete genome sequences of CCHFV isolates has revealed that the genomic plasticity of the virus is surprisingly high for an arthropod-borne virus. We have determined the complete nucleotide and deduced amino acid sequences of strain CCHFV Turkey-Kelkit06 isolated from the blood of a patient in an endemic region of Turkey in 2006. The complete sequence length of the CCHFV Turkey-Kelkit06 strain is 19,186 nt, consisting of a 1673 nt S segment, a 5364 nt M segment, and a 12,149 nt L segment. Based on the analysis of S, M, and L segments, CCHFV Turkey-Kelkit06 clustered in Group V, which represents the Europe/Turkey geographic lineage. Although glycoproteins encoded by the M gene are the most variable part of the CCHFV Turkey-Kelkit06 strain, some functional domains of the glycoproteins are well conserved. Here, we report the complete sequence and genome organization of the CCHFV Turkey-Kelkit06 strain and its phylogenetic relationship to other strains of CCHFV."

The full article can be found at: (A. Ozdarendeli, et. al., "The complete genome analysis of Crimean-Congo hemorrhagic fever virus isolated in Turkey". *Virus Research*, 2010;147(2):288-93). Link not available.

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### **GUIDANCE FOR INDUSTRY: CHARACTERIZATION AND QUALIFICATION OF CELL SUBSTRATES AND OTHER BIOLOGICAL MATERIALS USED IN THE PRODUCTION OF VIRAL VACCINES FOR INFECTIOUS DISEASE INDICATIONS**

US Food and Drug Administration

February 2010

## I. INTRODUCTION

We, FDA, are providing you, manufacturers of viral vaccines, guidance for the characterization and qualification of cell substrates, viral seeds, and other biological materials used for the production of viral vaccines for human use.

This guidance applies to the development of viral vaccines for the prevention and treatment of infectious diseases that are regulated by the Office of Vaccines Research and Review (OVR) of the Center for Biologics Evaluation and Research (CBER) under section 351 of the Public Health Service (PHS) Act (42 U.S.C. 262).

Cell substrates are cells used to produce vaccines. The scope of this guidance document is limited to cell substrates of human or animal (including insect) origin and does not cover characterization of unicellular organisms, such as bacteria or yeast. In this document, cell substrates are categorized as primary (cells, including eggs, derived directly from an animal source and that are not stored as cell banks), diploid (cells with a normal or near-normal karyotype and that are stored as cell banks prior to use in vaccine manufacture), or continuous (cells that are immortal and do not undergo senescence). This guidance also applies to the characterization and qualification of viral seeds and other biological materials (including vaccine intermediates) used in vaccine manufacture.

This guidance finalizes the draft guidance entitled "Guidance for Industry: Characterization and Qualification of Cell Substrates and Other Biological Starting Materials Used in the Production of Viral Vaccines for the Prevention and Treatment of Infectious Diseases," dated September 2006 (71 FR 57547). In addition, this document replaces the information pertaining to viral vaccines for the prevention and treatment of infectious diseases that we provided in the document entitled "Points to Consider in the Characterization of Cell Lines Used to Produce Biologicals," dated 1993 (Ref. 1). This document also supplements the recommendations on the production of viral vaccines for the prevention and treatment of infectious diseases, provided in International Conference on Harmonization (ICH) documents Q5A and Q5D (Refs. 2 and 3, respectively). For the production of biological products not covered under this guidance, we recommend that you refer to the "Points to Consider in the Characterization of Cell Lines Used to Produce Biologicals," dated 1993 (Ref. 1).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word should in a guidance document means that something is recommended, but not required.

The full article can be found at:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM202439.pdf>

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## **TRANSIT THROUGH THE FLEA VECTOR INDUCES A PRETRANSMISSION INNATE IMMUNITY RESISTANCE PHENOTYPE IN YERSINIA PESTIS**

By Viveka Vadyvaloo, Clayton Jarrett, Daniel E. Sturdevant, Florent Sebbane, B. Joseph Hinnebusch  
PLoS Pathogens  
February 26, 2010

"Yersinia pestis, the agent of plague, is transmitted to mammals by infected fleas. *Y. pestis* exhibits a distinct life stage in the flea, where it grows in the form of a cohesive biofilm that promotes transmission. After transmission, the temperature shift to 37°C induces many known virulence factors of *Y. pestis* that confer resistance to innate immunity. These factors are not produced in the low-temperature environment of the flea, however, suggesting that *Y. pestis* is vulnerable to the initial encounter with innate immune cells at the flea bite site. In this study, we used whole-genome microarrays to compare the *Y. pestis* in vivo transcriptome in infective fleas to in vitro transcriptomes in temperature-matched biofilm and planktonic cultures, and to the previously characterized in vivo gene

expression profile in the rat bubo. In addition to genes involved in metabolic adaptation to the flea gut and biofilm formation, several genes with known or predicted roles in resistance to innate immunity and pathogenicity in the mammal were upregulated in the flea. *Y. pestis* from infected fleas were more resistant to phagocytosis by macrophages than in vitro-grown bacteria, in part attributable to a cluster of insecticidal-like toxin genes that were highly expressed only in the flea. Our results suggest that transit through the flea vector induces a phenotype that enhances survival and dissemination of *Y. pestis* after transmission to the mammalian host.

The full article can be found at: <http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000783;jsessionid=E5D53485768A4FED9DA0925B23ED267B>

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## **PREPARING A COMMUNITY HOSPITAL TO MANAGE WORK-RELATED EXPOSURES TO INFECTIOUS AGENTS IN BIOSAFETY LEVEL 3 AND 4 LABORATORIES**

By George F. Risi, Marshall E. Bloom, Nancy P. Hoe, Thomas Arminio, Paul Carlson, Tamara Powers, Heinz Feldmann, and Deborah Wilson

Emerging Infectious Diseases

March, 2010

### “Abstract

Construction of new BioSafety Level (BSL) 3 and 4 laboratories has raised concerns regarding provision of care to exposed workers because of healthcare worker (HCW) unfamiliarity with precautions required. When the National Institutes of Health began construction of a new BSL-4 laboratory in Hamilton, Montana, USA, in 2005, they contracted with St. Patrick Hospital in Missoula, Montana, for care of those exposed. A care and isolation unit is described. We developed a training program for HCWs that emphasized the optimal use of barrier precautions and used pathogen-specific modules and simulations with mannequins and fluorescent liquids that represented infectious body fluids. The facility and training led to increased willingness among HCWs to care for patients with all types of communicable diseases. This model may be useful for other hospitals, whether they support a BSL-4 facility, are in the proximity of a BSL-3 facility, or are interested in upgrading their facilities to prepare for exotic and novel infectious diseases.”

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“To satisfy the NIH requirements for the CIU, the following elements were needed: 1) access control, i.e., the ability to restrict entrance into the CIU to authorized persons only; 2) three separate stand-alone rooms, each with a bathroom and shower, separate air handling, and an anteroom separating the patient room from the hallway; 3) directional air flow from the hallway into the anteroom and from the anteroom into the patient room; 4) a dedicated exhaust system providing >12 air exchanges per hour to the patient rooms (including >2 outside air changes per hour); 5) passage of exhaust through a HEPA filter to the building exterior >8 feet above the rooftop and well removed from air intake ducts; 6) room surfaces constructed of seamless materials amenable to topical disinfection; 7) the capability for the full range of intensive care unit (ICU) monitoring and support, including the ability to perform limited surgery, hemodialysis or peritoneal dialysis, Swan-Ganz catheter placement, and hemodynamic monitoring; and 8) a separate autoclave within the CIU for sterilizing all items that come out of a patient room.”

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“In addition to the physical aspects of the CIU, several other elements were developed. Specific policies and procedures were written that deal with all aspects from admission to discharge, including unique aspects such as clean up of infected bodily spills, donning and doffing of personal protective equipment (PPE), and use of the autoclave. Support of hospital administration, physicians, nurses, and support personnel was critical. This backing was enlisted primarily by mounting an educational campaign that stressed the true risk for nosocomial transmission of these agents, as well as the recognition that the increased resources that would be provided to the hospital could greatly enhance capacity for handling community-acquired infections.

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To maintain readiness, a series of drills and exercises have been performed and will continue, in collaboration with RML and local emergency medical services providers. These readiness exercises have encompassed all aspects of care from arrival to the hospital through discharge.”

The full article can be found at: <http://www.cdc.gov/eid/content/16/3/373.htm>  
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### **'PAINLESS' VACCINE NEEDLE INVENTED IN JAPAN**

By Julian Ryall  
The Telegraph (UK)  
March 04, 2010

“Kanji Takada, a professor of pharmacokinetics - or the study of the absorption, distribution and fate of substances delivered to the human body - has developed a round vaccine "chip" measuring just 1.5 cm in diameter that contains as many as 300 micro needles. The device can deliver drugs to the body without breaking the dermis layer of skin.

By penetrating just 0.5 millimetres before the needles dissolve and administer the vaccine, the patient feels no discomfort and there is no bleeding, said Professor Takada, of Kyoto Pharmaceutical University.”

The full article can be found at:  
<http://www.telegraph.co.uk/news/worldnews/asia/japan/7365134/Painless-vaccine-needle-invented-in-Japan.html>  
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