

UCRL-PROC-223237



LAWRENCE
LIVERMORE
NATIONAL
LABORATORY

Characterization of Pathogenicity, Virulence and Host-Pathogen Interactions

A. Krishnan, P. Folta

July 28, 2006

Characterization of Pathogenicity, Virulence and Host-
Pathogen Interactions

Livermore, CA, United States

September 13, 2006 through September 14, 2006

Disclaimer

This document was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor the University of California nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or the University of California, and shall not be used for advertising or product endorsement purposes.

This work was performed under the auspices of the U. S. Department of Energy by the University of California, Lawrence Livermore National Laboratory under Contract No. W-7405-Eng-48.

Characterization of Pathogenicity, Virulence and Host-Pathogen Interactions

The threats of bio-terrorism and newly emerging infectious diseases pose serious challenges to the national security infrastructure. Rapid detection and diagnosis of infectious disease in human populations, as well as characterizing pathogen biology, are critical for reducing the morbidity and mortality associated with such threats. One of the key challenges in managing an infectious disease outbreak, whether through natural causes or acts of overt terrorism, is detection early enough to initiate effective countermeasures. Much recent attention has been directed towards the utility of biomarkers or molecular signatures that result from the interaction of the pathogen with the host for improving our ability to diagnose and mitigate the impact of a developing infection during the time window when effective countermeasures can be instituted. Host responses may provide early signals in blood even from localized infections. Multiple innate and adaptive immune molecules, in combination with other biochemical markers, may provide disease-specific information and new targets for countermeasures. The presence of pathogen specific markers and an understanding of the molecular capabilities and adaptations of the pathogen when it interacts with its host may likewise assist in early detection and provide opportunities for targeting countermeasures. An important question that needs to be addressed is whether these molecular-based approaches will prove useful for early diagnosis, complement current methods of direct agent detection, and aid development and use of countermeasures.

Lawrence Livermore National Laboratory (LLNL) will host a workshop to explore the utility of host- and pathogen-based molecular diagnostics, prioritize key research issues, and determine the critical steps needed to transition host-pathogen research to tools that can be applied towards a more effective national bio-defense strategy. The workshop will bring together leading researchers/scientists in the area of host-pathogen interactions as well as policy makers from federal agencies. The main objectives of the workshop are:

- to assess the current national needs, capabilities, near-term technologies, and future challenges in applying various diagnostics tools to public health and bio-defense
- to evaluate the utility and feasibility of host-response and pathogen biomarker profiling in the diagnosis and management of infectious diseases
- to create a comprehensive developmental strategy from proof-of-concept, through validation, to deployment of appropriate advanced technology for the clinical/public health and bio-defense environments

The workshop will be a 2-day event (to be held at Livermore, CA) scheduled for September 13 and 14, 2006. An additional day (September 15) will be reserved for laboratory tours and site visits.

LLNL has a long history of successfully developing and deploying technologies and systems for rapid detection and identification of biological pathogens in support of national security. Additionally, LLNL has unique resources such as the High Performance Computing Center (HPCC), Center for Accelerator Mass Spectrometry (CAMS), Livermore Micro-Array Center (LMAC), National Atmospheric Release Advisory Center (NARAC) and a range of other infrastructure capabilities to support development, testing and evaluation of technologies/systems for bio-defense applications. LLNL is committed to researching and continuing to develop the next-generation tools for diagnosis and mitigation of the risk from both emerging infectious diseases and threats from bioterrorism.

Workshop on

Characterization of Pathogenicity, Virulence and Host-Pathogen Interactions

Sept. 13-15, 2006 ; LLNL- B543 Auditorium

Wednesday, September 13, 2006 (8:00 AM – 5:00 PM)

Session 1 : Role of Host-Pathogen Science in Public Health & Bio-Defense

- **Talks by speakers from HHS, CDC, NIH, DHS + Leading academics : Key issues facing bio-defense and public health, emerging/unknown/engineered (EUE) pathogens**
- **Discussion of public preparedness, current state-of-the-art, future requirements and priorities for bio-defense, challenges to be addressed, ...**

Session 2 : Mechanisms of pathogen virulence and host immune evasion

- **Viral/Bacterial/fungal mechanisms of pathogenesis**
- **Zoonoses and animal models**
- **Key pathogens and appropriate model systems**
- **Bio-defense issues/relevance, EUE pathogens**
- **Panel Discussion**

Thursday, September 14, 2006 (8:00 AM – 5:00 PM)

Session 3 : Mechanisms of host response

- **Innate and cellular response to pathogens (bio-markers, signatures of infections)**
- **Animal models and relevance to human studies**
- **Technologies for diagnosis of infections**
- **Bio-defense issues & relevance, EUE pathogens**
- **Panel Discussion**

Session 4 : Applications to bio-defense (Detection, diagnosis, mitigation)

- **Applications to detection, diagnosis, public response & containment**
- **Novel therapeutic strategies & technologies for detection & diagnosis**
- **Discussion of above in the context of emerging pathogens (i.e., bird flu) & bio-threats**
- **Panel Discussion**

Friday, September 15, 2006

Lab Tours/Demos for External Attendees : TSF, CAMS, NARAC, BAMS, Bio-Briefcase