

**US HUPO THIRD ANNUAL CONFERENCE
SEATTLE, WASHINGTON
March 5-8, 2007**

EVENING WORKSHOPS

Emphasis on progress made, obstacles encountered, needed specimen and reagent resources and data sharing, with active discussion and audience participation

Tuesday evening theme: Current Challenges and Opportunities in Proteomics

**NIAID Biodefense Proteomics Workshop: Biodefense Proteomics and Beyond
March 6, 7:00-8:15pm**

Objectives

The NIAID (National Institute of Allergy and Infectious Diseases) Biodefense Proteomics Research Program provides the scientific community with newly discovered proteomic information about pathogens and hosts to identify potential targets for the next generation of vaccines, therapeutics and diagnostics. New research and novel proteomic approaches are being developed at the Proteomics Research Centers, and data and reagents are being publicly disseminated through the Resource Center at <http://www.proteomicsresource.org/>. This workshop will present and discuss the current state-of-the-art research, technologies and resources generated by the Proteomics Research Program, as an outreach to the broad scientific community. The topic areas will be of general interest to researchers in proteomics, functional and structural genomics, bioinformatics, and systems biology, as well as developers of vaccines, therapeutics and diagnostics.

Program Moderator: Joseph J. Breen, NIAID

7:00-7:15pm Kimberly J. Stemple, NIAID
NIAID Proteomics and Related Programs: Addressing Challenges and Opportunities

7:15-7:35pm Joshua N. Adkins, Pacific Northwest National Laboratory
Towards a Proteomics Data Resource for the Salmonella and Orthopox Research Communities with Emphasis on Therapeutic Targets

7:35-7:55pm Philip C. Hanna, University of Michigan Medical School
Integrated Proteomics and Gene Expression Analysis of Host-Pathogen Interactions

7:55-8:15pm Cathy H Wu, Georgetown University Medical Center
Integrated Proteomic Bioinformatics: Challenges and Solutions for NIAID Biodefense Proteomics

Lognumber: 175
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NIAID Proteomics and Related Programs: addressing challenges and opportunities

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Nat'l Institute of Allergy and Infectious Disease, Bethesda, MD

AbstractThe primary goal of the seven NIAID (National Institute of Allergy and Infectious Diseases) Biodefense Proteomics Research Centers (PRCs) is to characterize the pathogen and/or host cell proteome, including the identification of proteins associated with innate and adaptive immune responses to infectious agents. PRC researchers are focused on the proteomic evaluation of NIAID Category A-C priority pathogens and microorganisms responsible for emerging and re-emerging infectious diseases. All data generated by the PRCs is being consolidated and made available to the scientific community via the related initiative, Administrative Resource Center. This publicly accessible Web site contains data and technology protocols generated by each PRC. This site serves as a central information source for reagents and validated protein targets (www.proteomicsresource.org). The NIAID portion of this workshop will present and discuss several current state-of-the-art research efforts, including technologies and resources generated by the Proteomics Research Program, as a mechanism of outreach to the broad scientific community. This presentation will also highlight current challenges and discuss related opportunities and resources available to the scientific community through NIAID proteomics, genomics, and bioinformatics programs as well. In addition to the PRCs, NIAID has established comprehensive genomic centers (<http://www3.niaid.nih.gov/research/topics/pathogen/default.htm>) to develop reagents and resources for the scientific community to conduct basic and applied research. The Microbial Sequencing Centers (MSCs) provide rapid and cost efficient resources for producing high quality genome sequences of pathogens and invertebrate vectors of infectious diseases. The Pathogen Functional Genomics Resource Center (PFGRC) provides scientists with free-of-charge genomic resources and reagents, such as microarrays, protein expression clones, genotyping resources, and bioinformatics services. The primary goal of the eight Bioinformatics Resource Centers (BRCs) is to provide scientists with genomic and related data for NIAID Category A-C priority pathogens, pathogens causing emerging and re-emerging infectious diseases, and invertebrate vectors of infectious diseases. Genomic sequence data is being integrated with gene expression and proteomics information, host/pathogen interactions and pathways data. In 2007 NIAID plans to award several Structural Genomics Centers that will provide a collection of three-dimensional structures that will serve as blueprints for development of structure-based drugs, vaccines, and diagnostics for infectious diseases.

Lognumber: 177

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Towards a Proteomics Data Resource for the Salmonella and Orthopox Research Communities with Emphasis on Therapeutic Targets

Joshua N. Adkins¹; Liang Shi¹; Fred Heffron²; Scott Wong³; Hyunjin Yoon²; Nathan P. Manes¹; Ryan D. Estep³; Charles K. Anson¹; Angela D. Norbeck¹; Kenneth J. Auberry¹; Jean K. Gustin³; Heather M. Mottaz¹; Richard D. Smith¹

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AbstractThe research enabled in recent years through the use of liquid chromatography coupled with mass spectrometry to study the proteomes of tissues, cells, and organisms has lead to a better understanding of the variety and types of proteins present in biological materials. Increasingly, the challenge for proteomics research is to provide improved measures of protein abundance in both relative and absolute terms. This research challenge is in contrast with needs for standardization across groups and experiments, especially when future users of the produced data are expected. A combined effort between our Biodefense Proteomics Research Center and the Administrative Resource Center for Biodefense Proteomics Research is developing a data resource that will be web accessible to allow online data mining as well as providing quick access to peptide identification scores and supporting spectrum files. Data resources developed under this program are to be made widely accessible, presenting opportunities for other scientists to improve genome annotation efforts through the use of proteome information, to perform novel searches for post-translational modifications, and to study protein content with regard to environmental transitions in a pathogenic microbe. In this presentation, some initial applications of this data are described in terms of the development of several possible targets for therapeutic intervention with respect to the pathogen *Salmonella typhimurium*. These include studies both from model culture conditions as well as analysis of the *Salmonella typhimurium* proteome when isolated from macrophages. In the context of these applications we will also discuss solutions and decisions made to address experimental challenges. Additionally, very recent datasets will be presented which will soon be available and demonstrate on-going and future opportunities for *Salmonella* and Orthopox virus research using mass spectrometry-based proteomics.

Lognumber: 179

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Integrated Proteomic Bioinformatics: Challenges and Solutions for NIAID Biodefense Proteomics

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AbstractThe accelerated growth of proteomics data presents both opportunities and challenges. Large-scale proteomic profiling of biological samples has led to discovery of novel proteins involved in many biological processes. The NIAID Biodefense Proteomics program aims to identify targets for potential vaccines, therapeutics, and diagnostics, for infectious agents of concern in bioterrorism, including intracellular bacterial, parasitic, and viral pathogens. The program consists of seven Proteomics Research Centers, which are generating host-pathogen data, covering diverse data types ranging from mass spectrometry (MS) data, yeast two-hybrid protein interaction data and transcriptional profiles to biological reagents such as clones. In addition, an Administrative Resource Center (www.proteomicsresource.org) has been developed for public dissemination of the data and reagents. Administering such a program presented unique challenges as large and heterogeneous data have to be integrated for knowledge discovery. To meet these challenges, we have developed a bioinformatics framework that adopts common standards, integrates high-quality data sources, and supports protein mapping and functional analysis. We have created protocols for data submission, exchange, and dissemination, adopting common data standards such as the HUPO PSI (Proteomics Standards Initiative) when possible. A Proteomics Data Center has been developed to house underlying experimental results, protocols and visualization tools, and to allow data downloads for additional analysis. A Master Protein Directory, serving as a protein knowledge system, integrates genes/proteins across organisms and across experiments in the Biodefense Proteomics program, along with functional and pathway information from UniProtKB and over 90 databases, as well as search and analysis tools. The system uses UniProt ID mapping and UniRef sequence mapping to improve protein identification from MS data. A major issue in protein identification is that many commonly used protein sequence databases contain redundant sequences, while leaving out alternative splice isoforms. Another problem is the lack of standardization, where the same proteins may be referred to by different IDs and names due to the use of different target databases for protein search, or even different versions of the same database. As the most comprehensive, non-redundant protein sequence database with links to rich UniProtKB annotations, UniRef100 is applied to proteomic data mapping. Protein profiles are then identified by functional categorization based on Gene Ontology, pathways and other protein annotations, revealing the functional significance of expressed proteins and their hidden relationships. The NIAID Biodefense Proteomic Resource Center represents an integrated proteomic bioinformatics resource that can facilitate target discoveries from host-pathogen proteomic data. The availability of the data in an integrated system with analytical tools allows comparative analysis at many levels, and can be useful in better understanding these organisms and aid in finding proteins that might be potential targets for intervention.

Lognumber: 185
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Integrated Proteomics and Gene Expression Analysis of Host-Pathogen Interactions

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AbstractThe NIAID-UM Biodefense PRC goals are focused on determining key choke-points in the *Bacillus anthracis* infectious cycle suitable to be defined as targets for anthrax countermeasure development. Appropriate models of anthrax infections are utilized and global mRNA and protein expression profiles determined from the bacterium, and the host, by microarray, tandem LC/LC-MS/MS (with MudPIT) and bioinformatic analyses. Validation of potential bacterial targets is scored by mutational disruption of targeted genes to determine loss of virulence and relevant phenotypic traits. So far, we have found that the combination of the technologies allows for an integrated profiling stronger than the sum of their individual parts. Examples will be presented. Data from the mRNA and protein analyses, and the custom anthrax array chips themselves, are now available to the scientific community