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UAB Center for Emerging Infections and Emergency Preparedness (CEIEP)

Emergency Preparedness and Community Mitigation Symposium
December 6, 2007

- Recent History of Biodefense and Emerging Infections Research
- Importance for Emergency Preparedness
- Current efforts at UAB
- Future research and challenges
Chronology of Biodefense & Emerging Infections Research

Federal Level
- February 2002: NIH Blue Ribbon Panel (Category A Agents), announces $1.5 billion in new research dollars
- May 2002: Second NIH Blue Ribbon Panel (Category B and C Agents)
- October 2002: Planning of RCEs
- September 2003: 1st RCE awards made

Category A
- Bacillus anthracis (anthrax)
- Clostridium botulinum toxin (botulism)
- Yersinia pestis (plague)
- Yersinia pestis (plague) and other related pathovars
- Francisella tularensis (tularemia)
- Viral hemorrhagic fevers
  - Arenaviruses
    - LCM, Jaun virus, Machupo virus, Guanarito virus
  - Lassa Fever
  - Bunyaviruses
    - Hantaviruses
  - Rift Valley Fever
  - Filoviruses
  - Dengue
  - Flaviviruses
- Ebola
- Marburg

Category B
- Burkholderia pseudomallei
- Brucella species
- Francisella tularensis
- Chlamydia trachomatis
- Rickettsia species
- Brucella species
- Mycobacterium tuberculosis
- Mycobacterium leprae
- Clostridium difficile
- Campylobacter jejuni
- Yersinia enterocolitica
- Helicobacter pylori

Additional viral encephalitides
- West Nile Virus
- LACITida
- California encephalitis
- VEE
- EEE
- Japanese encephalitis Virus
- Kusakura Footed Virus
Federal Level (cont.)

- June 2003: BSL-3 and BSL-4 Laboratory Construction Applications
- RBLs Awarded October 2003
- Biodefense and Emerging Infection Training Grants Approved in September, 2003
- 2004 – vaccine supply and development
- 2004 NIH Roadmap – Clinical and Translational Science Award: Emphasis on bench to bedside research.

NAID Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases

- University of Washington
- Washington University
- University of Chicago
- Harvard Medical School
- NY State Dept of Health
- University of Maryland
- Colorado State University (Fort Collins)
- Duke University
- University of California, Irvine
- University of Texas Medical Branch
UAB level

- March 2002: Strategy Meetings begun
- September 2002: Submission of Pilot Center Application
- October 2002: Planning of SERCEB
- Late 2003 – SERCEB, SEBLAB, UAB Centers received funding
- 2003 – CASG began clinical trials on emerging infections
- 2006 – CEIEP created merging two existing centers

Importance of Basic and Clinical Research to Preparedness Efforts

- Federally mandated approach to develop medical countermeasures
- Need for vaccines (prevention), diagnostics, and therapeutics
- Determine type and amounts of products for national stockpile
UAB Projects

Basic Research (SERCEB)
Development of Therapies for Orthopox viruses

- Cores:
  - Structural Biology: DeLucas
  - Protein Expression: Luo
  - Monoclonal Antibodies: Accavitti-Loper
  - Small Animals: Kern/Quenelle
  - Policy and Ethics: Tilden

Basic Research (cont.)

- Drug Candidate Screening and Animal Models: Kern, Prichard, Whitley
- Drug Synthesis: Secrist and Maddry at SRI

Vaccinia virus UDG structure

Structure has been determined to 2.3 Å Resolution. Currently R and Rfree Values are 29 and 32%. Approximately 86% of protein residues lie in the core region of Ramachandran plot.
Clinical Trials

- Collaborative Antiviral Study Group (CASG): international multi-center group conducting trials at more than 70 institutions.
- Mandated by NIAID to study West Nile virus in 2003. Study closed in December 2006.
- Began pediatric study of Tamiflu in late 2006 (children 0-2 years old).
- Developed protocol templates for smallpox and SARS.

Future of research - Federal level

- NIAID Strategic Plan for Biodefense Research - September 2007
  - Continued emphasis on vaccines, diagnostics and therapeutics, particularly drug discovery
- CTSA- NIH Roadmap initiative
  - More emphasis on interdisciplinary research to “speed up” bench to bedside process
Emerging Viral Diseases: 21st Century

Future of research - UAB level

- SERCEB – emphasis on drug discovery for the upcoming recompetition
- UAB Drug will be the first RCE developed drug in humans
- Compound will be studied through the NIAID CASG
- Increased emphasis on interdisciplinary efforts - CCTS

Challenges to Biodefense and Emerging Infections Research

- Understanding of Natural History and Pathogenesis of Disease
- Definition of Molecular Targets
  - Lack of Pharmaceutical Incentive
- Controlled Trial Evaluations during ‘Outbreaks’
  - Lack of controlled trials
  - Compassionate release of unproven medications
  - Regulatory Impediments