
***Regional Centers of Excellence for
Biodefense and Emerging Infectious
Diseases (RCEs)***

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***National Institute of Allergy & Infectious Diseases
National Institutes of Health
USA***

The NIH Mission

“Science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.”

NIH Pursues its Mission by...

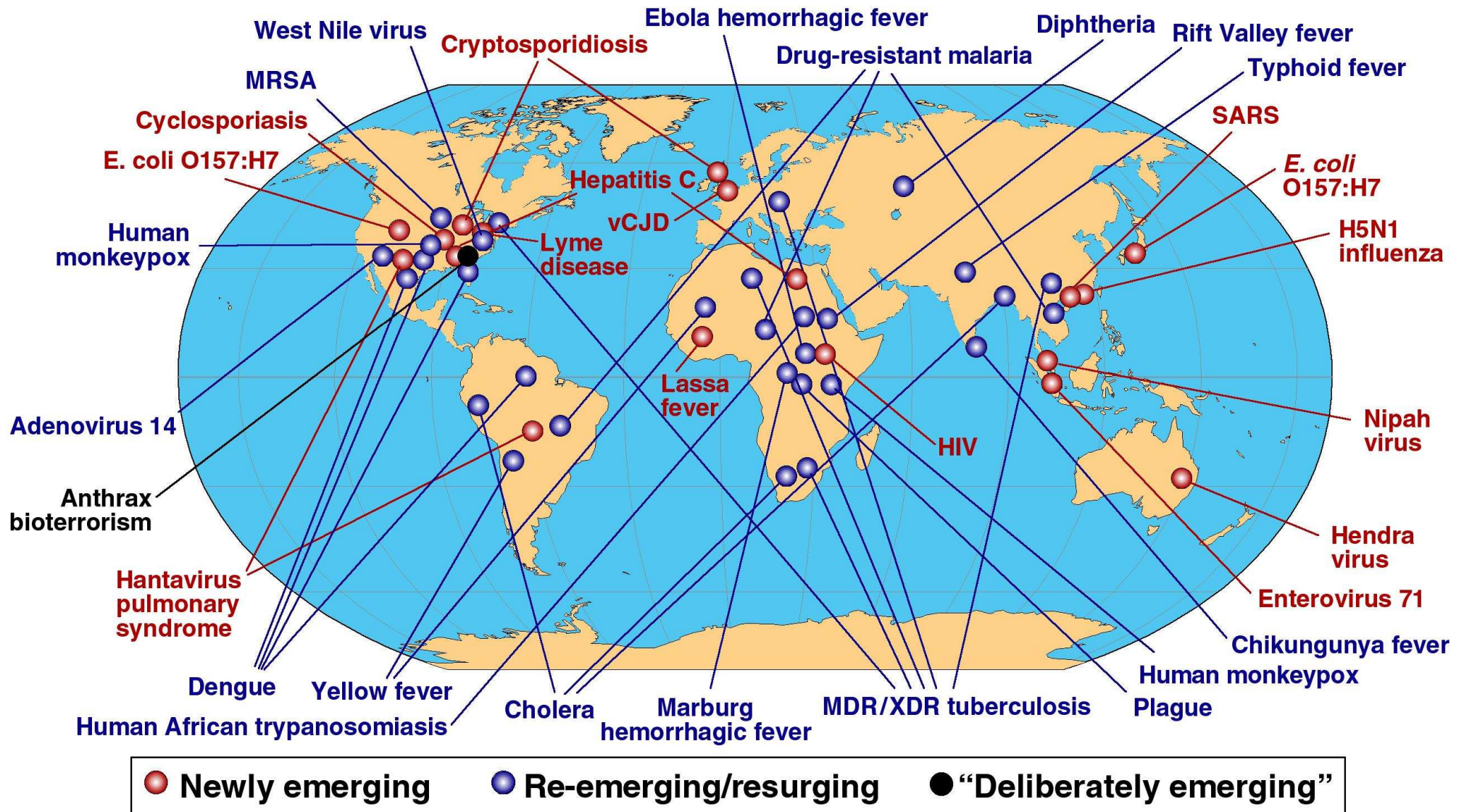
- ***Extramural research support (~85% of budget) for...***
 - ***Research by non-Federal scientists in universities & other research institutions***
 - ***Training research investigators***
 - ***Communicating biomedical information***
- ***Intramural research (~10% of budget)
Conducted in NIH's own laboratories***

Dr. Collins: Global Health an NIH Priority

- ***New NIH Director Francis Collins singled out global health as one of five areas he wants to emphasize during his tenure.***
- ***Focus “...not just on doing research in those countries but helping them develop their own research capacity for the longer term.”***



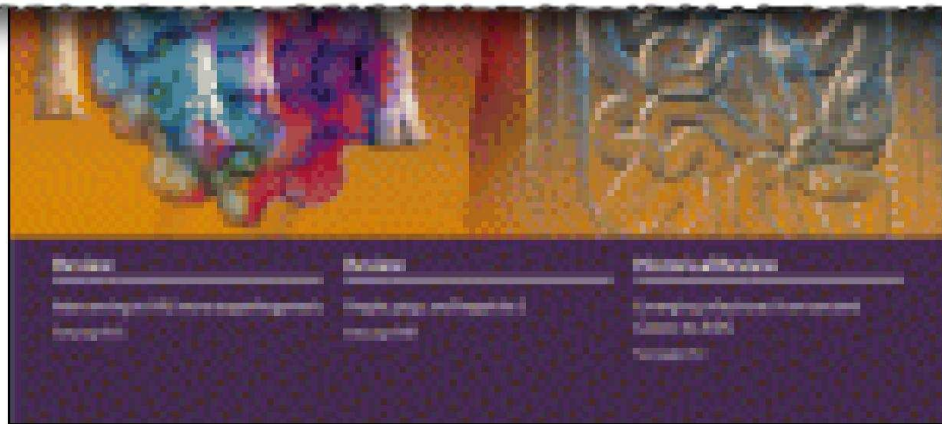
Global Examples of Emerging and Re-Emerging Infectious Diseases





Emerging Infections: A Perpetual Challenge

DM Morens, GK Folkers & AS Fauci

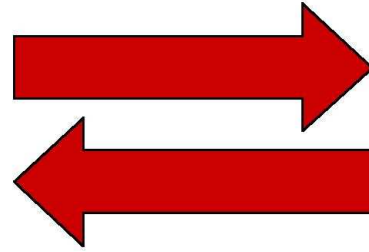


"For centuries a fundamental challenge to the existence and well-being of societies -- as reflected by scientific attention, as well as in art, religion, and culture -- emerging infections remain among the principal challenges to human survival."

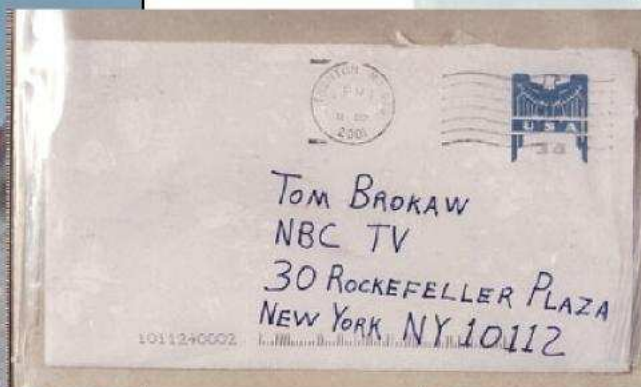
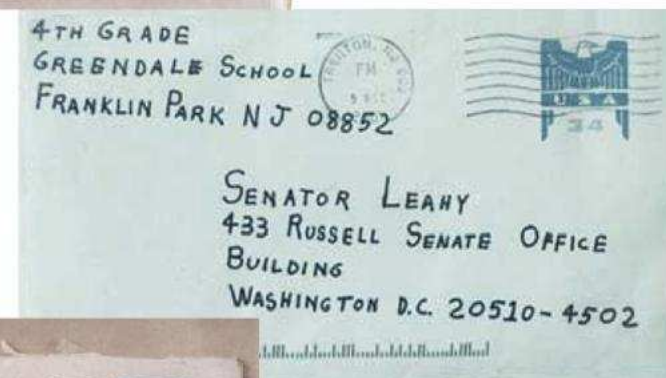
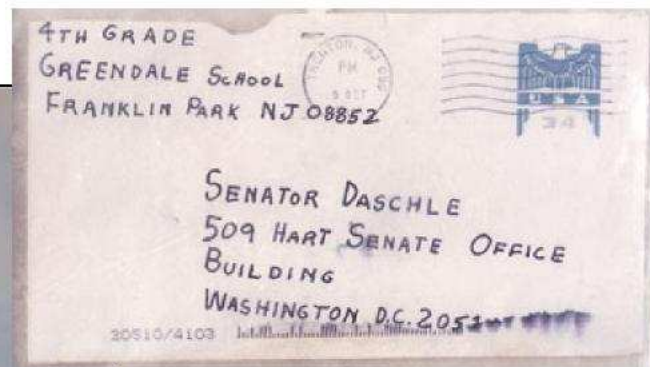
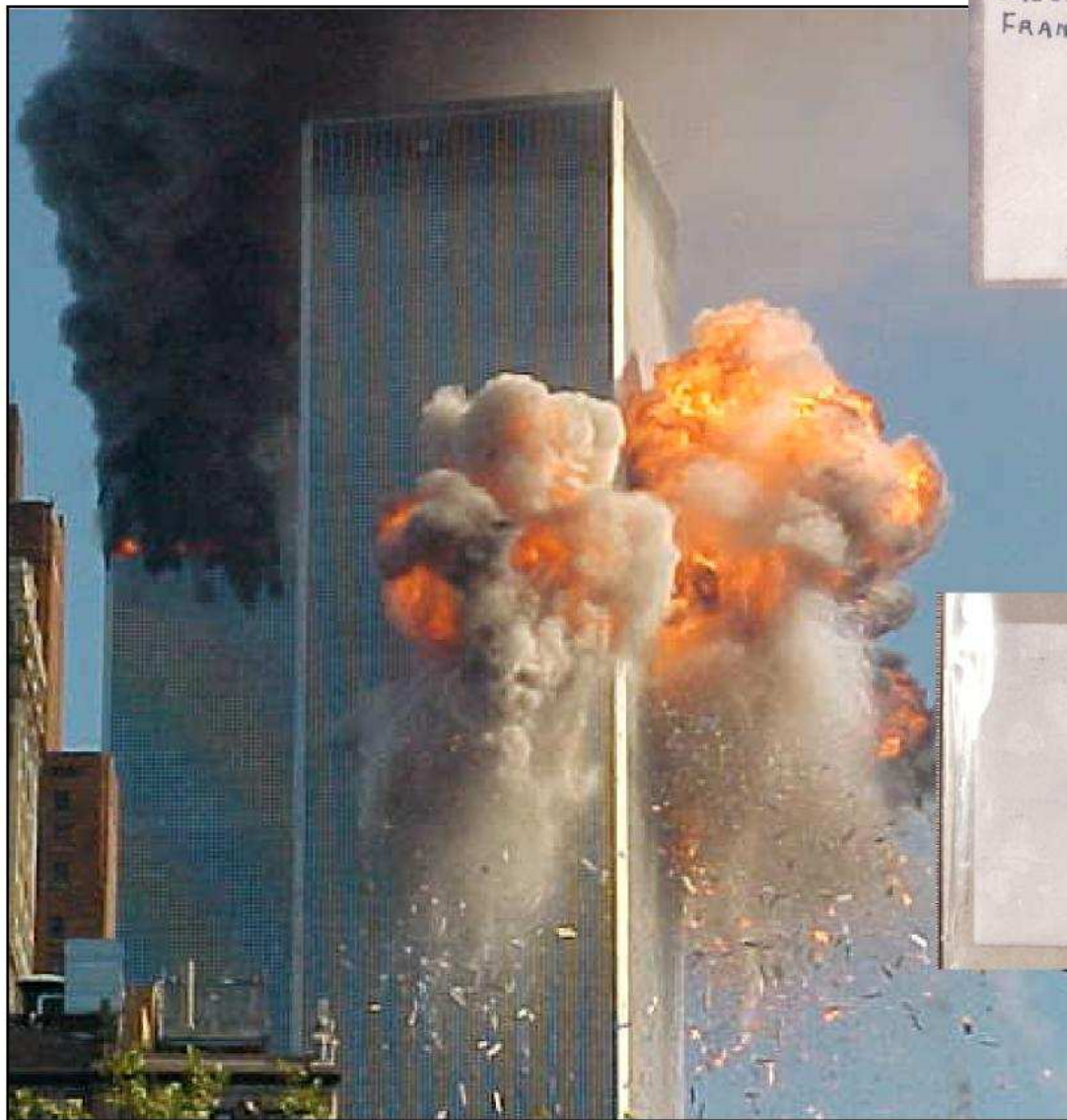
Examples of Human Disease Outbreaks, 2006-2008

- H5N1 avian influenza
- Chikungunya fever
- Dengue
- *E. coli* O157:H7
- *Fusarium* keratitis
- Poliomyelitis
- Rift Valley fever
- XDR-TB
- Ebola hemorrhagic fever
- Marburg hemorrhagic fever
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Adenovirus Serotype 14
- Yellow fever
- *Salmonella* Saintpaul

**Bierror
Threats**

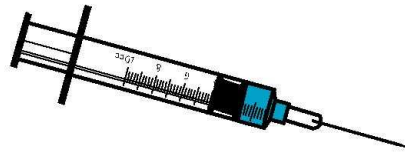


**Naturally
Occurring
Infectious
Disease
Threats**



NIAID Category A, B and C Priority Pathogens

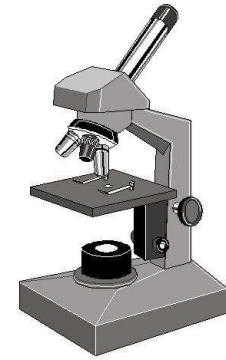
Category A	Category B	Category C
<p><i>Bacillus anthracis</i> (anthrax)</p> <p><i>Clostridium botulinum</i> toxin (botulism)</p> <p><i>Yersinia pestis</i> (plague)</p> <p><i>Variola major</i> (smallpox) and related pox viruses</p> <p><i>Francisella tularensis</i> (tularemia)</p> <p>Viral hemorrhagic fevers</p> <p> Arenaviruses (including LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever)</p> <p> Bunyaviruses (including Hantaviruses, Rift Valley Fever)</p> <p> Flaviruses (Dengue)</p> <p> Filoviruses (Ebola, Marburg)</p>	<p><i>Burkholderia pseudomallei</i></p> <p><i>Coxiella burnetii</i> (Q fever)</p> <p><i>Brucella</i> species (brucellosis)</p> <p><i>Burkholderia mallei</i> (glanders)</p> <p><i>Chlamydia psittaci</i> (Psittacosis)</p> <p>Ricin toxin (from <i>Ricinus communis</i>)</p> <p>Epsilon toxin of <i>Clostridium perfringens</i></p> <p><i>Staphylococcus enterotoxin B</i></p> <p>Typhus fever (<i>Rickettsia prowazekii</i>)</p> <p>Food- and Waterborne Pathogens</p> <p>Bacteria (<i>Diarrheagenic E.coli</i>, Pathogenic <i>Vibrios</i>, <i>Shigella</i> sp., <i>Salmonella</i>, <i>Listeria monocytogenes</i>, <i>Campylobacter jejuni</i>, <i>Yersinia enterocolitica</i>)</p> <p>Viruses (<i>Caliciviruses</i>, Hepatitis A)</p> <p>Protozoa (<i>Cryptosporidium parvum</i>, <i>Cyclospora cayatanensis</i>, <i>Giardia lamblia</i>, <i>Entamoeba histolytica</i>, <i>Toxoplasma</i>)</p> <p>Fungi (<i>Microsporidia</i>)</p> <p>Additional viral encephalitides (West Nile Virus, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus)</p>	<p>Nipah virus</p> <p>Additional hantaviruses</p> <p>Tickborne hemorrhagic fever viruses (Crimean-Congo Hemorrhagic fever virus, Tickborne encephalitis viruses)</p> <p>Yellow fever</p> <p>Multi-drug resistant TB</p> <p>Influenza</p> <p>Other Rickettsias</p> <p>Rabies</p> <p>Prions</p> <p><i>Chikungunya</i> virus</p> <p>Severe acute respiratory syndrome associated coronavirus (SARS-CoV)</p> <p><i>Coccidioides immitis</i></p> <p><i>Coccidioides posadasii</i></p> <p>Antimicrobial resistance (excluding research on sexually transmitted organisms)</p> <p>Innate immunity (non-adaptive immune mechanisms that recognize, and respond to, microorganisms, microbial products, and antigens)</p>



Vaccines

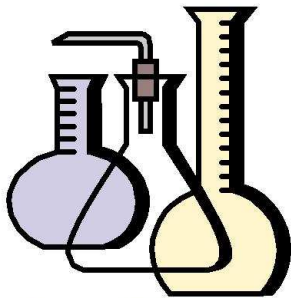


Therapeutics



Diagnostics

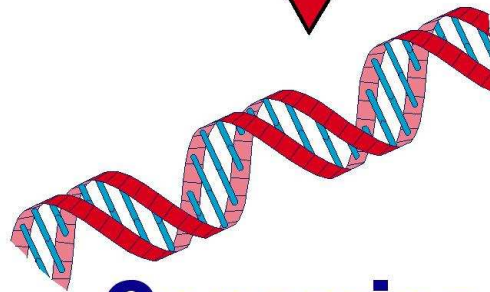
**Biodefense and
Emerging Infectious
Diseases (EID)
Research Priorities**



Basic Research



**Expansion of
Research
Capacity**



Genomics

Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases (RCEs)

Program Goals

- ***Basic research to understand category A-C and EID agents***
- ***Translational capacity leading to drugs, vaccines, and diagnostics***
- ***Expand the pool of researchers and technical personnel for biodefense and EID research***
- ***Regional facilities for research***
- ***Assist emergency responses***

RCE History

2003 ***Initial award of eight Centers.***

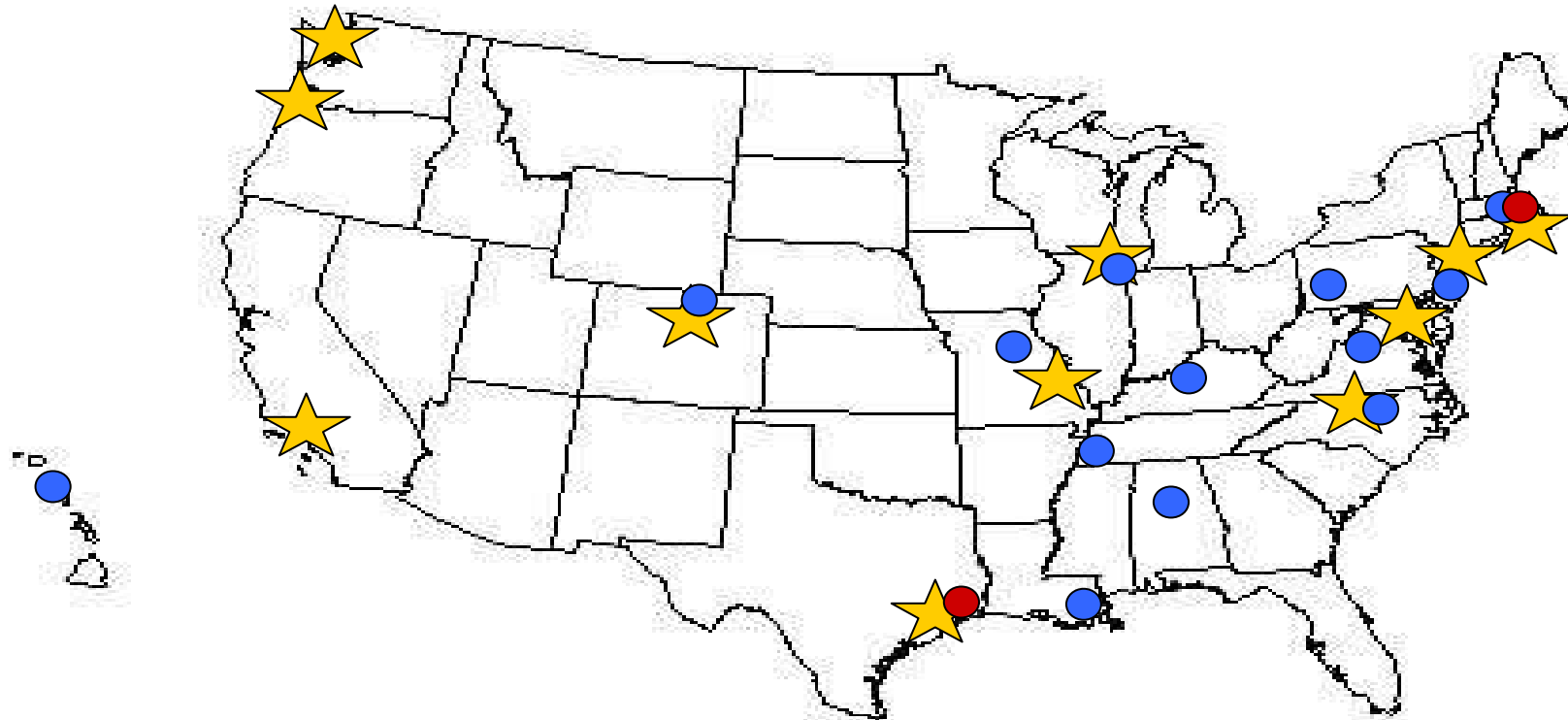
2005 ***Two additional Centers awarded.***

2009 ***Renewed funding for 10 previously established Centers.***

Established a new RCE (Oregon Health & Science University).

NIAID funding for the 11 RCEs will total up to ~\$455 million over five years.

Current NIAID RCE Network



- ★ Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research - 11**
- Regional Biocontainment Laboratories (BSL3) - 13**
- National Biocontainment Laboratories (BSL4) - 2**

RCE Accomplishments

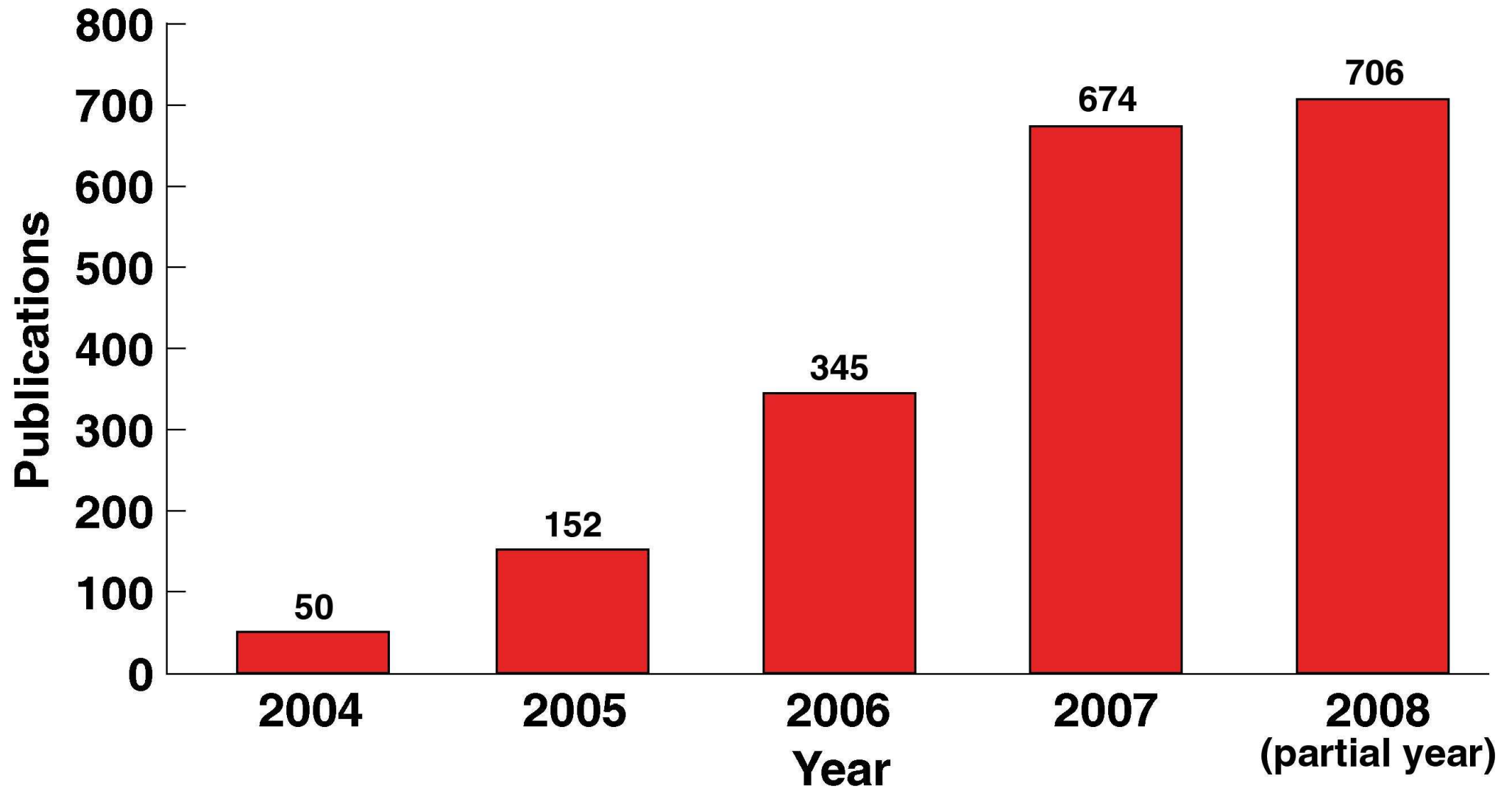
“The Regional Centers of Excellence are a critical component of our national research infrastructure for infectious diseases...”

Research studies conducted by the RCEs are central to our efforts to develop countermeasures against both endemic and emergent diseases.”

***Anthony Fauci, M.D.
Director, NIAID***



Total RCE Publications



Derived by searching PubMed by RCE grant numbers March 18, 2008

RCE: Selected Scientific Highlights

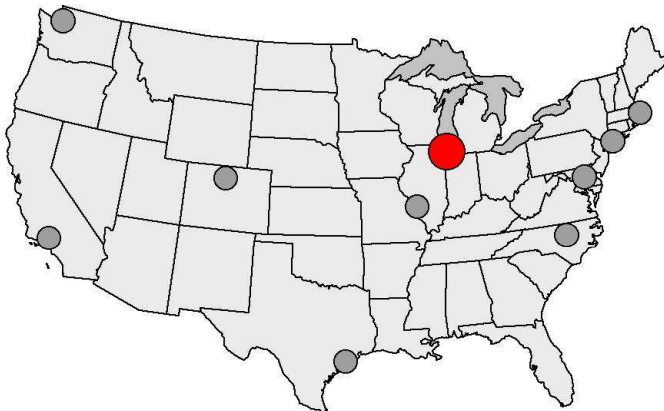
January 29, 2008

PNAS

Generation of Biologically Contained Ebola Viruses

P Halfmann, Y Kawaoka, et al.

Great Lakes RCE



- Understanding the biology of Ebola viruses and its interactions with host cells, with the aim of developing vaccines and antivirals

RCE: Selected Scientific Highlights

February 13, 2008

The Journal of
Infectious
Diseases

Exceptionally Potent Cross-reactive Neutralization of Nipah and Hendra Viruses by a Human Monoclonal Antibody

Z Zhu, DS Dimitrov, et al.

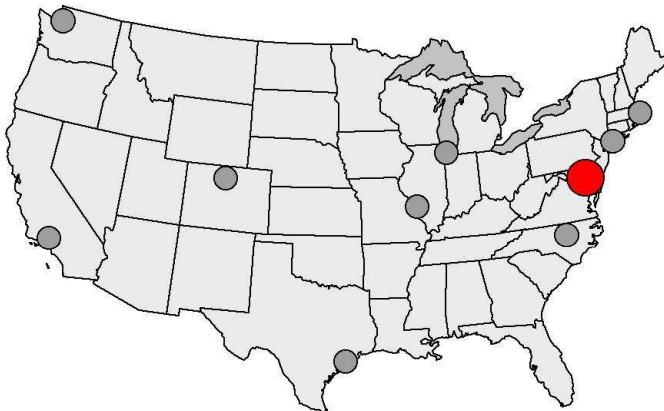
July 26, 2005

PNAS

Ephrin-B2 Ligand is a Functional Receptor for Hendra and Nipah Virus

MI Bonaparte, CC Broder, et al.

Mid-Atlantic RCE



- **Development of vaccine and post-exposure therapeutic strategies for Nipah and Hendra virus infections**

RCE: Selected Scientific Highlights

July 15, 2007

The Journal of
Infectious
Diseases

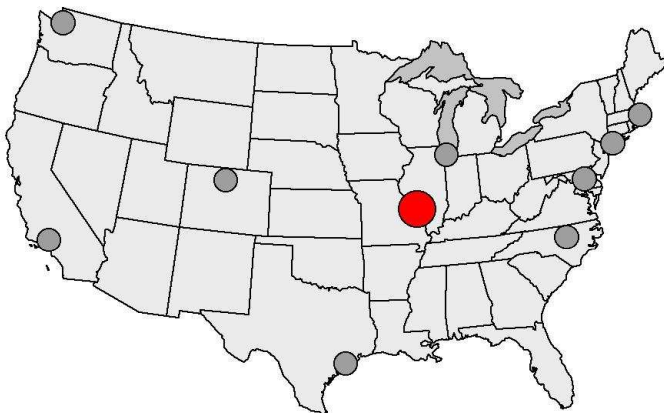
Antibody Responses to Vaccinia Membrane Proteins after Smallpox Vaccination

SJ Lawrence, SE Frey, et al.

The Immunogenetics of Smallpox Vaccination

SL Stanley, RB Belsche, et al.

Midwest RCE



- **Determined common DNA variations that can be used to identify patients likely to develop vaccine-related fever following smallpox immunization**

RCE: Selected Scientific Highlights

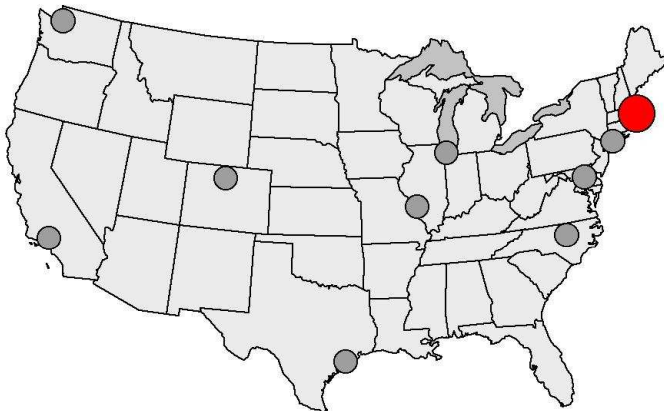
March 20, 2008

PNAS

COPI Coatomer Complex Proteins Facilitate the Translocation of Anthrax Lethal Factor Across Vesicular Membranes *in vitro*

AG Tamayo, JR Murphy, et al.

New England RCE



- Showed the mechanism of anthrax toxin entry into host cell cytosol is similar to that of diphtheria toxin

RCE: Selected Scientific Highlights



The New England Journal of Medicine

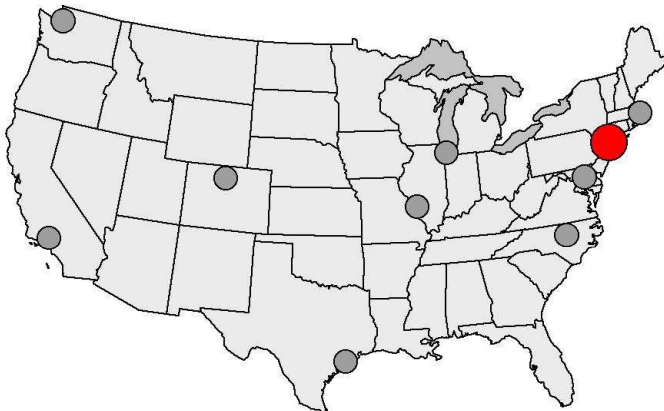
Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

MARCH 6, 2008

A New Arenavirus in a Cluster of Fatal Transplant-associated Diseases

G Palacios, WI Lipkin, et al.

Northeast RCE



■ Novel techniques for pathogen surveillance

■ Discovery of a new arenavirus responsible for the deaths of 3 transplant recipients in Victoria, Australia

RCE: Selected Scientific Highlights

January 16, 2007

PNAS

A Comprehensive Transposon Mutant Library of *Francisella novicida*, a Bioweapon Surrogate

LA Gallaher, C. Manoil, et al.

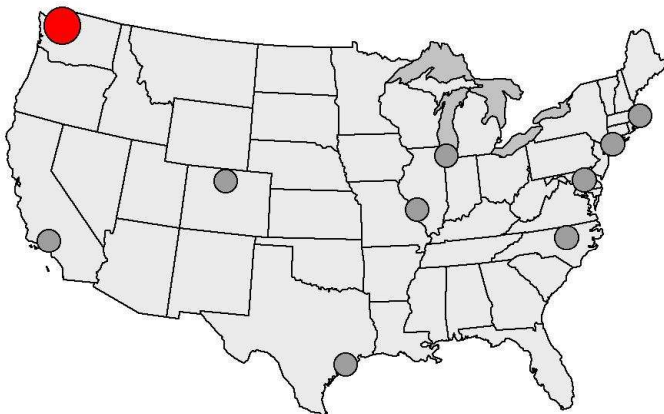
October 2006

molecular
microbiology

Type IV Pili-mediated Secretion Modulates *Francisella* Virulence

AJ Hager, T Guina, et al.

Northwest RCE



- Development and use of tools to understand *Francisella tularensis* virulence, pathogenesis determinants and mechanisms of attenuation in potential vaccine strains

RCE: Selected Scientific Highlights



PLOS one

Publishing science, accelerating research

In Press

Attomolar Detection of Botulinum Toxin Type A in Complex Biological Matrices

K Bagramyan, M Kalkum, et al.

Pacific-Southwest RCE



- **Development of sensitive, specific, rapid and simple method to detect the presence of botulinum neurotoxin in complex biological samples such as serum or food**

RCE: Selected Scientific Highlights

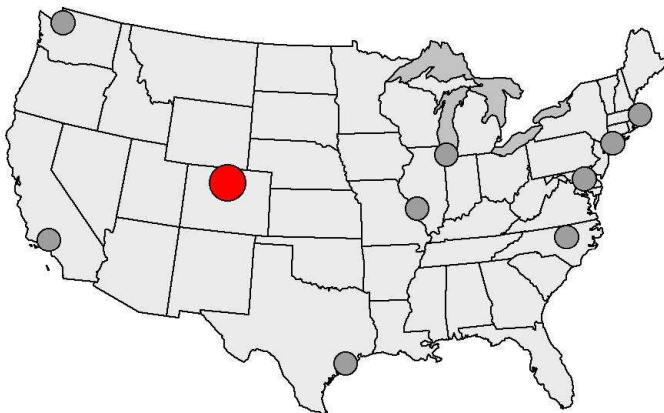
February, 2008

Applied and
Environmental
Microbiology

Genetic Tools for Select-agent-compliant Manipulation of *Burkholderia pseudomallei*

KH Choi, HP Schweizer, et al.

Rocky Mountain RCE



- Engineered completely attenuated strain of *Burkholderia pseudomallei* as potential vaccine candidate
- Developed select agent-compliant genetic tools for broad research use in the study of *Burkholderia* species

RCE: Selected Scientific Highlights

November 2007

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY

Synergistic Efficacy of the Combination of ST-246 with CMX001 against Orthopoxviruses

DC Quenelle, ER Kern, et al.

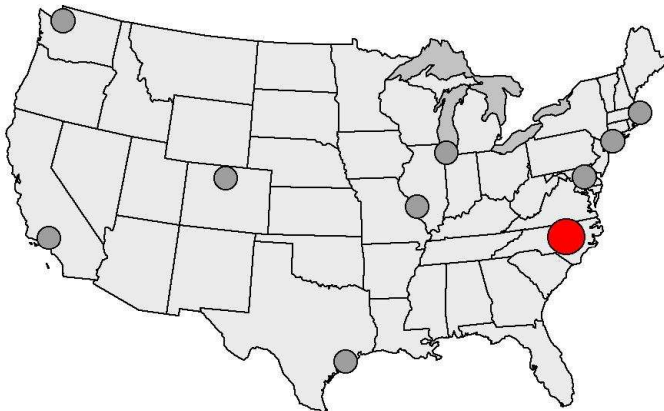
November 2007

Journal of Virology

Rabbitpox Virus and Vaccinia Virus Infection of Rabbits as a Model for Human Smallpox

MM Adams, AD Rice, RW Moyer

Southeast RCE



- Key preclinical data for IND submission for current clinical trials of CMX001 (oral derivative of cidofovir) to treat orthopoxvirus infections

RCE: Selected Scientific Highlights

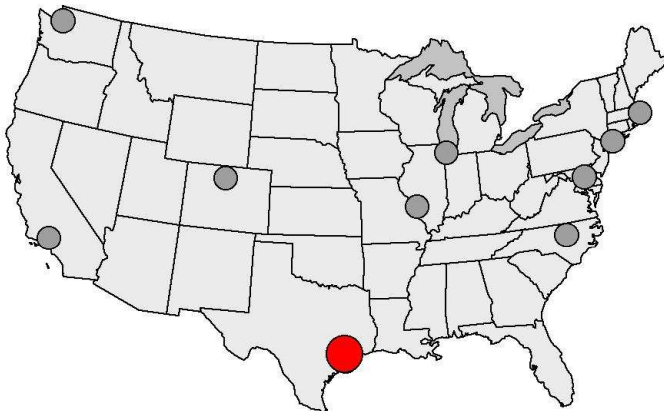
November 2007

Journal of
Virology

Production of Pseudoinfectious Yellow Fever Virus with a Two-component Genome

AV Shustov, PW Mason, I Frolov

Western RCE



■ **Development of RepliVAX as a potential universal vaccine platform for flaviviruses**

RCE Components

- ***Research Projects (RP)***
- ***Core Facilities (CO)***
- ***Developmental Projects (DP)***
- ***Career Development Projects (CD)***
- ***New Ops (NO)***

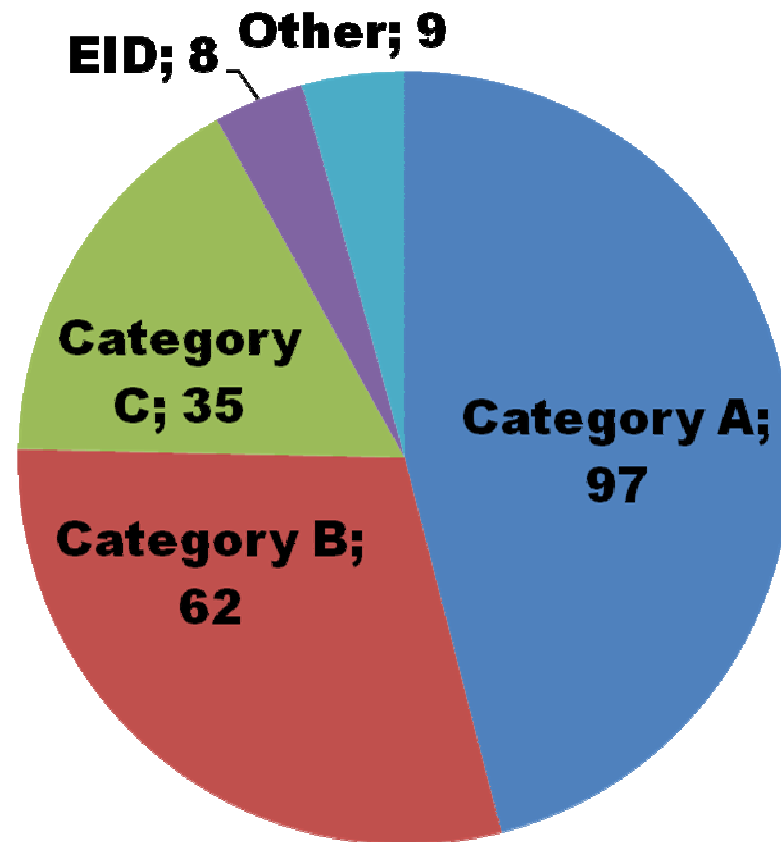
RCE Facts and Figures (2009)

<i>Research Projects</i>	<i>160</i>
<i>Investigators</i>	<i>262</i>
<i>Institutions</i>	<i>103</i>
<i>States with Research Projects</i>	<i>34</i>
<i>International sites</i>	<i>5</i>
<i>Cores</i>	<i>39</i>
<i>DPs and CDs (est., still being selected)</i>	<i>50-60</i>

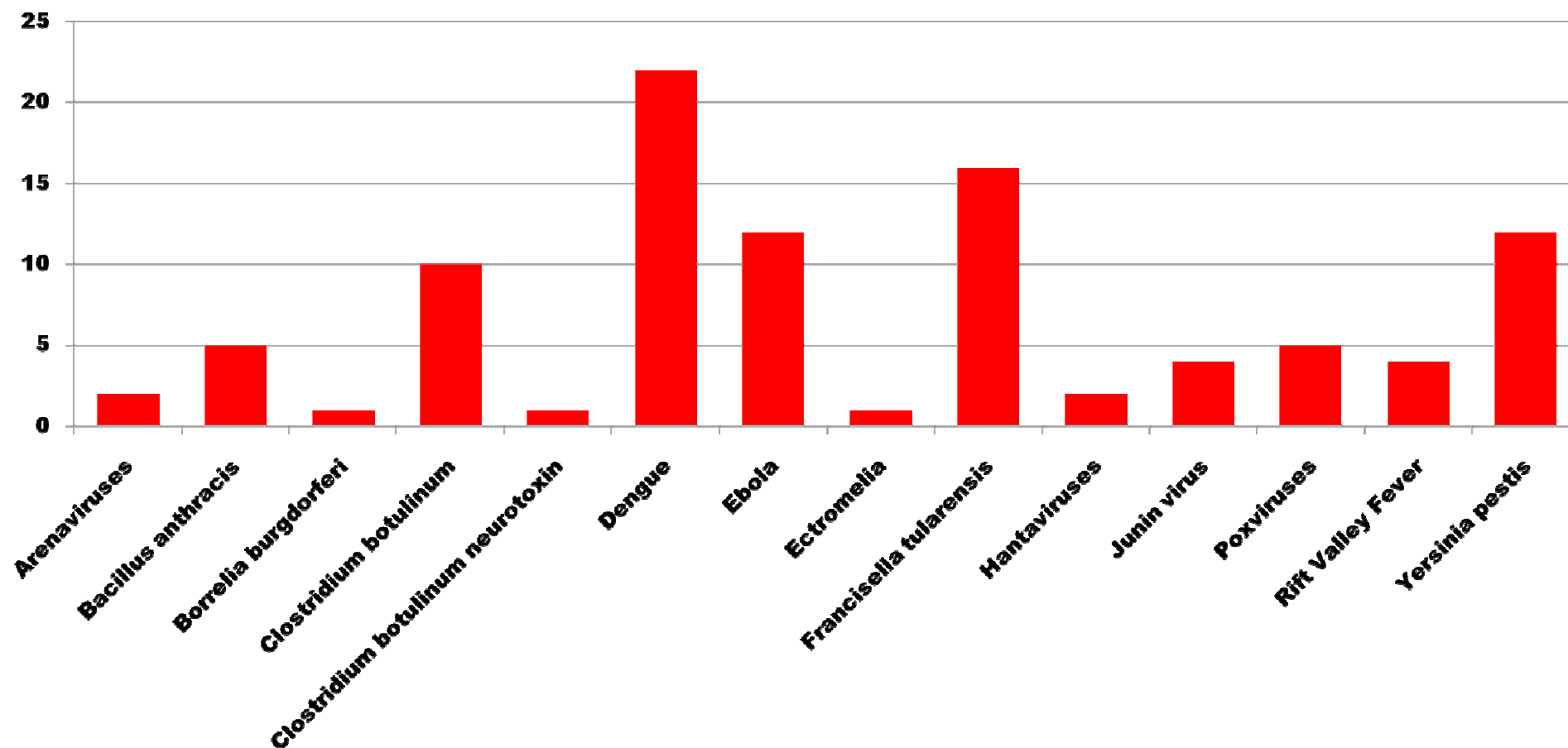
RCEs and Non-U.S. Collaborators

- ***Research projects may include non-U.S. collaborations if they are integral to a research project***
- ***The research project must have a Project Leader from a U.S. institution.***
- ***Non-U.S. collaborations must offer significant benefits that cannot be duplicated within the U.S.***
- ***May not exceed \$100,000 per project per year, direct costs.***
- ***Clinical trials at non-U.S. sites will not be supported.***

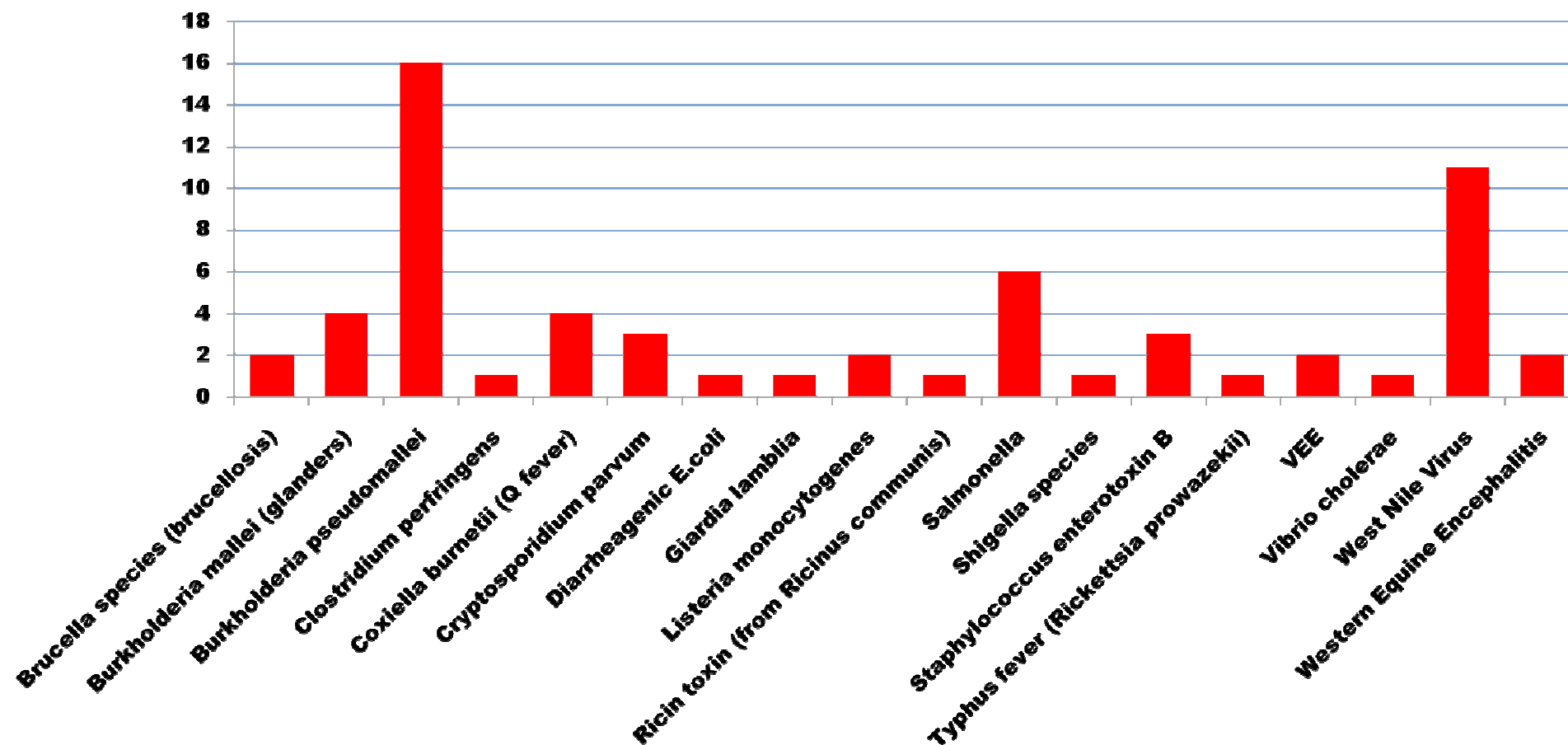
RCE Research Projects by Category (2009)



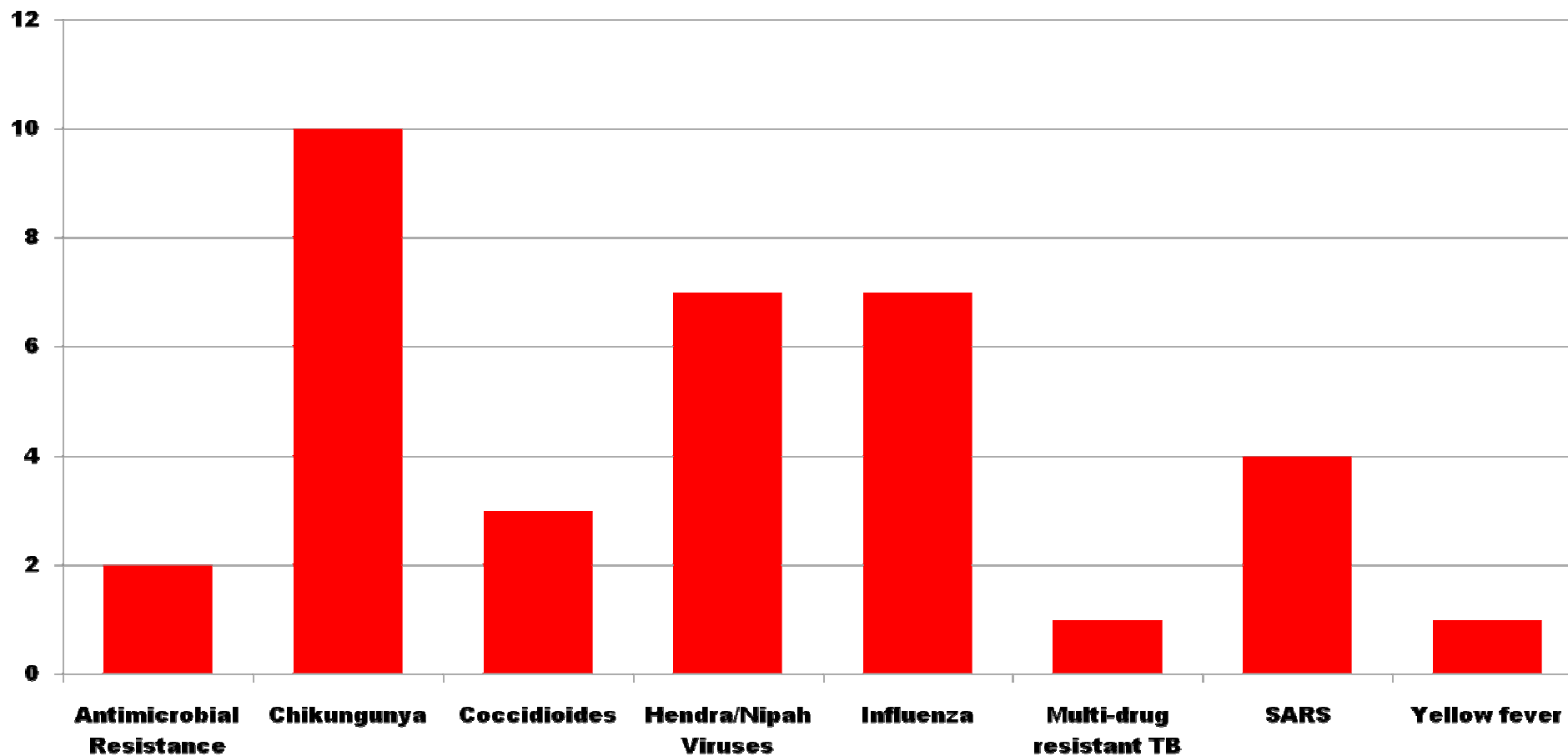
Category A Projects (2009)



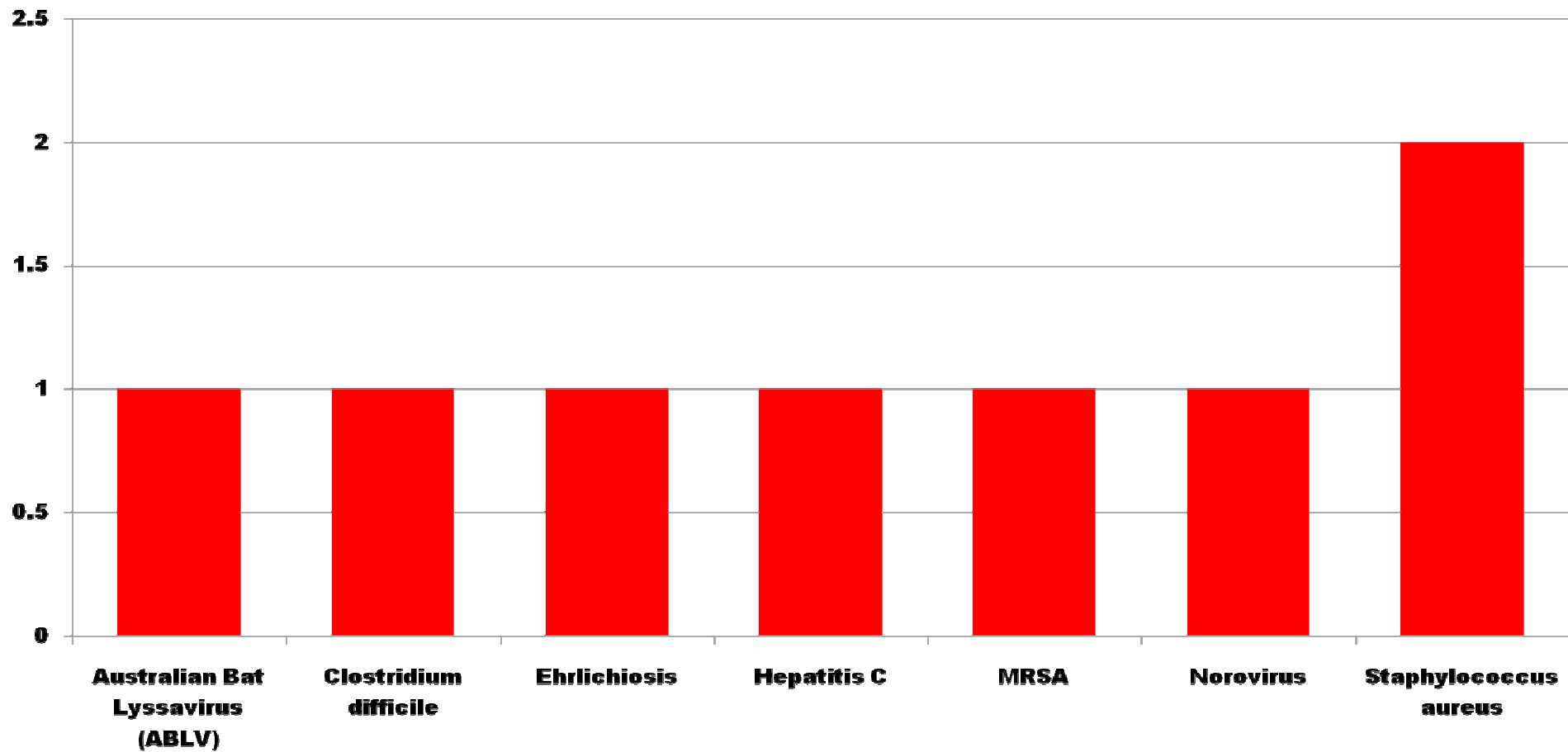
Category B Projects (2009)



Category C Projects (2009)



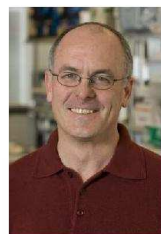
EID Projects (2009)



NIAID Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases



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Chicago, IL



PI – Dr. Dennis Kasper
Harvard Medical School
Boston, MA



PI – Dr. W. Ian Lipkin
Columbia University
New York, NY



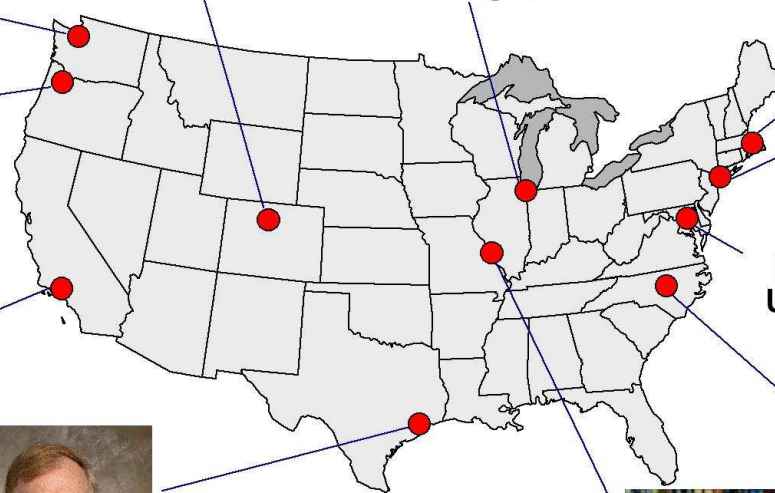
PI – Dr. Jay A. Nelson
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PI – Dr. Alan G. Barbour
University of California
Irvine, CA



PI – Dr. David Walker
University of Texas Medical Branch
Galveston, TX



PI – Dr. Samuel Stanley
Washington University
St. Louis, MO



PI – Dr. Myron Levine
University of Maryland
Baltimore, MD



PI - Dr. Fred Sparling
University of North Carolina
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