Council of Councils

February 1, 2012

Louise E. Ramm, Ph.D.
Director, Office of Research Infrastructure Programs

Office of Research Infrastructure Programs

Components

- Division of Comparative Medicine
- Division of Instruments, Infrastructure Resources, and Construction
- Science Education Partnership Awards (SEPA)
- Office of Science Education

Office of Research Infrastructure Programs

Division of Comparative Medicine (DCM)

- National Primate Research Centers
- Chimpanzee Management Program and Sanctuary
- Biorepositories and Other Resources
- Career Development and Training Programs
- Research Project Grants

Office of Research Infrastructure Programs

Division of Comparative Medicine (DCM)

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William (Bill) Watson, D.V.M., M.S.

Office of Research Infrastructure Programs

Division of Comparative Medicine (DCM)

- **National Primate Research Centers**

- Chimpanzee Management Program and Sanctuary
- Biorepositories and Other Resources
- Career Development and Training Programs
- Research Project Grants

National Primate Research Centers

- Network of 8 nonhuman primate biomedical research and resource centers
- Provides for access to >27,500 nonhuman primates, representing over 20 species
- Provides scientific expertise, professional care, facilities, and equipment
- Provides infrastructure support for more than 1,200 hundred scientists, funded by over 1,000 NIH grants (excess of $ 590M)
- Research Activities - HIV/AIDS, Age-Related diseases Neurosciences (AD, PD), Reproductive Biology, Re-emerging Infectious Diseases

Office of Research Infrastructure Programs

Division of Comparative Medicine (DCM)

- National Primate Research Centers
- **Chimpanzee Management Program and Sanctuary**
- Biorepositories and Other Resources (Animal and Biological models)
- Career Development and Training Programs
- Research Project Grants

NIH-supported Research Use of Chimpanzees

- The Chimpanzee Management Plan develops, coordinates, and implements policies for DHHS-supported research using chimpanzees.
- Chimpanzees are the only well-validated animal model for studies of Hepatitis C virus.
- Cooperative agreements or contracts support long-term housing and maintenance at facilities nationwide.
- Support is provided to a reserve a colony of chimpanzees previously used in HIV, HCV, and HBV research.

Chimpanzee Sanctuary

- NIH awarded a contract and two construction grants to build and operate the sanctuary.
- First animals arrived in April 2005.
- Housing for approx. 130 animals.
- New Request for Proposals released in 2011 with proposals reviewed in January. Award anticipated in FY2012.

Office of Research Infrastructure Programs

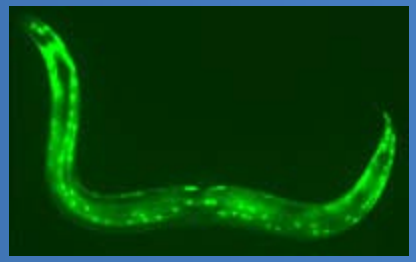
Division of Comparative Medicine (DCM)

- National Primate Research Centers
- Chimpanzee Management Program and Sanctuary
- **Biorepositories and Other Resources**

- **Career Development and Training Programs**
- Research Project Grants

Biorepositories - Non-Mammalian Models
Development and Support

- **National Resource for Zebrafish**
  - Wild-type, transgenic, and mutant stocks and database resource of zebrafish, genetic, genomic, and developmental research information. Over 1,000 lines and ~100,000 strains distributed.
- **Bloomington Drosophila Stock Center**
  - Collection of over 23,300 different stocks that carry 31,100 unique genetic components. Over 155,000 distributed/yr.
- **Caenorhabditis Genetics Center**
  - Over 7,000 strains available
- **National Stem Cell Resource**
  - Accessions, characterizes, expands, preserves, d distributes nonhuman embryonic stem cells



Biorepositories – Mammalian Models
Development and Support

- **The Mutant Mouse Regional Resource Center (MMRRC) consortium**
  - Network of four archiving/distribution centers and one coordinating/informatics Center
  - Consortium inventory includes over 28,000 mutant stem cell lines and 3,500 germline mutant mouse lines

- **Rat Resource**
  - Performs research on germ line cryopreservation and knockout rat technology to produce high-quality, well-characterized inbred, hybrid and mutant strains
  - 500+ rat strains available for distribution
- **Swine Resource**
  - Repository and distribution center for valuable swine models.
  - Models imported are rederived to a pathogen-free status, and gametes and embryos cryopreserved to prevent future loss.

- **NHP Disease models**
  - Neurologic disorders – Huntington's Disease, Multiple sclerosis
  - Genetic disorders - Krabbe disease

Office of Research Infrastructure Programs

Division of Comparative Medicine (DCM)

- National Primate Research Centers
- Chimpanzee Management Program and Sanctuary
- Biorepositories and Other Resources

- **Career Development and Training Programs**

- Research Project Grants

Career Development Programs

- **Research career development for veterinarians**
  - Promoting research interest during DVM training (=pre-doctoral training)
  - Post-residency/doctoral training – systems/integrated research combined with molecular expertise
- **Post-doctoral and mid-career career development (to attract veterinary scientists into research careers)**
- **Educational programs for laboratory animal veterinarians**

National Center for Research Resources

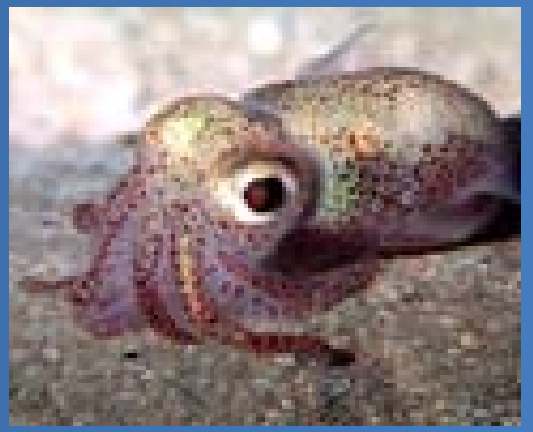
Division of Comparative Medicine (DCM)

- National Primate Research Centers
- Chimpanzee Management Program and Sanctuary
- Biorepositories and Other Resources
- **Career Development and Training Programs**

- **Research Project Grants**

Research Project Grants

- Studies on symbiosis between squid and bacterial toxin promote insight into organ development - Ruby and Ngai-McFall, UW-Madison
- Reproduction of Transgenic Pigs by Nuclear Transplantation - Prather, U Missouri



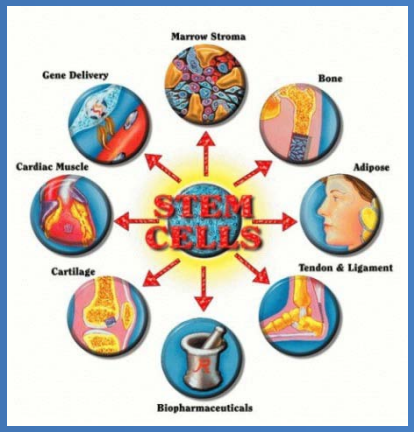
Aquarium to Bedside: The Zebrafish Role in Fatal Disease Research

- Development of a zebrafish model system for studying Fanconi anemia (FA), a hereditary disease of bone marrow failure and enormous cancer risk (2 R01RR020833; PI: John Postlethwait).
- Zebrafish FA system shares characteristics with the human system. Discovered that zebrafish with mutations in FA genes were unable to repair breaks in the DNA of their cells.
- Developed a small molecule screen for compounds to rescue zebrafish FA mutants to identify potential therapeutics for human FA patients and to understand disease mechanisms.
- Screening 3 libraries of drug-like molecules: 1) Approved Oncology Drugs Set II; 2) Microsource US Drug Library, 1040 FDA-approved compounds; and 3) the NIH Clinical Collection.

Stem cell therapies for tissue repair

Prockop DJ, *Texas A&M Health Science Center, College of Medicine, Institute for Regenerative Medicine, Scott and White Hospital, Temple, Texas*

P40RR017447 - Preparation and Distribution of Adult Mesenchymal Stem Cells (MSCs) from mice, rats, humans



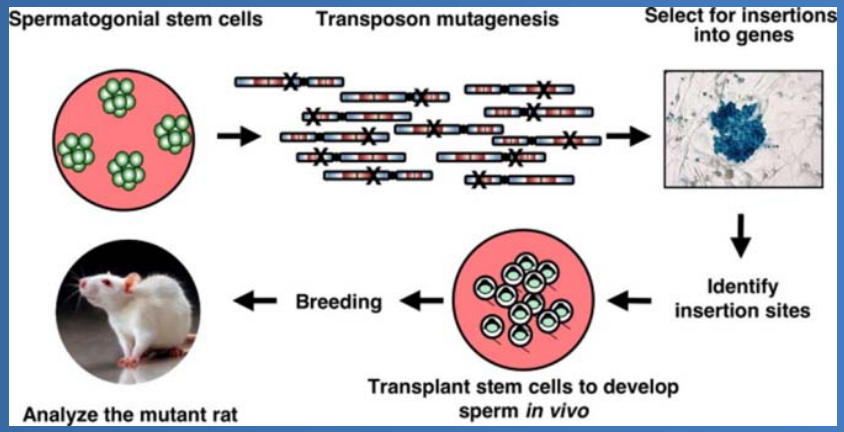
- Center prepares MSCs from human volunteers and rodents, defines the quality of the cells, and then distributes them to multiple investigators.
- Grant support enabled development of improved methods for isolation and characterization of the MSCs.
- Last year supplied frozen MSCs to 120 individual investigators, 23 NIH grants were funded which are using Center MSCs, 25 articles were published in peer review journals by PI laboratory.
- Disease models under investigation in PI laboratory: Myocardial infarction, Huntington disease, Progressive pulmonary hypertension, Transient global ischemia, Peritonitis, Autoimmune diseases

Development of rat genome modification technologies and new disease models

Current progress made by DCM/ORIP supported grants and rat resource significantly improves rat models for human disease conditions such as cancer, behavioral
biology, toxicology, alcoholism, diabetes, transplantation, cardiovascular and autoimmune diseases.

- **Mutagenesis via sperm manipulation**
  (R24, Hamra, Kent; University of Texas Southwestern Medical Center, TX)
- **Embryonic stem cells and gene knockouts via homologous recombination**
  (R01, Ying, Qi-Long; University of South California, CA)
- **Zinc finger nucleases technology**
  (P40, RRRC, Bryda, Elizabeth; University of Missouri, MO)

1. Nat Methods. 2010 Jun;7(6):443-5
2. Nature. 2010 Sep 9;467(7312):211-3
3. Nat Protoc. 2011;6(10):1521-354
4. Nat Protoc. 2011;6(6):827-44
5. J Clin Invest. 2011;121(9):3456-665.
6. Cell Cycle. 2011;10(7):1059-66



Division of Comparative Medicine

Oregon National Primate Research Center

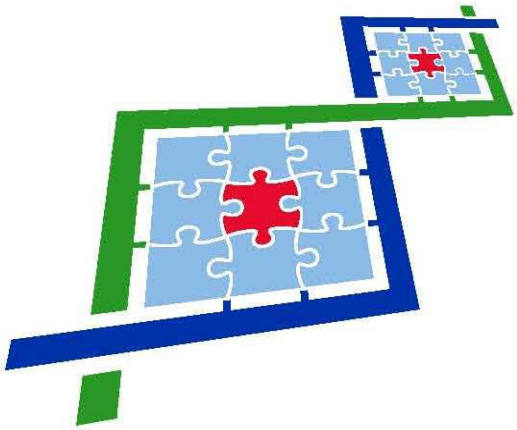
Title: Profound early control of highly pathogenic SIV by an effector memory T-cell vaccine

Publication: *Nature*. 2011 May 26; 473, (7348):523–527

- Researchers developed a novel vaccine strategy that helps control the virus at the initial mucosal exposure site before progressive, systemic infection occurs.
- Tested their new vaccine strategy in non-human primates using the monkey form of HIV (Simian Immunodeficiency Virus - SIV).
- Just over half of the monkeys that received the vaccine, controlled the replication of the SIV after one year of infection.
- This new vaccine strategy might clear viruses from infected animals compared to antiretroviral therapy that controls disease but cannot clear the virus.
- Findings may eventually lead to an AIDS vaccine for humans.

A Monkey Model of Huntington's Disease

- Development of monkeys transgenic for Huntington's disease at the Yerkes National Primate Research Center, Emory University. PI, Dr. Anthony Chan.
- Accomplished by using viral transgenesis with a dominant Huntington's mutation and use of Assisted Reproductive Technologies
- Animals show phenotypes characteristic of human Huntington's patients.
- The investigators have also developed a cell line derived from the HD monkeys that develops key HD phenotypes during neural differentiation in vitro.
- These animals and cells provide a system for studying the etiology of HD and for testing therapeutics.



LAMHDI

LINKING ANIMAL MODELS TO HUMAN DISEASE INITIATIVE

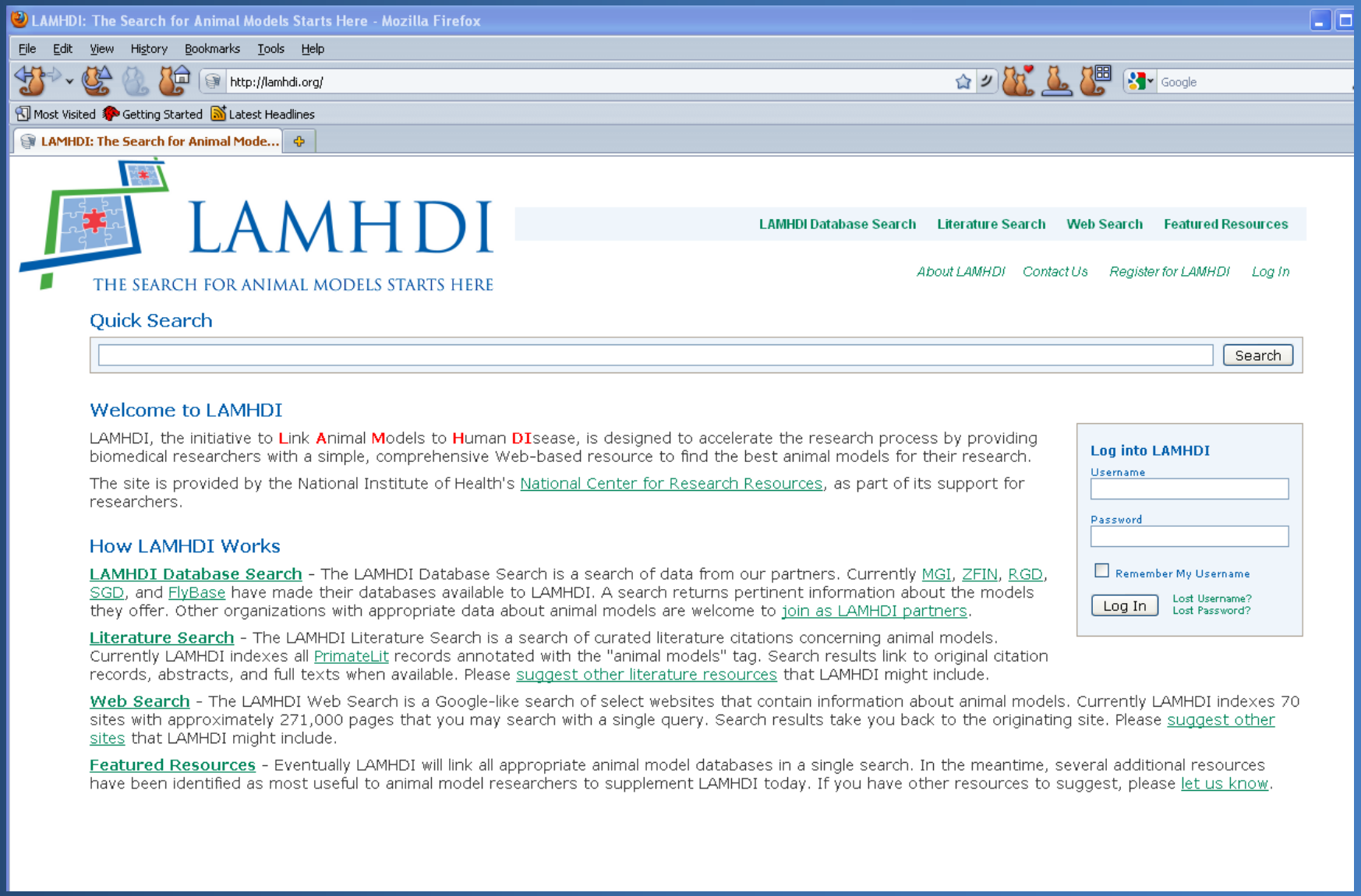
PHASE I

A Web-based resource to provide the best match between model and disease. Researchers can find what models are available and where they are located. Provides access to the data and functions at the different resource sites.

PHASE II

Identify and provide cross-resource tools to interplay data in different formats, from different species, from different diseases.

LAMHDI.org


LAMHDI: The Search for Animal Models Starts Here - Mozilla Firefox
File Edit View History Bookmarks Tools Help
http://lamhdi.org/
Most Visited Getting Started Latest Headlines
LAMHDI: The Search for Animal Mode...
LAMHDI
THE SEARCH FOR ANIMAL MODELS STARTS HERE
LAMHDI Database Search
Literature Search
Web Search
Featured Resources
About LAMHDI
Contact Us
Register for LAMHDI
Log In
Quick Search
Search
Welcome to LAMHDI
LAMHDI, the initiative to Link Animal Models to Human DIsease, is designed to accelerate the research process by providing biomedical researchers with a simple, comprehensive Web-based resource to find the best animal models for their research.
The site is provided by the National Institute of Health's National Center for Research Resources, as part of its support for researchers.
How LAMHDI Works
LAMHDI Database Search - The LAMHDI Database Search is a search of data from our partners. Currently MGI, ZFIN, RGD, SGD, and FlyBase have made their databases available to LAMHDI. A search returns pertinent information about the models they offer. Other organizations with appropriate data about animal models are welcome to join as LAMHDI partners.
Literature Search - The LAMHDI Literature Search is a search of curated literature citations concerning animal models. Currently LAMHDI indexes all PrimateLit records annotated with the "animal models" tag. Search results link to original citation records, abstracts, and full texts when available. Please suggest other literature resources that LAMHDI might include.
Web Search - The LAMHDI Web Search is a Google-like search of select websites that contain information about animal models. Currently LAMHDI indexes 70 sites with approximately 271,000 pages that you may search with a single query. Search results take you back to the originating site. Please suggest other sites that LAMHDI might include.
Featured Resources - Eventually LAMHDI will link all appropriate animal model databases in a single search. In the meantime, several additional resources have been identified as most useful to animal model researchers to supplement LAMHDI today. If you have other resources to suggest, please let us know.
Log into LAMHDI
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Division of Instruments, Infrastructure Resources, and Construction

- Shared Instrumentation (S10)
- High-end Instrumentation (S10)
- Recovery Act Instrumentation Awards
- Extramural Construction (C06)
- Animal Facilities Improvement (G20)

Division of Instruments, Infrastructure Resources, and Construction

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Shared Instrumentation Grant (SIG) Program
High-End Instrumentation (HEI) Program

Overview

- Unique and critical NIH mechanisms
- Equipment which is too costly to obtain with regular NIH research grants
- Highly cost-effective mechanisms
- Shared by an average of 8-10 NIH grantees
- Specialized research instruments
- Key tools in accelerating NIH research projects

SIG and HEI Program (S10)

Requirements

- Demonstrated need for the new instrument
- Enhancement of the NIH-funded research projects
- Appropriate technical expertise
- Administrative plan to assure sharing and maximum use
- Financial plan for long-term operation
- Institutional commitment

Shared Instrumentation Grant (SIG) Program

- Supports the purchase of research equipment in the $100,000 to $600,000 price range
- Provides a cost-effective mechanism for groups of at least three NIH-supported investigators to obtain commercially-available equipment that costs more than $100,000
  - Which are typically too expensive to be obtained through a research project grant
- Covers the direct costs of the instruments
  - Grantee pays for maintenance, service contracts, and technical support
- Awards are for one year only and are not renewable

High-End Instrumentation (HEI) Program

- Supports the purchase of a single major piece of research equipment that costs $750,000 to $2.0 million
- Assists NIH-supported investigators to keep at the forefront of modern biology and medicine
- Complements the Shared Instrumentation Grant program

SIG and HEI Program (S10) Facts

	Pre-ARRA (average of 5 years)		ARRA (FY10 non-ARRA)	
	SIG Program	**HEI Program**	**SIG Program**	**HEI Program**
Receipt dates	Annually (Mar)	Biannually (Sept)	Mar 2009	May 2009
# of Applications	350	100	1,898 ¥	834 ¥
$ range	100-500K	750K-2M	100-500K	600K-8M
Total $ requested	142.8M	152.3M	731M	1.76B
# of Awards	150	14-15*	378 † (+114)	80 † (+13)
Average $ per award	365K	1.62M	375K	1.98M
Budget	43M	20M	142M (+42M)	158M (+22M)
Success rate	30%	30%	26%	11%

* Annually

† Includes 84 ARRA FY09 (68 SIG, 16 HEI)

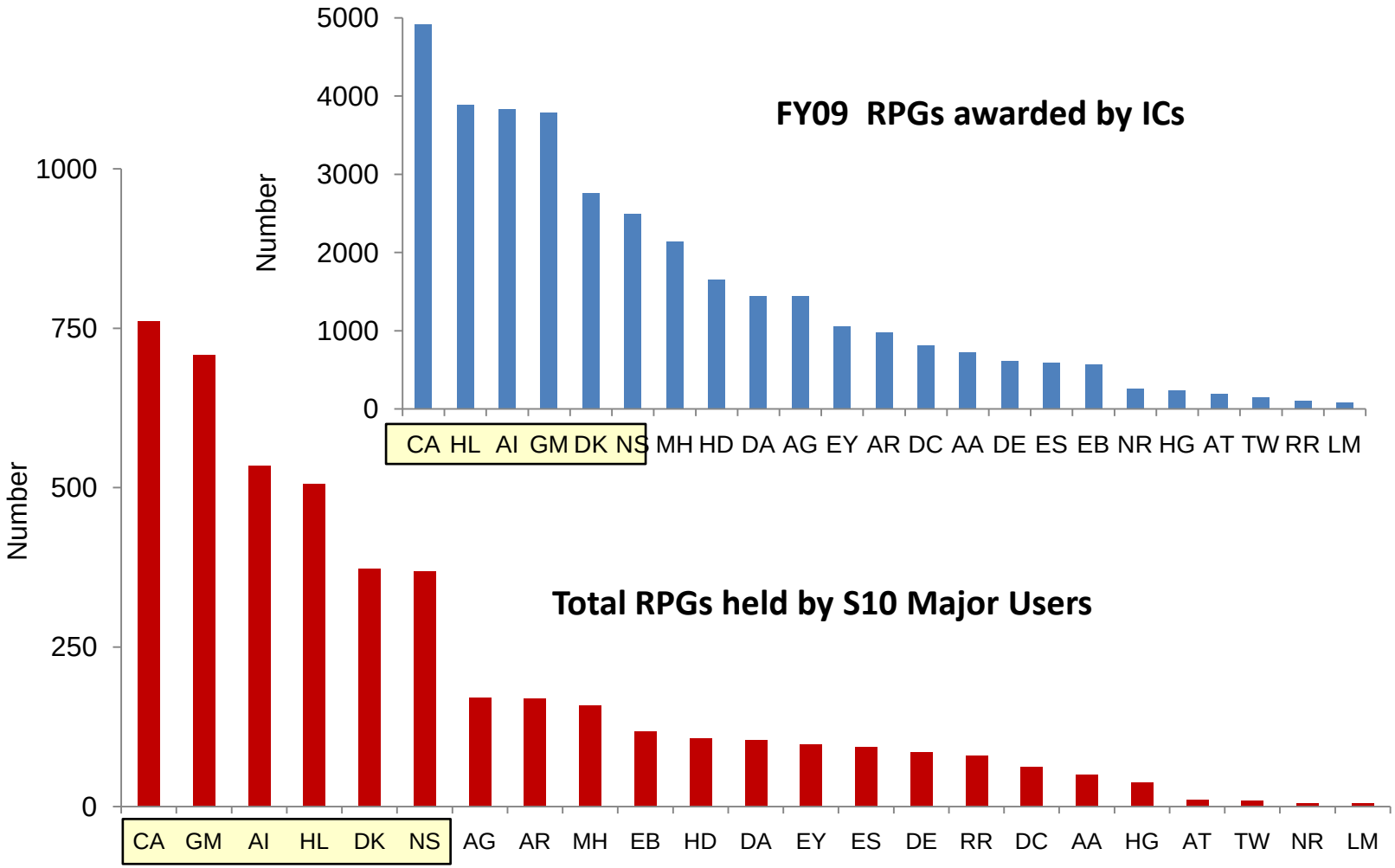
¥ Reviewed by more than 50 different CSR study sections

SIG and HEI Program (S10)
Impact on NIH Biomedical Research

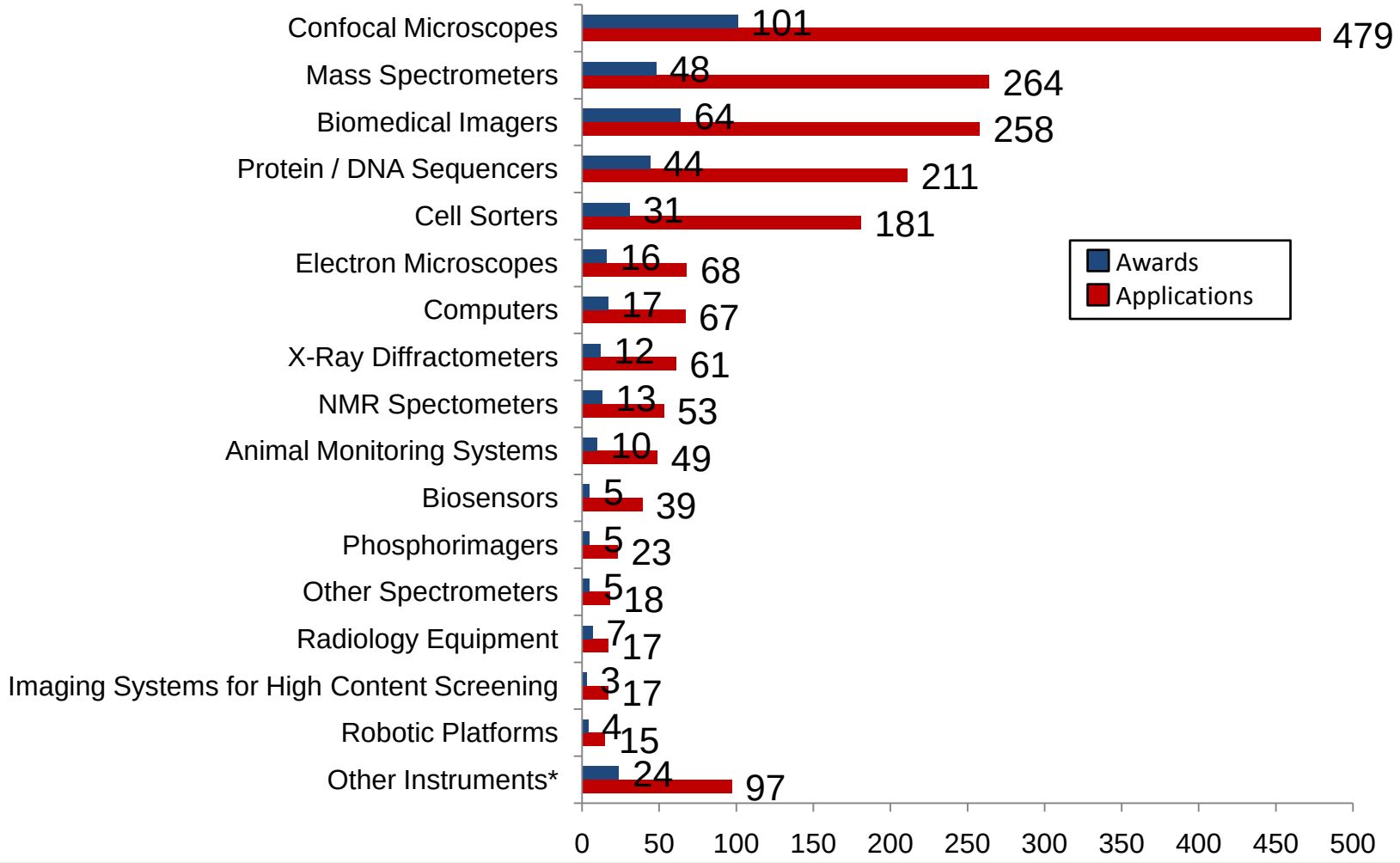
ARRA Awards

- 458 awards (378 SIG, 80 HEI)
- 3,500 individual major users
  - PIs on a total of 6,500 NIH grants
  - Totaling $2.5 billion in NIH funds
- Underestimate: other NIH users (minor or new) not included in analysis

NIH Support for S10 Major Users

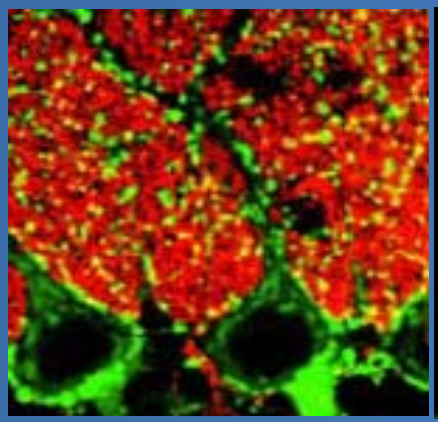


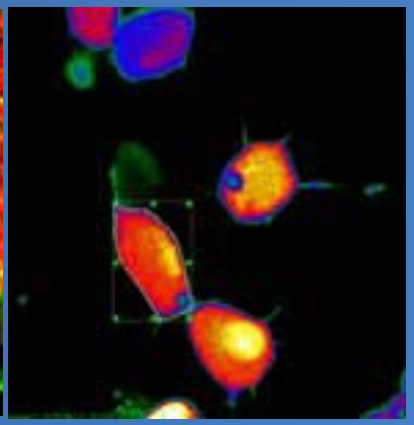
SIG Program: Applications and Awards (ARRA and Non-ARRA) by Instrument

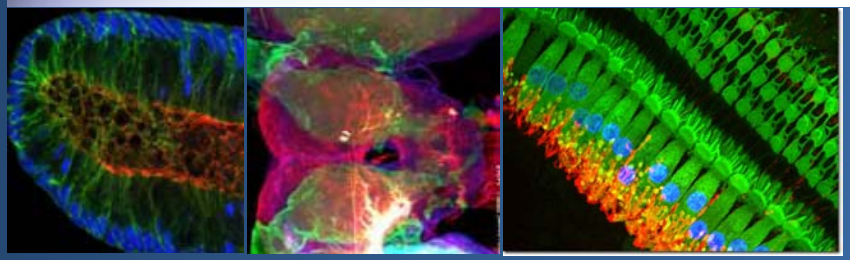


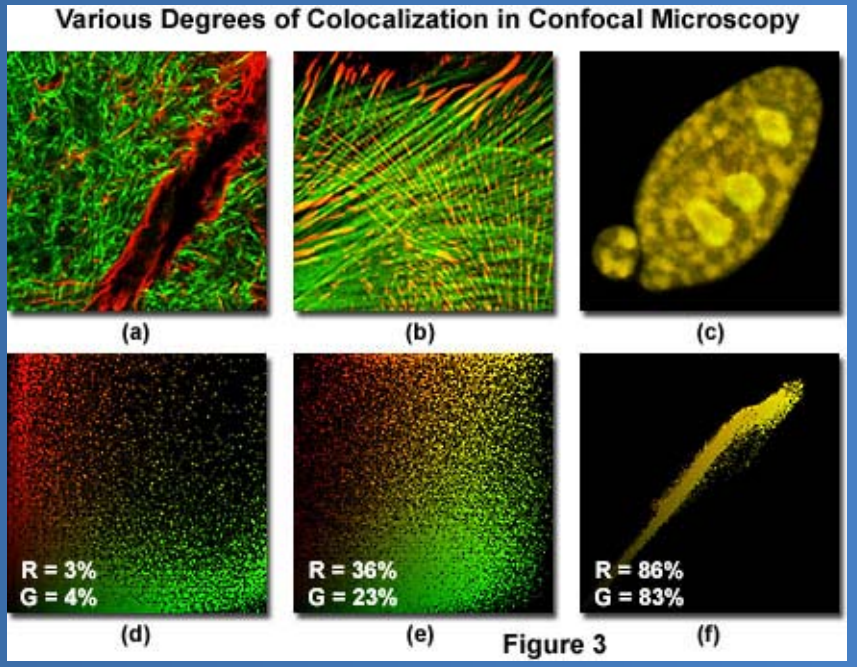
* Includes Clinical Chemistry Analyzers, EPRs, Fermentors, HPLCs, Nanotechnology Equipment, and Preparative Workstations

Confocal Laser Scanning Microscope









Illumina DNA Sequencer (HiSeq 2000)

- Comprehensive applications
  - DNA sequencing
  - Genotyping
  - Gene regulation & Epigenetic analysis
  - Gene expression
  - Real-time PCR
- High throughput
  - 5 X more output
  - Half cost/base

High-End Instrumentation Program: Supercomputers

- CRAY XE6 with ultra-high capabilities
  - 82 teraflop/sec
  - 1800 terabyte storage
- Approx. $6.9M awarded to U. Chicago
- Supports 12 NIH funded research teams
- Built on
  - CTSA bioinformatics bus (U. Chicago)
  - BIRN (NCRR)
  - caGRID (NCI)
  - Pathogen Data Resources (NIAID)

High-End Instrumentation Program
950 MHz NMR

950 MHz NMR (supermagnet) with cryoprobe

- $7.9M ARRA to University of Maryland
- Partnership among UMB, UMBC and UMCP
- One of the two sites in the US
- Superior sensitivity/resolutionto tackle most difficult biomolecular NMR problems
- Supports 35 NIH-funded projects
- Will be a mid-Atlantic regional resource

Construction – History at NCRR

- **The general extramural facilities improvement program (C06) began in NCRR in 1994**
  - Funding gradually increased to ~$115M in FY 2004
  - In FY2005, funding was cut to $30M
  - Until ARRA, no funding has been provided for the program since 2005
  - This program is for major alterations and renovations (over $500K)
- **Since the 1980s, NCRR has supported minor alterations and renovations (up to $500K) to develop and improve institutional animal resources (G20)**
  - Funding for this program (non-ARRA) was $7M in FY2011

Construction/Renovation Awards

- Prior to 2006, Congress appropriated funds each year for major construction/renovation awards
- The terms and conditions for the major construction/renovation awards (those above $500,000) require that ORIP certify that the improved facilities be used for biomedical research for 20 years following the completion of construction
- ORIP monitoring more than 350 awards that have not yet reached their 20-year milestone

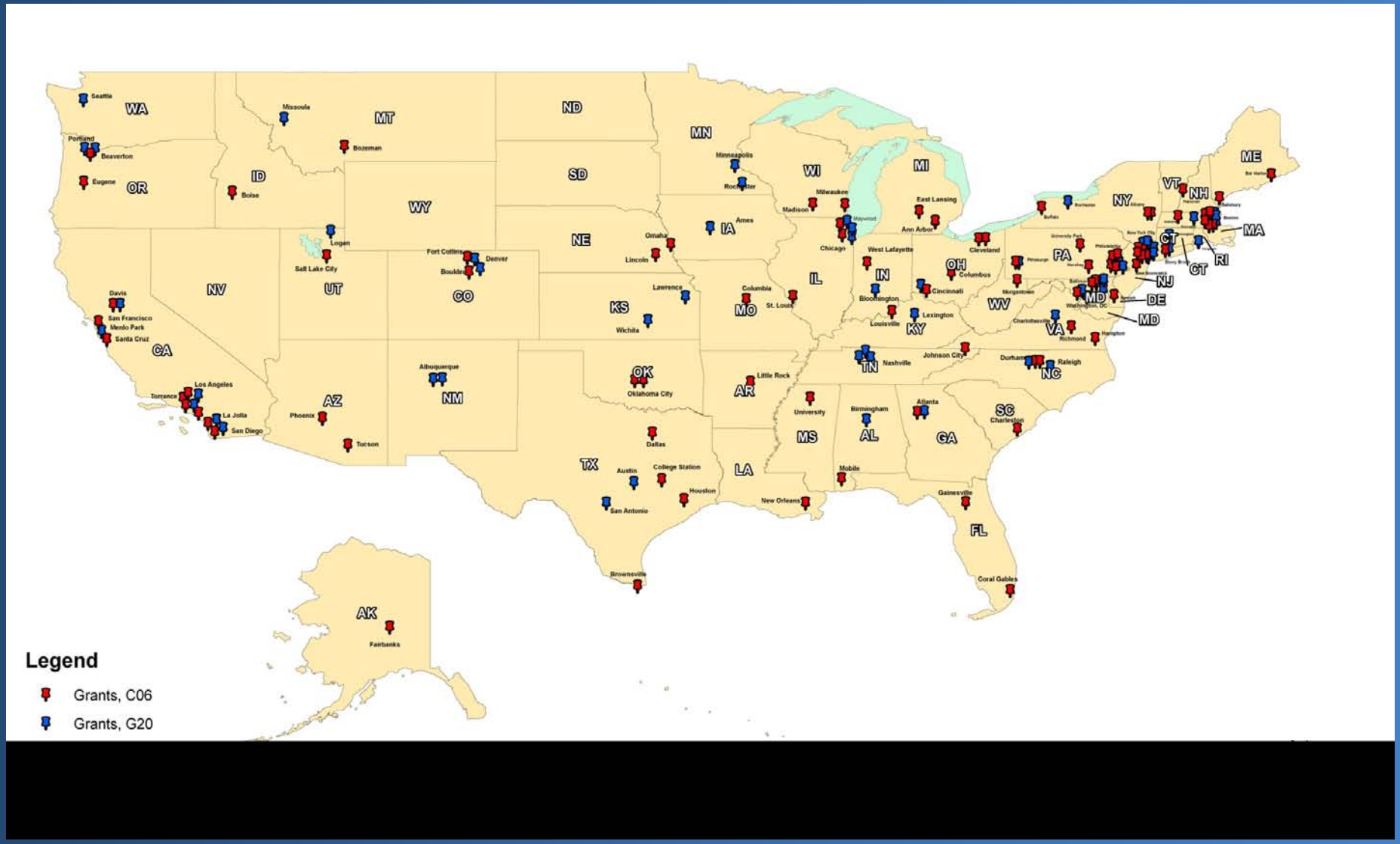
American Recovery and Reinvestment Act (*ARRA*) of 2009

Research Facilities Improvement – 2009

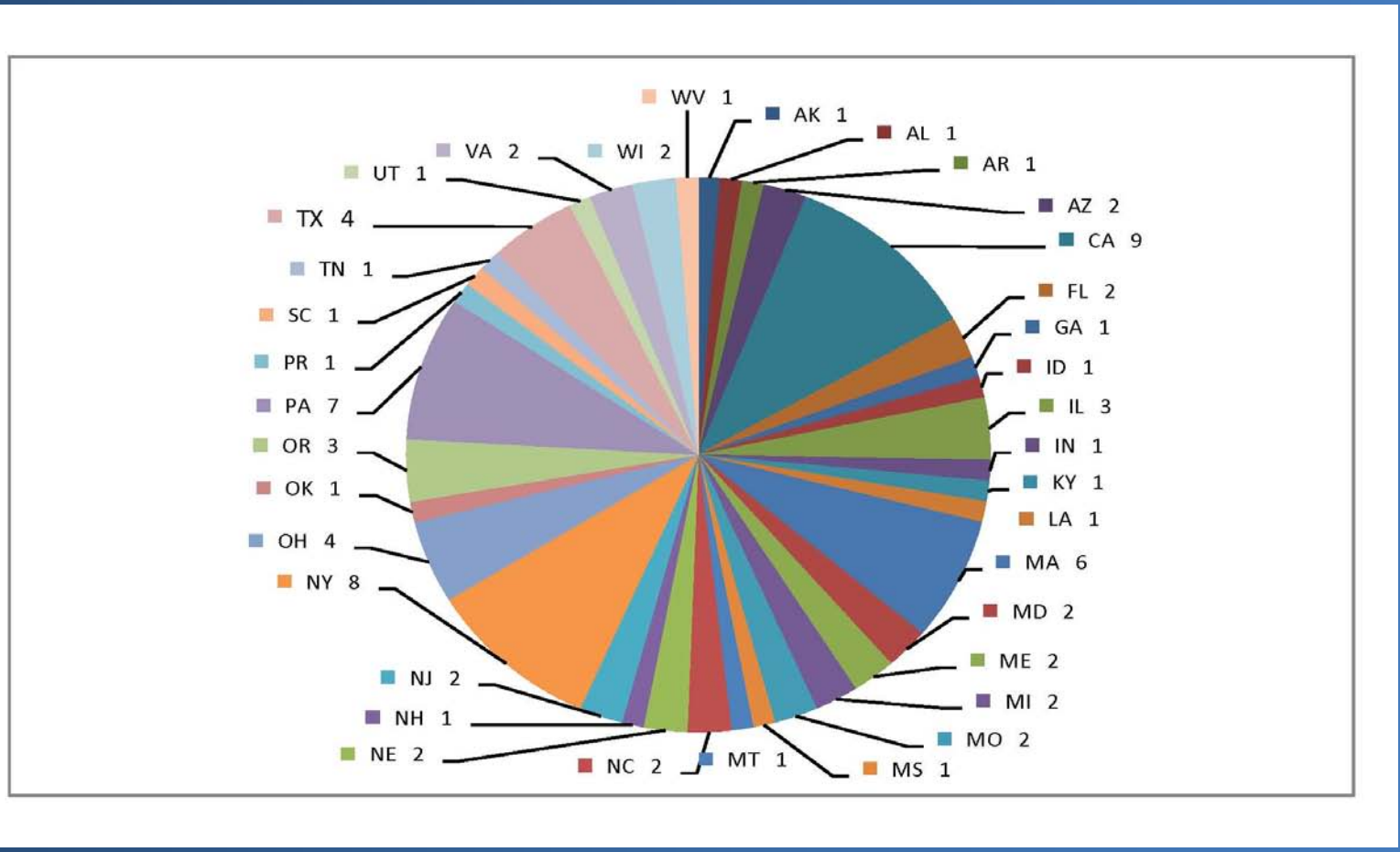
American Recovery and Reinvestment Act of 2009 (*ARRA*) provided NCRR with $1 billion for construction awards

- Core Facility Repair, Renovation, and Improvement (G20, RFA-RR-09-007)
- Extramural Research Facilities Improvement Program (C06, RFA-RR-09-008)

American Recovery and Reinvestment Act (ARRA)
C06 and G20 Construction Awards



American Recovery and Reinvestment Act (ARRA)
C06 Awards



Construction – ARRA Program Announcements

- Core Facility Repair, Renovation, and Improvement (G20, RFA-RR-09-007)
  - One receipt date (Sept 17, 2009)
  - Each institution limited to two applications
  - Applications between $1M and $10M
- Extramural Research Facilities Improvement Program (C06, RFA-RR-09-008)
  - Three receipt dates
  - Each institution limited to three applications
  - Applications between $2M and $15M

Construction – Awards

- $10.6B in responsive applications from both applications
- Nearly 1,200 responsive applications reviewed
- 18 study sections were empaneled using over 250 reviewers

Guidelines for Making Awards

The RFAs allow the following to be considered when making funding decisions:

- Scientific merit
- Geographic distribution of awards
- Program balance and Recovery Act priorities (energy efficiency, job creation)

Overview of the Current Program

- Long standing program at NCRR focused on Animal Facility Improvements
- Current program is restricted to budget amounts under $500K - minor alterations and renovations (A&R)
- Applications can request minor A&R, equipment such as caging or cage washers, or both
- Applications for scientific instruments (mass spectrometers…) are not accepted. Those go to the Shared Instrument program