

# US Large Mutant Mouse facilities (KOMP and MMRRC)

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*Session 4: Biological and Medical Sciences (14:00-16:00)*

Kent Lloyd



International Cooperation in Research Infrastructures:  
Symposium on transatlantic EU-U.S. cooperation in the field of research infrastructures

CNR - Piazzale Aldo Moro, Rome, Italy  
01 October 2010

# US measures

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~6million mice used annually in science (>10 million “snake food”)

NIH budget US\$30billion...

50% (\$15billion) supports studies using research animals

→ 90% (\$14 billion) supports studies using mice

NIH funded mutant mouse facilities infrastructure:

Repositories

Molecular biology, ES cell, genetics laboratories

Phenotyping facilities

Informatics and data management resources

# US mutant mouse facilities

*...come in a variety of flavors...*



## Taconic Knockout Repository

Taconic Knockout Model Repository of over 3,200 KO lines provides commercial researchers world-wide with unparalleled access to fully-licensed, healthy knockout mouse models. Our repository offers the scientific community immediate access to expertly-derived, highly valuable research tools that rapidly accelerate the drug discovery and development processes. Eliminating the time associated with increasing the design and development of these mouse models provides a tremendous competitive advantage.



## Mouse Resources

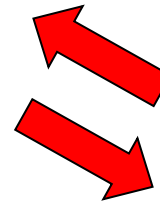
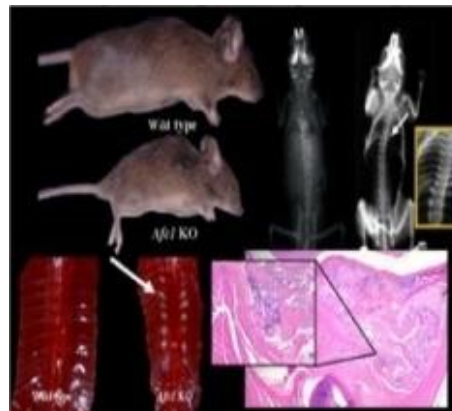
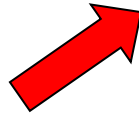
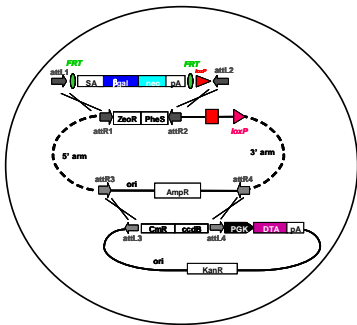
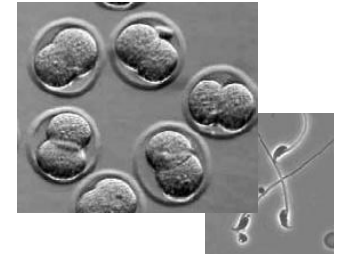
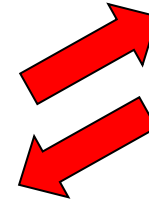
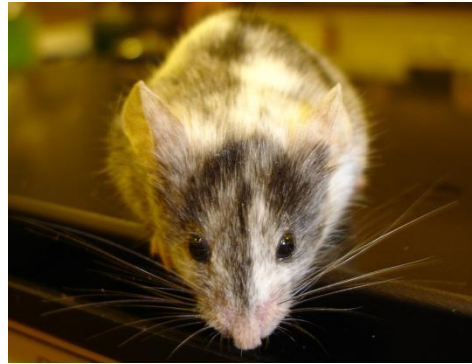
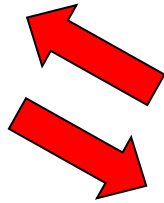
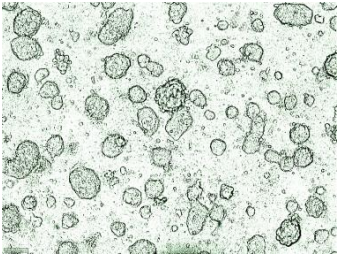
[Alzheimer's Disease](#)    [Mouse Mutant](#)  
[Craniofacial Mutant](#)    [Neural Tube Defect](#)  
[JAX Cre Repository](#)    [Parkinson's Disease](#)  
[Cytogenetic Models](#)    [Special Mouse Strains](#)  
[Mouse DNA Resource](#)    [Type 1 Diabetes](#)

# Yesterday's facilities...





# More than just a mouse house...



# What mouse facilities do now...

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- ❑ Identify, seek, import, preserve, distribute models
- ❑ Mice, germplasm, ES cells, vectors, data
- ❑ Conduct quality control (eg, genetic, pathogens, etc)
- ❑ Provide relevant information (eg, genotyping protocols)
- ❑ Health certificates, tech transfer (MTA, COU), customs
- ❑ Offer value-added products and services (gene targeting)
- ❑ Customer service
- ❑ Advertising & marketing
- ❑ Facilitate sharing



# Raison d'être (public repositories)

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- ☐ Serve the scientific community
- ☐ Ensure quality, accuracy, reliability
- ☐ Facilitate availability & accessibility
- ☐ Extend value and utility at reasonable cost
- ☐ Stewardship, security, protection, perpetuity

# Two examples

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- ❑ Mutant Mouse Regional Resource Center
- ❑ Knockout Mouse Project Repository



- ***established 1999...“availability, accessibility, acquisition” of mutant mouse lines from and for the biomedical research community***
- ***renewed 2005...an internationally-recognized, credible, reputable, competent, and reliable international resource***
- ***renewal and expansion 2010...largest academic resource in world***



*Sponsored by (U42):*



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
**National Institutes of Health**





~30,000 mutant lines deposited by individual researchers, including major collections....

Trans-NIH Mouse Initiatives



~14,000 gene trap ES cells and mice (+WTSL, Soriano)



Deltagen and Lexicon Knockout Mice and Phenotypic Data

~200 knockouts, ES cells and mice, and data



~497 mouse lines, ES cells, and phenotyping data



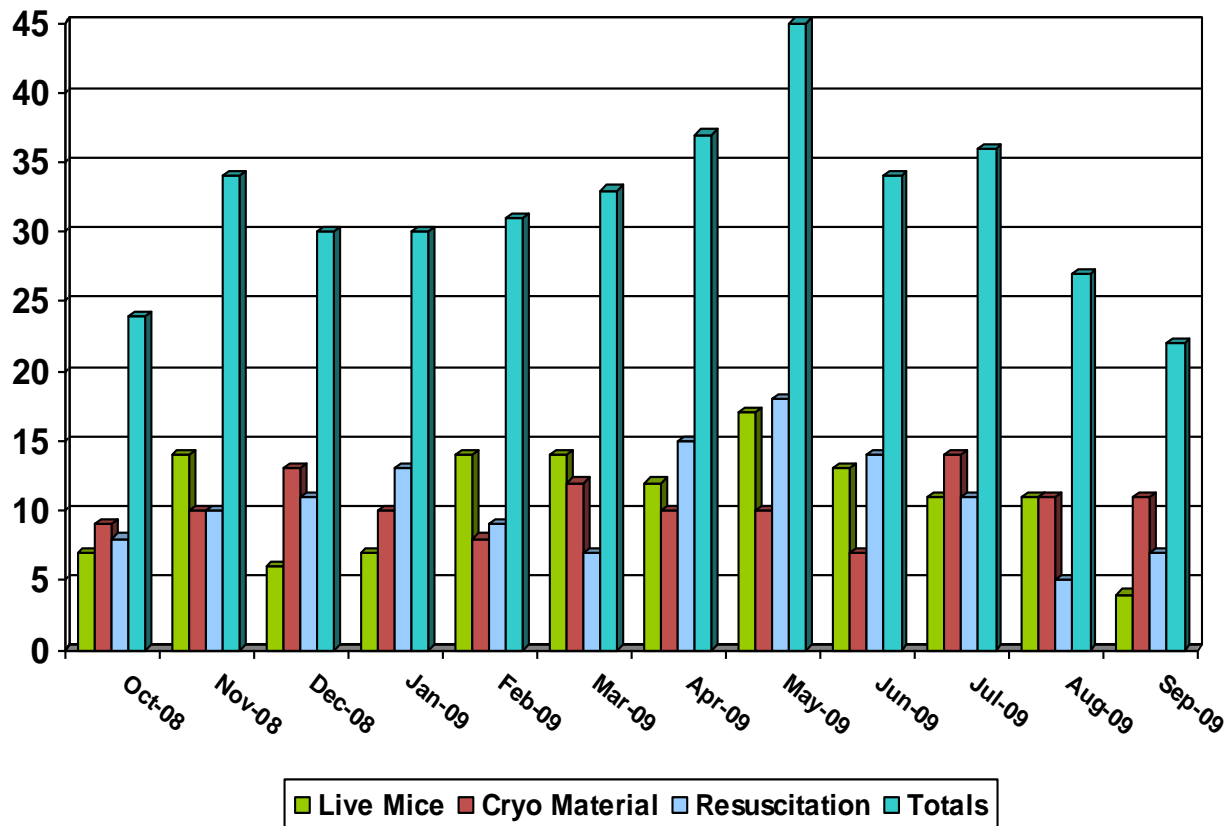
>50 ENU immune and other phenotypes, mice and germplasm



~800 BAC-tg and CRE mouse lines & data

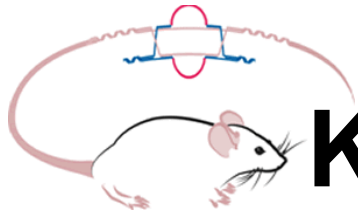
# MMRRC-UCD Orders

**2008-09**

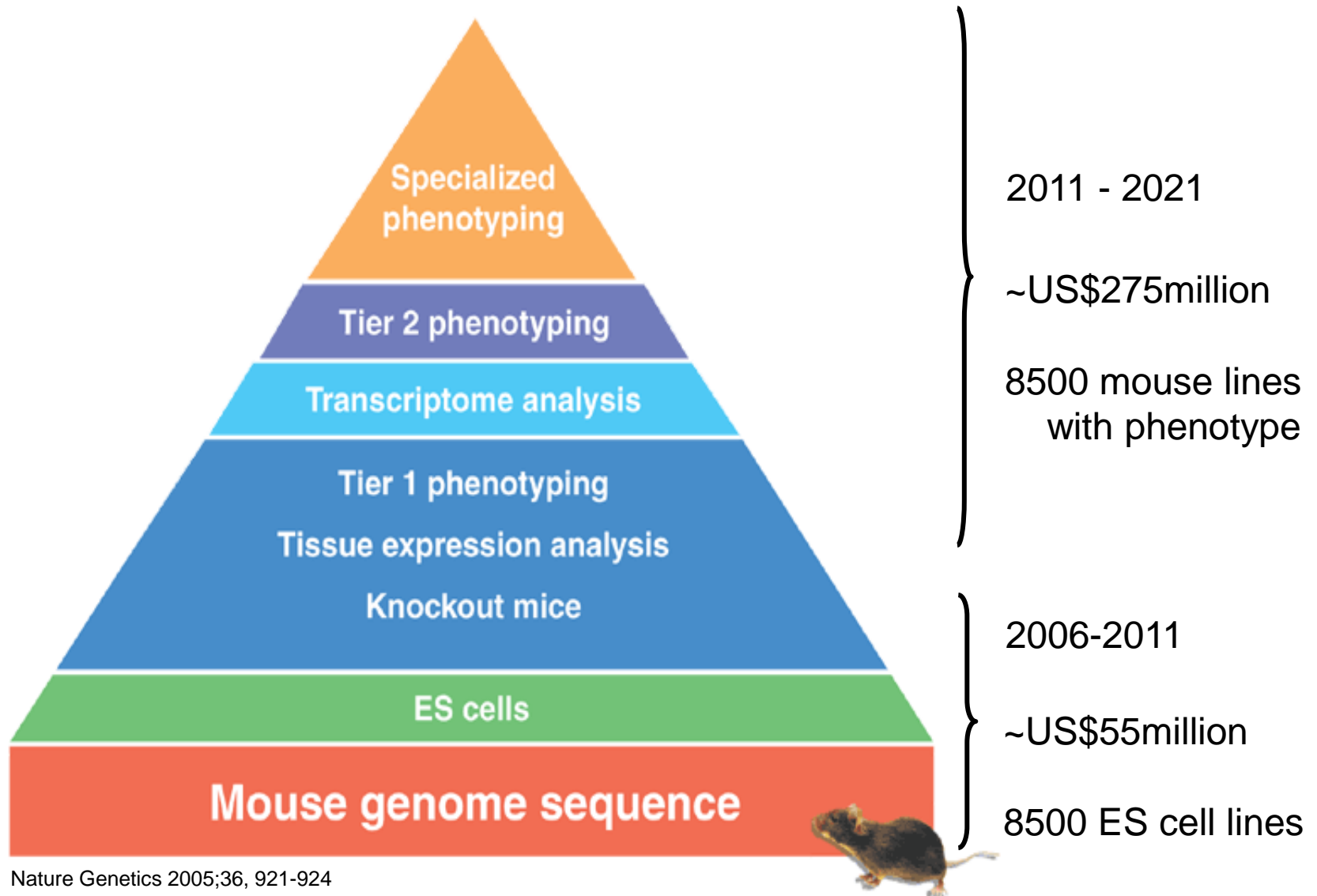


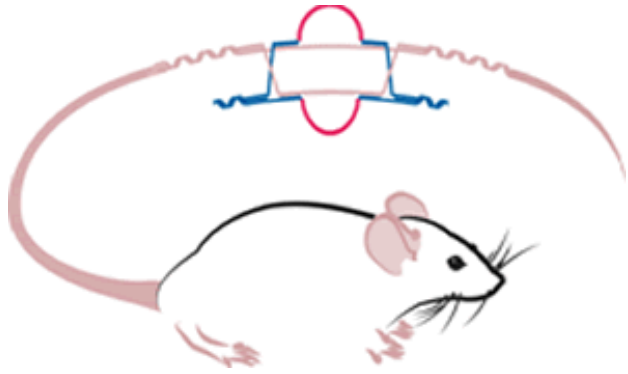
**Totals:**

**>6000 orders**  
**--1,500 investigators**  
**--900 institutions**  
**--33 countries**

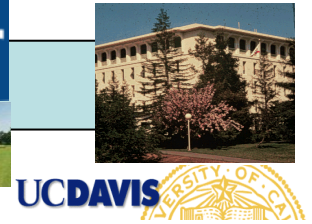


# Knockout Mouse Project (KOMP)





**CSD**  
consortium



***REGENERON, INC***

**8500 genes**



**Mutant ES cell  
resource**

**+**

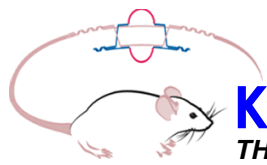
**Vector  
resource**



**150-200 mutant mouse lines**

**-C57BL6/N**  
**-lacZ-tagged**  
**-K/O alleles:**  
**conditional null**  
**targeted trap**  
**deletion**



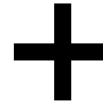


**KOMP Repository**  
THE KNOCKOUT MOUSE PROJECT

# Archive & Distribution



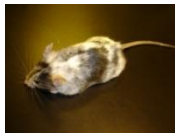
**UC DAVIS**



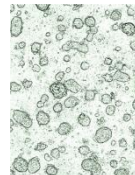
**C · H · O · R · I**  
Children's Hospital Oakland Research Institute



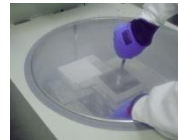
*microinjection*



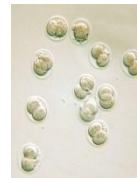
*mice*



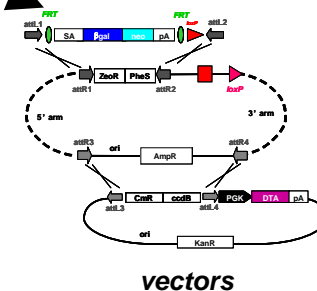
*ES cells*



*cryopreservation/  
cryorecovery*



*sperm & embryos*



*vectors*

Sponsored by (U42):

- Acquire, import products from KOMP mutagenesis teams
- Conduct Quality Control assays
- Archive and distribute KOMP products
- Provide comprehensive customer and technical services
- Market, promote, and extend utilization via KOMP.org
- Engage and coordinate efforts with international partners

# Common features:

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- ❑ Novel products and specialized services
  - Mice, ES cells, microinjection, cryo
- ❑ Resource-related research & development
  - iPS cells, RMCE, pathogen control
- ❑ Education, training, outreach
  - Curation, nomenclature, pathology

# Examples of EU-US cooperation:

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## FRAMEWORK FOR ADVANCING TRANSATLANTIC ECONOMIC INTEGRATION BETWEEN THE EUROPEAN UNION AND THE UNITED STATES OF AMERICA

We, leaders of the European Union and the United States of America:

Establish a joint research infrastructure for mouse functional genomics (following a joint meeting in 2007 in Belgium);

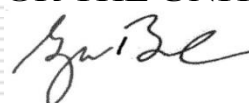
Signed at Washington on this 30<sup>th</sup> day of April, 2007, in two originals.

FOR THE EUROPEAN UNION:



Angela Merkel  
President of the European Council

FOR THE UNITED STATES OF AMERICA:

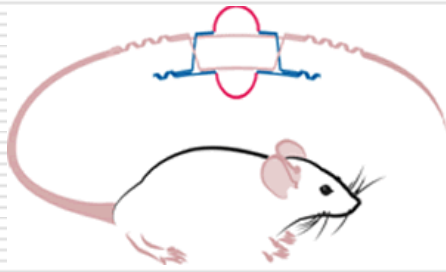


George W. Bush  
President

José Manuel Barroso  
President of the European Commission

# Examples of EU-US cooperation:

## International Knockout Mouse Consortium



**-C57BL6/N**  
**-lacZ-tagged**  
**-K/O alleles:**  
**conditional null**  
**targeted trap**  
**deletion**

**Mutant ES cell**  
**resource**

+

**Vector**  
**resource**

**17,000 genes**

**8,500 genes (KOMP)**  
**8,000 genes (EUCOMM)**  
**500 genes (NorCOMM)**

**250-500 mutant mouse lines**



# Examples of EU-US cooperation:

## Resource & Data Sharing

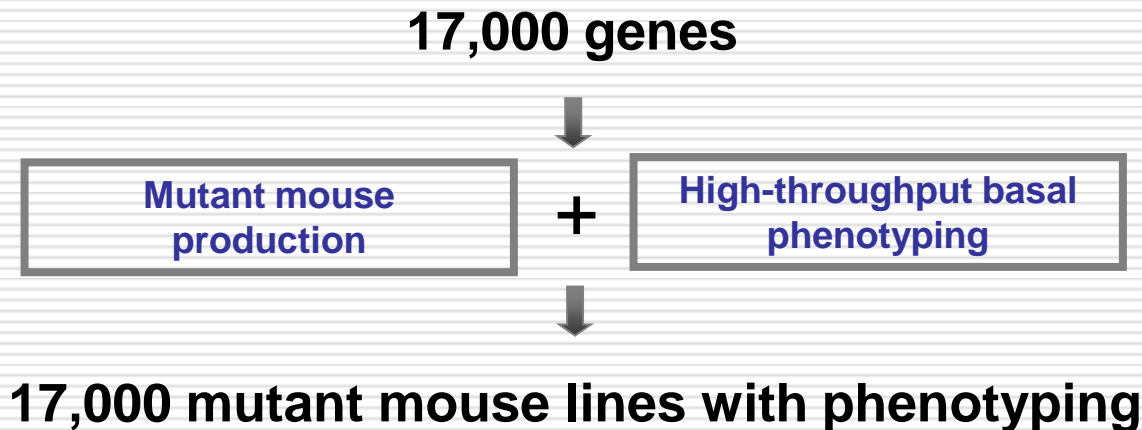


# Examples of EU-US cooperation:

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## International Mouse Phenotyping Consortium

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Data and information available fully, free, and fast  
Mutant mouse and associated resources accessible  
Technical, support, and value-added services

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# Challenges

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- ❑ Researcher (user) expectations (e.g., qc)
- ❑ Originator (provider) expectations (e.g., costs)
- ❑ Customs and other national laws & regs
- ❑ Transportation issues (e.g., infectious diseases)
- ❑ Informatics & data management consistencies
- ❑ IP & Technology Transfer issues (e.g., MTA's)
- ❑ Harmonization of husbandry, handling, health

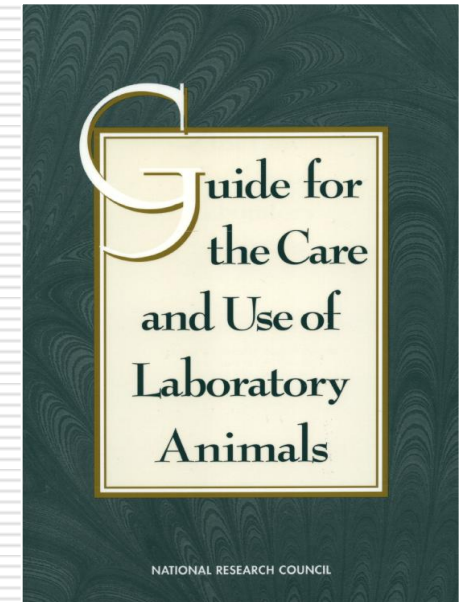
# Attempt to reconcile animal care differences

- 2010 update of the ILAR Guide
- 2010 update of the FASS Ag Guide
- ETS 123 / European Directive 86/609

**Performance  
Standards**



**Engineering  
Standards**



# What's driving the changes?

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- ☐ Researcher needs
- ☐ Animal needs
- ☐ Public needs





[www.mousebiology.org](http://www.mousebiology.org)

*Celebrating*  
**Mouse Biology  
Program**  
[www.mousebiologyprogram.org](http://www.mousebiologyprogram.org)  
**10 YEARS**

