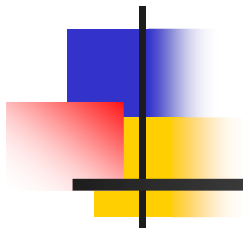


NIH Funded Animal Resource Centers at the University of Missouri



Genetically-modified Animals:
Powerful tools for biomedical
research



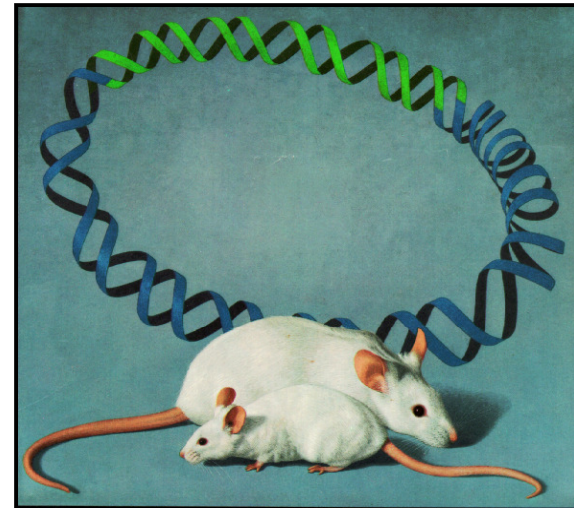
Mice, Rats and Pigs

- Mutant Mouse Regional Resource Center (MMRRC)
- Rat Resource and Research Center (RRRC)
- National Swine Resource and Research Center (NSRRC)



Overall Goals

- Provide valuable animal models to investigators
- Shift the burden for maintaining and distributing unique animal models from investigators to a National Resource Center
- Perform research aimed at improving GM animal models



Functions

- Import animals
- Confirm genotype
- Cryopreserve germplasm
- Rederive animals free of infectious pathogens
- Maintain strains/lines as live animal or cryopreserved material
- Produce and Distribute animals and cryopreserved materials to biomedical investigators



Create Genetically-Modified Swine

- Genetically-modified swine models are be created for NIH-funded investigators
- Proposals submitted on-line and reviewed by NSRRC Advisory Panel
- No cost to the requesting investigator



Genetically Modified Mice

- 1980 – 1st transgenic mouse
- 1987 – 1st knockout mouse
- The MMRRC currently holds ~30,000 lines
- JAX currently holds ~10,000 lines
- MMRRC: www.mmrrc.org



Mice as the predominant species for GM models

- Short gestation
- Small, relatively inexpensive to keep
- Well-defined genetics



Genetically Modified Rats

- Transgenic Rats
- Targeted Mutations in Rats
 - Transposon/Transposase
 - Zinc Fingers
 - Embryonic Stem Cells





Rat models accepted into RRRC

- **Cell/Tissue Markers**
 - EGFP (SD, F344, Lewis, Wistar)
 - Alk Phos (F344)
 - LacZ (SD)
 - DS red 2- liver specific (Wistar)
- **Human Transgenes**
 - ICAM2-DAF
 - HLA B7
 - HLA B27
- **Polycystic Kidney Disease**
 - RRRChan:SPRD-Pkdr1
- **Behavioral Models**
 - Syracuse low & high avoidance
 - Alcohol-Tolerant/ Alcohol-Normal
 - High & Low Alcohol Sensitive
- **Hypertension**
 - SS/jrctr & SR/jr
 - Lyon hypertensive, normotensive, hypotensive
- **Hydrocephalus**
 - H-Tx/Hcj
 - LEW/Jms
- **Dietary/Obesity**
 - DIO & DR
 - F.DIO
- **Miscellaneous**
 - Ia osteopetrotic model
 - Spontaneous dwarf rat
 - Belgrade (anemia model)

**182 rat models
currently available**

Rats vs. Mice

- Rats: Advantages
 - Increased size
 - Used extensively for physiologic studies
 - Large Toxicology databases
- Rats: Disadvantages
 - More expensive
 - Genetics – less defined
 - Embryo manipulations more difficult





Swine in Biomedical Research

- GM pigs made using somatic cell nuclear transfer (cloning)
- Both random and targeted mutations possible
- Currently 20 GM pig models available from the NSRRC





NSRRC Facilities

- The NSRRC has a separate, new state-of-the-art facility
- Facility:
 - houses 175-200 pigs
 - provides biosecurity to prevent pathogen entry
 - contains laboratory and surgery space





Genetic Modifications and Wild Type Animals within the SPF Facility

▪ Genetically Modified Models

- Alpha gal KO and hDAF
- EGFP (CMV Chicken beta actin promoters)
- Omega Fatty Acid (Fat-1)
- Human coagulation factor IX; Human alpha-antitrypsin; von Willibrand factor

▪ Miniature Swine

- NIH miniature pigs (SLA^{C/C})
- Minnesota miniature pigs

▪ Wild type Models

- Ossabaw
- Yucatan



Training the Future

- Graduate students from the schools of Medicine, Veterinary Medicine and Engineering
- Veterinarians from a nationally recognized Comparative Medicine Program (CMP)
 - Trains veterinarian in comparative medicine research and the specialty of laboratory animal medicine
- Veterinary students in the Veterinary Research Scholars Program (VRSP)
 - Provides veterinary students opportunity to explore research career opportunities
 - Strong collaborations with Kansas State University
- Future trainees in the Institute for Clinical and Translational Science
 - Integration of research and clinical training for medical students

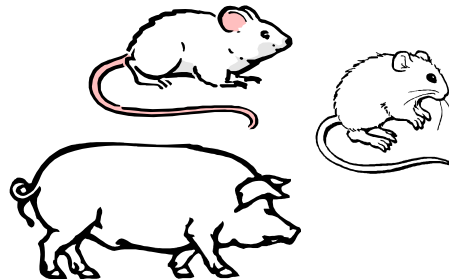
Do you worry that your animal model may be lost due to disease or genetic instability?

Is the demand for your animal model by other investigators more than you can accommodate?

The NIH-funded **Animal Resource Centers** for mice, rats & swine can help!

The Resource Centers provide the following services:

- ✓ **Cryopreserve and store models to prevent loss**
- ✓ **Rederive models to eliminate pathogens**
- ✓ **Distribute valuable models to investigators**
- ✓ **Provide health and genetic monitoring**



Mutant Mouse Regional Resource Centers
www.mmrrc.missouri.edu

Rat Resource & Research Center
www.nrrrc.missouri.edu

National Swine Resource & Resource Center
www.nsrrc.missouri.edu

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