Mice and Rats in Biomedical Research

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MDSC 402

Content Warning

Use of animals in research.
Eugenics

The next slides discuss the use of animals (rodents) in scientific experiments.

The next slides discuss people who were eugenicists.

Lecture Outcomes

- By the end of this lecture, students will be able to:
  - Identify the main species in biomedical research
  - Discuss pros and cons for using mice and rats in biomedical research
  - Select the ideal model organism for example experiments
  - List the three “R”’s for rodent biomedical research
  - List the tetrad behaviours

Overview and History of Laboratory Mice and Rats

Species of Laboratory Mice

- *Mus musculus* (house mouse)
- Many strain varieties
- Mostly inbred (20+ generations)

The Jackson Laboratory

History of Laboratory Mice

- Mouse fanciers (Asia, Europe and North America) were origin of most laboratory mice
  - Mix of 4 different subspecies
    - *Mus musculus musculus*
    - ***Mus musculus domesticus***
    - *Mus musculus castaneus*
    - *Mus musculus molossinus*

History of Laboratory Mice

- Many inbred strains derive from fancy mice colonies generated by Abbie Lathrop
  - Researchers realized that mouse fanciers had routinized mouse breeding, but also created inbred colonies with genetic control
  - Dr. William Castle (Harvard) placed first order to study genetics in mice

An Interlude

- Dr. William Castle (Harvard) placed first order to study genetics in mice in 1902
  - In his laboratory C.C. Little was in charge of the mouse colonies, who went on the found Jax Labs
    - Not only did he not credit work Abbie Lathrop did,
    - But, he was also an avowed eugenicist
      - Important to understand where our tools come from, history

Species of Laboratory Rats

- *Rattus norvegicus*
- Also many strain varieties
- Mostly inbred (20+ generations)

Bioresource Now Newsletter

History of Laboratory Mice

- Rat fanciers (Asia, Europe and North America) were origin of most laboratory rats
  - Breeding for rat pits and fancy rats
  - First used in experimental studies in the 1850s

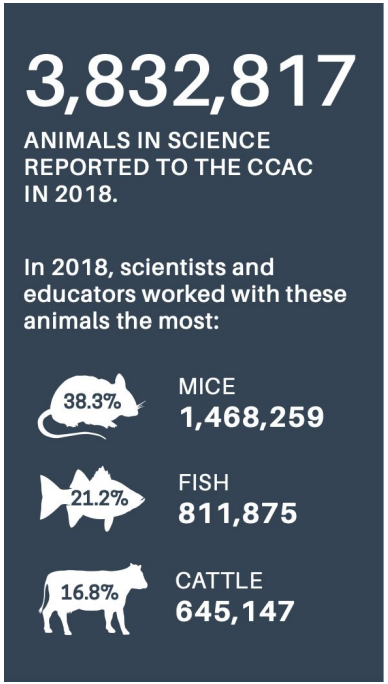
Milestones for Rodents in Biomedical Research

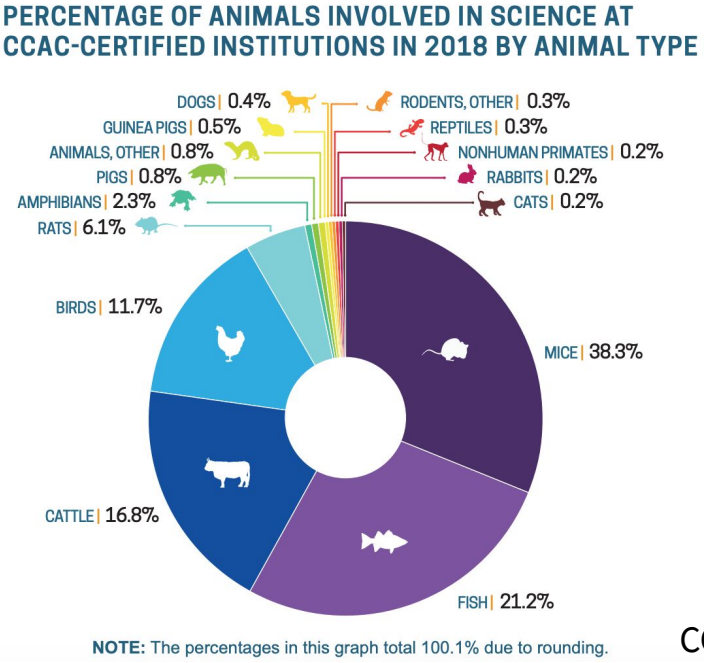
- 1976—First developed transgenic mouse
- 1987—First knockout mouse
- 2002—Mouse genome sequenced
- 2004—Rat genome sequenced
- 2009—First knockout rat

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3979591/

Mice and Rats in Biomedical Research Overview

- Mice and rats make up 95 % of animals utilized in biomedical research
- Canada numbers:





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Benefits and Pitfalls in Using Mice and Rats

Let's Brainstorm!

Think
Pair
Share

1. Take a few minutes and think about potential pros and cons to using mice and rats in biomedical research.
2. Take a few minutes and share with a partner or two near you.
3. Let's create a list as a class!

Pros to Using Mice

Pros to Using Mice

- Similar homology to humans
- Similar genetic function and inheritance to humans
- Small (easy to store a lot)
- Relatively economical
- Short(ish) lifespan (2 years)
- Quick breeding
- Altricial (born immature)
- Infrastructure
- Know a lot about their genetics
  - Genetics tools (including conditional knockouts/in; tissue specific manipulations; cell identification)
- Inbred

Pros to Using Rats

Pros to Using Rats

- Similar homology to humans
- Similar genetic function and inheritance to humans
- Small (larger than mice)
- Relatively economical
- Short(ish) lifespan (2 years)
- Quick breeding
- Altricial (born immature)
- Genome is sequenced
- Larger brains allow for more complex behaviour analysis
  - Training required but more easily trained to mice

Cons to Using Mice

Cons to Using Mice

- Smaller bodies/brains (compared to rats)
- Not the closest to humans
  - Especially immunologically
- Not great at performing complex behaviours
- Drugs developed for and work in mice do not always work
- Inbred strains not diverse (better to compare strains to get at human genetic diversity)
- Nocturnal
- Expensive to develop transgenic models
- Longer lifespans/gestation than worms/flies
- Influenced by researcher’s

Cons to Using Rats

Cons to Using Rats

- Not the closest to humans
- Drugs developed for and work in rats do not always work
- Genetic tools not as advanced
- Despite having more related immunological responses, tools not as developed
- Inbred (better to compare across strains)
- Nocturnal
- Social animal
- Allergies
- Expensive to develop transgenic models
- Longer lifespans/gestation than worms/flies
- Influenced by researcher's behaviour
- Larger than mice

What Makes Mice/Rats Unique for biomedical research?

What makes Mice/Rats unique for biomedical research?

Mammalia class (close-ish homology to humans)

AND

Easy/quick to breed and manipulate genetics

Which Model Organism?

Think Pair Share

1. Think for a minute or two about which organism and WHY?
2. Share with a partner.
3. We'll vote as a class.

1. Designing an experiment to test:

2. Which animal(s) and why?
   a. Rats
   b. Mice
   c. Both
   d. Neither

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1. Designing an experiment to test:
   a. Anxiety and cognitive behaviours
   b. Model of arthritis
   c. Contribution of T cells

2. Which animal(s) and why?
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1. Designing an experiment to test:
    a. Anxiety and cognitive behaviours
    b. Model of arthritis
    c. Contribution of T cells
2. Which animal(s) and why?
    a. Rats!
        i. Better for advance cognitive tasks
        ii. Immune cell contribution
    b. Mice
        i. Tools to inhibit T cells and study their phenotypes

Think Pair Share

1. Think for a minute or two about which organism and WHY?
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1. Designing an experiment to test:
   a. Disruption of circadian rhythms
   b. Embryonic development

2. Which animal(s) and why?
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2. Which animal(s) and why?
    a. Rats
    b. Mice
    c. Both
        i. Quick gestation, altricial
    d. Neither

Think Pair Share

1. Think for a minute or two about which organism and WHY?
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1. Designing an experiment to test:
    a. Genetic knockdown of hormone receptor
    b. Social behaviour
    c. Males and females

2. Which animal(s) and why?
    a. Rats
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    c. Both
    d. Neither

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1. Designing an experiment to test:
    a. Genetic knockdown of hormone receptor
    b. Social behaviour
    c. Males and females
2. Which animal(s) and why?
    a. Rats
    b. Mice
        i. Genetic knockdown most likely to be available or easy to create
    c. Both
    d. Neither

Think Pair Share

1. Think for a minute or two about which organism and WHY?
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1. Designing an experiment to test:
    a. Brain imaging
    b. Alzheimer's patients
    c. Drug trial

2. Which animal(s) and why?
    a. Rats
    b. Mice
    c. Both
    d. Neither

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    a. Brain imaging
    b. Alzheimer's patients
    c. Drug trial
2. Which animal(s) and why?
    a. Rats
    b. Mice
    c. Both
    d. Neither
        i. Not a good model and can't get AD; patient drug trial, would have already been tested in todents

Considerations for Using Rodents in Biomedical Research

Who Governs Animal Use?

- Canadian Council on Animal Care (CCAC)
  - Mission: “animal-based science in Canada takes place only when necessary and that the animals in the studies receive optimal care according to high quality, research-informed standards.”
- University of Calgary Animal Welfare Committee
  - Animal Care Committees

Best Practices—Three “R’s”

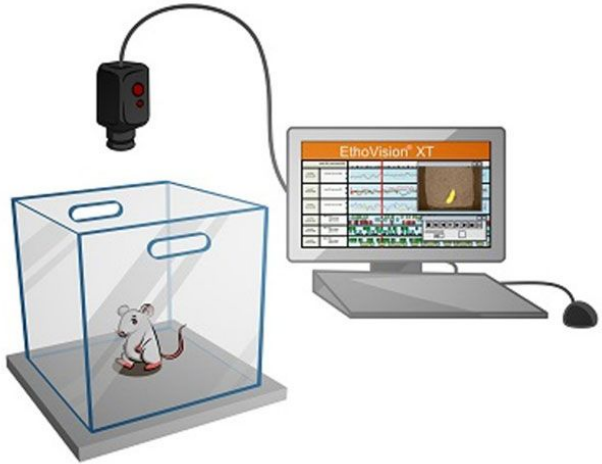
- Replacement
  - Avoid or replace use of animals
- Reduction
  - Less animals used
- Refinement
  - Minimizing pain and distress
- Important when designing and conducting studies to keep these principles in mind

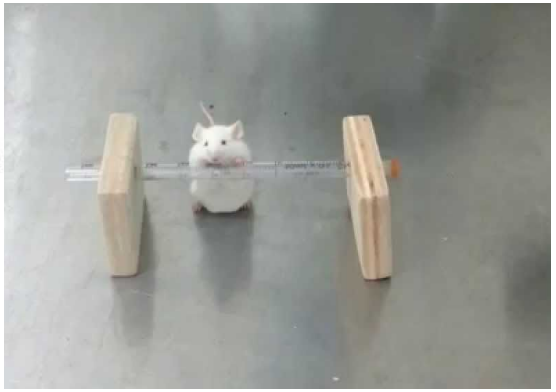
“Real” Research World Example of Rodents in Research

Cannabis Related Behaviours—Tetrad

Rodents will respond to THC and cannabinoids with a tetrad of behaviours

- Decreased spontaneous activity
- Catalepsy
- Hypothermia
- Analgesia





Thank you!

Questions/Comments/Concerns/Feedback:

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