Research Using Aged B6 Mice: Considerations, Applications, and Best Practices

Technical Information Services

May 18, 2017
The Jackson Laboratory’s Mission

“To discover precise genomic solutions for disease and empower the global biomedical community in the shared quest to improve human health.”

Performing Research
Investigating genetics and biology of human disease

Providing Resources
JAX® Mice, Clinical & Research Services, online data resources, technical publications, and more

Educating Scientists
World-class courses, internships, and other programs
JAX® Mice
The Gold Standard for Biomedical Research

- NIH-funded resource
- >8,000 strains and growing
  - 2.7 million mice shipped annually
- Unsurpassed genetic quality & animal health
- Best characterized & referenced ~100 new pubs/week
- Common inbred strains (C57BL/6J, BALB/cJ, DBA/2J) support development/collection of specialty strains and other valuable community research resources
Online Resources to Expedite Research

- **JAX® Mice Database**
  [www.jax.org/mouse-search](http://www.jax.org/mouse-search)

- **Mouse Genome Informatics**
  [www.informatics.jax.org](http://www.informatics.jax.org)

- **Mouse Phenome Database**
  [www.jax.org/phenome](http://www.jax.org/phenome)

- **Others**, including: **JAX-Clinical Knowledgebase**, **Mouse Tumor Biology Database**
Learning Goals

- Correlate life phases of mice with humans
- Locate resources for defining “normal” phenotypes of aging
- Recognize some common age-related health conditions in C57BL/6J mice
- Identify and communicate factors that can affect phenotype and reproducibility

Aged C57BL/6J mouse at 63 weeks
Learning Goals

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When are Mice “Old”? Life Phase Equivalencies for Mice vs Humans

- **Mature adult: 3–6 months**
  - Past development but not yet affected by senescence

- **Middle age: 10-14 months**
  - Senescent changes can be detected in some, but not all, biomarkers of aging

- **Old: 18-24 months**
  - Senescent changes can be detected in almost all biomarkers in all animals

Adapted from Figure 20-3: Flurkey, Currer, and Harrison, 2007. 'The mouse in biomedical research.' in James G. Fox (ed.), American College of Laboratory Animal Medicine series (Elsevier, AP: Amsterdam; Boston).

More information: [Life Span as a Biomarker](#)
Research Areas Involving Aged Mice

- Basic biology of mouse lifespan and healthspan
- Cognition, behavior, and sleep
- Bone density, osteoporosis, osteopenia
- Muscle mass, sarcopenia
- Metabolism
- Body composition, diet, exercise
- Cardiovascular disease
- Reproductive biology
- Age-related changes in immune function, wound repair
- Age-related hearing loss

Aged C57BL/6J mouse at 63 weeks displaying barbered muzzle

American Federation for Aging Research
https://www.afar.org/research/funding/

National Institute on Aging
Turning Discovery Into Health
https://www.nia.nih.gov/
Question 1

You want to study C57BL/6J mice that correspond, approximately, to a 56 – 69 year old human. Which age range of mice correlates best? (select one)

a) 3 – 6 months
b) 10 – 14 months
c) 18 – 24 months
d) 28 – 36 months
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Aged C57BL/6J mouse at 63 weeks
What is *Normal* for “Old”? Resources for Defining Phenotype

- Mouse Phenome Database, http://phenome.jax.org/

![Survival of C57BL/6J (000664)](image)

Data from the Nathan Shock Aging Center at The Jackson Laboratory ([Yuan2 data set](#))
Resources for Defining Phenotype

Mouse Phenome Database (MPD), http://phenome.jax.org/

Strains >

**Mouse strain: C57BL/6J**

*Available phenotype strain survey data for C57BL/6J:*

- By topic / anatomy / system
  - appearance and coat color
  - behavior
  - blood—clinical chemistry
  - blood—hematology
  - blood—lipids
  - blood—xenobiotics
  - body composition
  - body fat pads
  - body weight size and growth
  - bone
  - brain
  - cancer
  - cardiovascular
  - cell and tissue damage
  - ear

- By detailed phenotype category

- By methodology / procedure
  - By intervention study
    - (drugs, alcohol, diets, challenges)

- In aging-related studies

*Also available for this strain:*

- Appearance: black

- View pup appearance by age

- SNP / genotype variation data for C57BL/6J and comparisons vs. other strains

…and proper controls

Link to C57BL/6J Data in MPD

and Link to C57BL/6J Detailed Phenotype Categories
Resources for Defining Phenotype

Mouse Genome Informatics, www.informatics.jax.org

...and proper controls
Resources for Defining Phenotype

Books


The Mouse in Biomedical Research: Normative Biology, Immunology, and Husbandry (Foster, Small, Fox, 1983).

The Laboratory Mouse (Suckow, Danneman, Brayton, 2001)

2nd editions available

Now
## Resources for Defining Phenotype

**Published Literature**

| Table 3. Clinicopathological data from B6 mouse presented in Figures 2B, 5C, and 5D and CB6F1 mouse presented in 3B, 3D, and 4C |
|---|---|---|---|
| **Complete blood count** | B6 Female Figs. 2B and 5C,D | CB6F1 Male Figs. 3B, D and 4C | Reference values* |
| WBC, K/μl | 2.5 | 14.8 | 5.1–11.8 |
| RBC, M/μl | 8.5 | 11.1 | 8.7–10.3 |
| HGB, g/dl | 12.9 | 15.4 | 12.8–16.2 |
| HCT,% | 51.0 | 55.8 | 42.4–44 |
| MCV, fl | 60.1 | 50.1 | na |
| MCH, pg | 15.3 | 13.8 | na |
| MCHC | 0.3 | 27.8 | na |
| Platelet count, K/μl | 992.0 | 2043.0 | 100–1,000 |
| **Differential** | Absolute/μl (%) | Absolute/μl (%) | 0 |
| Bands | 0 (0.0) | 0 (0.0) | 0 |
| Polye | 960 (38.0) | 6,200 (42.0) | 6.7–37.2 |
| Lymph | 1,240 (49.0) | 7,090 (48.0) | 63–75 |
| Monos | 250 (10.0) | 1,030 (7.0) | 0.7–2.6 |
| Eos | 80 (3.0) | 440 (3.0) | 0.3–3.8 |
| Rasso | 0 (0.0) | 0 (0.0) | 0.1–1.6 |
| Comments | Polychromasia, +1 | Slight polychromasia Platelet count inaccurate due to clumps |

**Small mammal panel**

| Glucose mg/dl | 196.0 | 170.0 | 106–278 |
| Urea nitrogen (BUN), mg/dl | 24.0 | 30.0 | 19–34 |
| Calcium, mg/dl | 10.6 | 10.1 | 9–12 |
| Total protein, g/dl | 6.9 | 5.7 | 4.3–6.4 |
| Albumin, g/dl | 3.5 | 3.2 | 2.0–4.7 |
| Alanine aminotransferase, U/l | 43.0 | 47.0 | 26–120 |
| Aspartate aminotransferase, U/l | 83.0 | 107.0 | 69–191 |
| **Principal histologic diagnoses** | Pituitary adenocarcinoma | Harderian gland adenoma |
| | Histiocytic sarcoma | Preputial adenitis and seminal vesiculitis |
| | Keratitis and corneal ulceration | Mild nephropathy |
| | Poyartitis |

*Summarized from (58, 59).

...and proper controls

Pettan-Brewer and Treuting, 2011; PMID: 2953032

Summarized from (Foster, Small, Fox, 1983) and (Suckow, Danneman, Brayton, 2001)
Resources for Defining Phenotype

Strain datasheet

C57BL/6J males and females 25-78 weeks ready to order now, get your study started today.
Colonies are managed by our patented Genetic Stability Program to minimize genetic drift.
One of the most well-characterized models available; more than 15,799 studies have been published to date using the C57BL/6J mouse.
Mice are available from rooms that are free of pathogens and opportunistic agents to suit your research needs.

Research Applications

- Neurodegenerative Disease
- Bone Density
- Age-related Hearing Loss
- Immunology
- Oncology
- Diabetes and Obesity

Appearance & Care

Phenotype Information

References & Resources

Link to strain datasheet: https://www.jax.org/aged-b6
How to Find the Datasheet

1. Visit the JAX website and search for the strain by going to the "MOUSE STRAIN DATASHEET - 000664" page. You can find the strain C57BL/6J under the "POPULAR" section.

2. Search for "aged b6 jax" on Google to find additional information or related resources.
Appearance and Care

- Graying and/or thinning pelage
- Barbering – not a characteristic of aging; however, not excluded from colony

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Aged C57BL/6J mouse at 63 weeks displaying graying coat and thinning hair

Aged C57BL/6J mouse at 63 weeks displaying barbering

Aged C57BL/6J mouse at 63 weeks displaying barbered muzzle

Link to strain datasheet:  
https://www.jax.org/aged-b6
Phenotype Information

Click below to download detailed project data including:

- Organ Weight Summary
- Hematology Summary
- DEXA Summary
- Bio Chemistry Summary
- Flow Cytometry Summary

![Table Image]

Link to strain datasheet: https://www.jax.org/aged-b6
Question 2

You inherit a dataset from someone who has just recently left the lab – the datasets are labelled “effects of rapamycin on survival: B6, cBy, 129S1, C3, D2.” You know rapamycin is an agent that can extend lifespan, but the letter/numbers are confusing. Where can you get help?

a) The Mouse Phenome Database (http://phenome.jax.org/)
b) The Jackson Laboratory’s strain datasheet for aged B6J mice
c) Published literature, book chapters, textbooks
d) Google Scholar, PubMed
e) Facebook, Twitter, Instagram
f) The Mouse Genome Informatics Database (www.informatics.jax.org)
C57BL/6 Background: Related Conditions

- Hydrocephalus
- Microphthalmia, anophthalmia
- Age related hearing loss
- Malocclusion
- Ulcerative dermatitis
- Behavioral:
  - Barbering
  - Aggression (fight wounds)

Malocclusion References
- JAX Blog *How to spot and manage malocclusion in research mice*
- JAX Notes: *Malocclusion in the laboratory mouse*

Ulcerative Dermatitis References
- Burkholder et al. 2012; *Health Evaluation of Experimental Laboratory Mice*; PMID:22822473
- Sargent et al, 2015; *Systematic Literature Review of Risk Factors and Treatments for Ulcerative Dermatitis in C57BL/6 Mice*; PMID:26678363
- Also see Comment, Chue et al, 2016; PMID:27053561

Hydrocephalus Reference
JAX Notes: *Hydrocephalus in laboratory mice*
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Advance Planning with Staff for Age-Related Health Issues is Essential

“An effective aging research program includes the collaboration and education of the research, husbandry, and veterinary staff, and of the members of the institution animal care and use committee. This collaborative effort is critical to humanely maintaining older mice and preventing excessive censorship due to non-lethal diseases. Part of the educational process is becoming familiar with how old mice appear clinically, at necropsy and histopathologically. This baseline knowledge is important in making the determination of humane end points, defining health span, contributing causes of death and effects of interventions. The goal of this paper is to introduce investigators to age-associated diseases and lesion patterns in mice from clinical presentation to pathologic assessment”

End-of-life: Criteria for Euthanasia

- Nonresponse to touch
- Cool body temperature to the touch
- Slow or labored breathing
- Hunched posture with matted fur
- Poor body condition score

“It is important to optimize [end-of-life] EOL determination for humane and for scientific reasons. Timely euthanasia of mice based on validated markers of imminent death allow implementation of end points that alleviate terminal distress, minimally or insignificantly affect life span data, and permit timely collection of tissue specimens.”


BCS: Ullman-Cullere and Foltz 1999; PMID: 10403450
Body Condition (BC) Scoring System for Assessing Animal Health

<table>
<thead>
<tr>
<th>BC1</th>
<th>Skeletal structure extremely prominent; little or no flesh cover; Vertebrae distinctly segmented</th>
</tr>
</thead>
<tbody>
<tr>
<td>BC2</td>
<td>Segmentation of vertebral column evident; Dorsal pelvic bones are readily palpable</td>
</tr>
<tr>
<td>BC3</td>
<td>Vertebrae and dorsal pelvis not prominent; palpable with slight pressure</td>
</tr>
<tr>
<td>BC4</td>
<td>Spine is a continuous column; Vertebrae palpable with only firm pressure</td>
</tr>
<tr>
<td>BC5</td>
<td>Mouse is smooth and bulky; Bone structure disappears under flesh and subcutaneous fat</td>
</tr>
</tbody>
</table>

Burkholder et al. 2012; PMID:22822473
Ullman-Culleré and Foltz, 1999; PMID: 10403450
University of Washington (UW) Study of Aged C57BL/6J Mice: Clinical Presentations

- Rectal prolapse
- Alopecia and dermatitis
- Ocular lesions
- Palpable masses

Pettan-Brewer, C., and P. M. Treuting; 2011. PMID: 22953032
# UW Study of Aged C57BL/6J Mice: Neoplastic Lesions

<table>
<thead>
<tr>
<th>Neoplastic diseases</th>
<th>Location</th>
<th>% of mice with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosarcoma</td>
<td>Uterus, skin, perirenal, ear</td>
<td>4</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>Spleen</td>
<td>1</td>
</tr>
<tr>
<td>Hemangiosarcoma</td>
<td>Spleen, uterus, ovary, liver, skin</td>
<td>4</td>
</tr>
<tr>
<td>Hematopoietic neoplasia (Malignant lymphoma</td>
<td>Systemic</td>
<td>67</td>
</tr>
<tr>
<td>or Histiocytic sarcoma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic adenoma</td>
<td>Liver</td>
<td>1</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>Seminal vesicle, colon</td>
<td>3</td>
</tr>
<tr>
<td>Malignant Pheochromocytoma</td>
<td>Adrenal</td>
<td>1</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>Vertebra</td>
<td>1</td>
</tr>
<tr>
<td>Ovarian granulosa cell tumor</td>
<td>Ovary</td>
<td>1</td>
</tr>
<tr>
<td>Pituitary adenocarcinoma</td>
<td>Pituitary</td>
<td>1</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>Pituitary</td>
<td>6</td>
</tr>
<tr>
<td>Pulmonary adenocarcinoma</td>
<td>Lung</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary adenoma</td>
<td>Lung</td>
<td>1</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Skin</td>
<td>1</td>
</tr>
<tr>
<td>Squamous papilloma</td>
<td>Stomach</td>
<td>3</td>
</tr>
<tr>
<td>Testicular interstitial cell adenoma</td>
<td>Testicle</td>
<td>1</td>
</tr>
</tbody>
</table>

*Note: Retrospective review of clinical data, necropsy, and histology findings was tabulated. Results reported as percentage of mice with the disease (n=72; males=26, females=46). Age range 16–36 months.*
UW Study of Aged C57BL/6J Mice: Non-neoplastic Lesions

<table>
<thead>
<tr>
<th>Non-neoplastic diseases</th>
<th>Location</th>
<th>% of mice with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidophilic macrophage pneumonia</td>
<td>Lungs</td>
<td>13</td>
</tr>
<tr>
<td>Amyloid, glomerular</td>
<td>Kidney</td>
<td>41</td>
</tr>
<tr>
<td>Amyloid, intestinal</td>
<td>Small intestine</td>
<td>14</td>
</tr>
<tr>
<td>Biliary hyperplasia</td>
<td>Liver</td>
<td>3</td>
</tr>
<tr>
<td>Cataracts or cornea opacity</td>
<td>Eyes</td>
<td>30</td>
</tr>
<tr>
<td>Chronic endometrial hyperplasia</td>
<td>Uterus</td>
<td>14</td>
</tr>
<tr>
<td>Heart lesions(^a)</td>
<td>Heart</td>
<td>97</td>
</tr>
<tr>
<td>Hepatic cysts</td>
<td>Liver</td>
<td>3</td>
</tr>
<tr>
<td>Hydronephrosis(^b)</td>
<td>Kidney</td>
<td>19</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>Kidney</td>
<td>100</td>
</tr>
<tr>
<td>Ovarian atrophy</td>
<td>Ovary</td>
<td>6</td>
</tr>
<tr>
<td>Ovarian cysts</td>
<td>Ovary</td>
<td>3</td>
</tr>
<tr>
<td>Polyarteritis</td>
<td>Systemic arteries</td>
<td>10</td>
</tr>
<tr>
<td>Preputial cystic adenitis</td>
<td>Preputial glands</td>
<td>3</td>
</tr>
<tr>
<td>Rectal prolapse(^b)</td>
<td>Rectum(^b)</td>
<td>19(^e)</td>
</tr>
<tr>
<td>Seminal vesiculitis, cystic degeneration</td>
<td>Seminal vesicles</td>
<td>17</td>
</tr>
<tr>
<td>Skin lesions(^d)</td>
<td>Skin</td>
<td>17</td>
</tr>
<tr>
<td>Systemic antigenic stimulation</td>
<td>Most major organs</td>
<td>60</td>
</tr>
<tr>
<td>Testicular degeneration</td>
<td>Testes</td>
<td>19</td>
</tr>
<tr>
<td>Ulcerative keratitis</td>
<td>Eyes</td>
<td>13</td>
</tr>
</tbody>
</table>

Note: Retrospective review of clinical data, necropsy, and histology findings was tabulated. Results reported as percentage of mice with the disease (n=72; males=26, females=46). Age range 16–36 months.

\(^a\)Includes cardiomegaly, cardiomyopathy, arteriosclerosis, valvular lesions, and amyloidosis.

\(^b\)Diagnosed at cage level or at necropsy.

\(^c\)Out of total colony, \(n=711\).

\(^d\)Includes dermatitis and alopecia.
UW Study of Aged C57BL/6J Mice: Non-neoplastic Lesions

Pettan-Brewer, C., and P. M. Treuting; 2011. PMID: 22953032
Examples of Benign Degenerative and Inflammatory Lesions in Aged Mice (Not Exclusive to C57BL/6 Mice)

<table>
<thead>
<tr>
<th>Body System</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular</td>
<td>Cataracts</td>
</tr>
<tr>
<td></td>
<td>Corneal ulceration</td>
</tr>
<tr>
<td></td>
<td>Chronic keratitis</td>
</tr>
<tr>
<td></td>
<td>Harderian gland adenoma</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Cerebral mineralization, lipofuscin accumulation</td>
</tr>
<tr>
<td>Skin and subcutis</td>
<td>Alopecia</td>
</tr>
<tr>
<td></td>
<td>Mild dermatitis</td>
</tr>
<tr>
<td>Reproductive</td>
<td>Seminal vesicle, coagulating gland, and preputial gland dilation</td>
</tr>
<tr>
<td></td>
<td>Testicular degeneration/atrophy</td>
</tr>
<tr>
<td></td>
<td>Cystic endometrial hyperplasia</td>
</tr>
<tr>
<td></td>
<td>Uterine polyps</td>
</tr>
<tr>
<td></td>
<td>Ovarian atrophy</td>
</tr>
<tr>
<td></td>
<td>Ovarian cysts</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Thyroid cysts</td>
</tr>
<tr>
<td></td>
<td>Adrenal gland subcapsular spindle cell hyperplasia</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Hepatocyte karyomegaly and cytomegaly</td>
</tr>
<tr>
<td></td>
<td>Biliary hyperplasia</td>
</tr>
<tr>
<td></td>
<td>Hepatic cysts</td>
</tr>
<tr>
<td></td>
<td>Mild hyalinosis gall bladder epithelium</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Endo-/myo-/epicardial mineralization</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Mild hyalinosis respiratory epithelium</td>
</tr>
<tr>
<td></td>
<td>Mild alveolar macrophage accumulation</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Mild hyalinosis gastrointestinal epithelium</td>
</tr>
<tr>
<td></td>
<td>Mild rectal acute prolapse</td>
</tr>
</tbody>
</table>

Question 3

You have just started research with aged C57BL/6J mice. You receive your mice at 78 weeks of age, and a few months pass. You go to the vivarium and see the following animals in the colony. Which of them would you contact your veterinary staff about?

a) A  
b) B  
c) C

Photos from Pettan-Brewer and Treuting, 2011; PMID: 22953032
Question 4

Many more months pass and your aging study is still underway. You go to the vivarium and see the following animals in the colony. Which of them would you contact your veterinary staff about?

a) A
b) B
c) C

Images from Pettan-Brewer and Treuting, 2011; PMID: 2953032
Note: “A” is not C57BL/6 (different background); the condition occurs in multiple strains
Burkholder et al. 2012; Health Evaluation of Experimental Laboratory Mice; PMID: 22822473
Question 5

Another week or two passes. You go down to the vivarium on Friday night around 6pm to do your last cage checks. The veterinary staff have left for the weekend, but they have previously trained you to be one of two people in your lab responsible for cage checks and for making important decisions regarding end-of-life issues.

One mouse does not look well. What, specifically, will you examine to decide whether you need to stay and do a necropsy so you do not lose valuable data? (choose all that apply.)

a) Breathing rate  
b) Response to touch  
c) Body temperature to touch  
d) Posture  
e) Body condition score

Burkholder et al. 2012; PMID:22822473  
Ullman-Culleré and Foltz, 1999; PMID: 10403450
Summary Regarding Age-Related Health Conditions in Mice

- Investigators working with aged mice and veterinary/facility staff who support them should expect mice to develop multiple pathologies as a normal sequelae of aging.

- Advance plans and clear guidelines regarding end-of-life endpoints are critical.

- Experimental and control group sample sizes should be robust and include a buffer that will permit statistical significance even if several mice need to be taken off study.

- Phenotypes of aging can vary due to environmental factors.

Photo credit: P. Treuting, University of Washington
Learning Goals

- Correlate life phases of mice with humans
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Aged C57BL/6J mouse at 63 weeks
### Variables That Influence Phenotypes and Experimental Results in Aging Studies

<table>
<thead>
<tr>
<th>Experimental Condition or Variable</th>
<th>Affected Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet—additives: fenbendazole, vitamins</td>
<td>Tumors</td>
</tr>
<tr>
<td>Diet—additives: trimethoprim-sulfamethoxazole</td>
<td>Thyroid function</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Mammary tumors</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Immune responses, bone loss</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Alzheimer pathology</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Longevity, tumors, lesion burden</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Tumors, body weight, etc</td>
</tr>
<tr>
<td>Diet—fat/calories</td>
<td>Tumors, body weight, survival</td>
</tr>
<tr>
<td>Diet restriction</td>
<td>Body weights, organ weights, hematology</td>
</tr>
<tr>
<td>Diet type: purified AIN-76A vs natural ingredient diet (NIH-07)</td>
<td>Amyloid</td>
</tr>
<tr>
<td>Diet type: NIH-07, NTP-2000</td>
<td>Survival</td>
</tr>
<tr>
<td>Diet type: hardness, autoclaving</td>
<td>Cancer, drug metabolism</td>
</tr>
<tr>
<td>Enrichment</td>
<td>Urologic syndrome, survival</td>
</tr>
<tr>
<td>Enrichment</td>
<td>Body composition</td>
</tr>
<tr>
<td>Housing—cage type: suspended, shoebox</td>
<td>Cancer and/or chemotherapy response</td>
</tr>
<tr>
<td>Housing—bedding</td>
<td>Amyloidosis</td>
</tr>
<tr>
<td>Housing—bedding or cage type</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Housing—density/grouping</td>
<td>Tumors, proliferative lesions</td>
</tr>
<tr>
<td>Housing—density/grouping</td>
<td>Longevity, phenotypes, pathology</td>
</tr>
<tr>
<td>Housing—density/grouping and pathogen status</td>
<td>Tumor growth</td>
</tr>
<tr>
<td>Implant—ear tag</td>
<td>Immune function, tumor growth, toxicity</td>
</tr>
<tr>
<td>Implant—transponders</td>
<td></td>
</tr>
<tr>
<td>Infectious agents</td>
<td></td>
</tr>
<tr>
<td>Light cycle</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td></td>
</tr>
</tbody>
</table>

Brayton, Treuting, and Ward 2012; PMID: 22215684
Ideal Controls Are Matched with Respect to Age, Sex, and Environment

Mouse Phenome Database, [http://phenome.jax.org/](http://phenome.jax.org/)

Ideal controls:
Littermates and colony mates kept under same environmental conditions

Historical data from National Institute on Aging (NIA)
Colonies: C57BL/6NNia
- Males
- Females

NIA now distributes C57BL/6JNia / C57BL/6JN
(survival data not available)

Data from the Nathan Shock Aging Center at The Jackson Laboratory ([Yuan2 data set](http://phenome.jax.org/))
and adapted from historical [NIA Aged Colonies C57BL/6NNia Survival Data](http://phenome.jax.org/) (Turturro et al. 1999)
Better Reporting Will Lead to Better Reproducibility

“There needs to be increased awareness of these factors within the community but, as importantly, these parameters need to be captured and shared with publications. The ARRIVE guidelines cover all of the parameters identified here in detail and yet there is still a problem in persuading authors to provide this information and for journals to enforce their own policies. …

The bottom line, however, is that it is only with a firm commitment to disclosure and sharing by investigators, journals and funding agencies, and a recognition by the latter that, in many cases, ensuring reproducibility has a financial cost, that we will see better value for money from investment in model organism development and, in turn, a more robust translational pipeline.”


- Animal Research: Reporting of In Vivo Experiments (Download the ARRIVE Guidelines)
- Minimum Information for Publication of Experimental Pathology Data (Download the MINPEP Guidelines)
Question 6

Which of the following environmental factors can affect phenotype? (Select all that apply.)

a) Diet
b) Enrichment
c) Bedding
d) Density
e) Light cycle
f) Health status
g) Phase of the moon

Burkholder et al. 2012; PMID:22822473
Ullman-Cullerè and Foltz, 1999; PMID: 10403450
Images from http://www.bio-serv.com
Recommended Reading

- **Guide (White paper): Aged C57BL/6J Mice for Research Studies** – Reviews and elaborates on the content of this webinar


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  - Jun. 1, 2017, 2017, 1:00 pm (ET); 5:00 pm (GMT)

- CRISPR/Cas: Moving from Founder Mice to Phenotyping
  - Jun. 13, 2017, 9:00 am (ET); 1:00 PM (GMT); 3:00 pm (CEST)

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  - Jun. 22, 2017, 1:00 pm (ET); 5:00 pm (GMT)
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