

## **Guide to the use of rodents in aging research:**

If you are starting to think about the design of experiments using aged mice or rats, please consider the following aspects.

### Age selection, groups, group pooling, and strains

#### **1) Age selection**

Age selection is vital to differentiate aging effects from disease symptoms accurately. Combining data from different age groups can lead to erroneous interpretations. Use of various mouse or rat strains is recommended for broader applicability of findings.

- Using oldest (geriatrics) mice can yield results confounded by diseases, not just aging.
- Consider the specific mouse strain's median survival age for age group selection.
- Recognize that aging is a gradual process; changes occur well before median survival age.

#### **2) Using very young mice can be misleading due to maturational changes. Recommended young control age group is typically 4-6 months **Grouping and Age Range in Experiments****

- Avoid using only two age groups (young and old) to reduce costs, as this may miss progressive aging effects. Inclusion of a mid-age group is highly recommended, usually animals in the 12-18 months of age range
- Include spaced apart age groups with adequate intervals between young and old to capture aging manifestations.

#### **3) Diversifying strains**

- Inbred strains like C57BL/6 mice and F344 rats, often used in aging research, lack genetic diversity, limiting the generalizability of findings.
- These inbred mice often exhibit abnormal traits such as specific dominant pathologies and shorter lifespans.
- It's recommended to use a variety of strains, not just inbred ones, for more comprehensive aging research.

#### **4) Planning for Disease and Mortality in Old Mice:**

- Purchase about 30% more old mice than needed to compensate for potential disease and mortality. This ensures a sufficient number of healthy, old mice for reliable data at experiment completion.

### Specific pathogen free mice

- Specific pathogen free mice (SPF) mice are specifically free from common pathogens like Sendai virus and mouse hepatitis virus in mice, and sialodacryoadenitis virus in rats. Despite being SPF, they may not be free from all infections.
- It's essential to verify SPF status, even for mice sourced from SPF colonies. Regular in-house testing in animal facilities is crucial to maintain SPF status.

#### Quick autopsy or gross necropsy on each old mouse

- Perform a quick autopsy on each older mouse or rat to check for health issues. Examine major organs for enlargement or lesions and body for infected scars.
- Discard data from mice with significant lesions or infections to ensure accurate results.

#### Cost-adjusted power analysis

- Statisticians should perform power analysis aiming for maximum, rather than minimal, statistical power.
- Factor in the higher cost of older mice; conduct power analysis for the most statistical power per dollar.
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#### Inferring causal associations from correlated age effects

- Observing simultaneous declines in traits A and B in old mice may indicate correlation due to aging rather than a direct causative link between the traits.
- This principle of distinguishing correlation from causation also applies to human aging studies.

For more information refer to the following resources:

<https://academic.oup.com/biomedgerontology/article/55/3/B117/2947964>

<https://www.afar.org/guidelines-for-populations>