RARC
Research Animal Resources and Compliance
UNIVERSITY OF WISCONSIN-MADISON

JUNE 2020

NEWSLETTER

FOCUS ON THE RESEARCH MOUSE

A Word from Dr. Janet Welter, Chief Campus Veterinarian

We at RARC are committed to providing consistent and professional care and advice. As researchers begin returning to campus, we will continually assess the environment to see how we can best support labs during Research Reboot. Please let us know specific ways we can assist you, too.

We look forward to the return of a robust research environment. Until then we are adapting by focusing on what we can more readily achieve, which includes educating – ourselves and others. In this issue of our newsletter, with a focus on the research mouse, we review some basics and survey what is new and hope it provides you with a useful combination of fundamental and food-for-thought education.

I like to remind investigators to take a holistic view of the mouse. It's easy to zero in on the goals of research and forget to consider *Mus musculus* as an entire system with unique needs and behaviors that play a role in your research outcomes.

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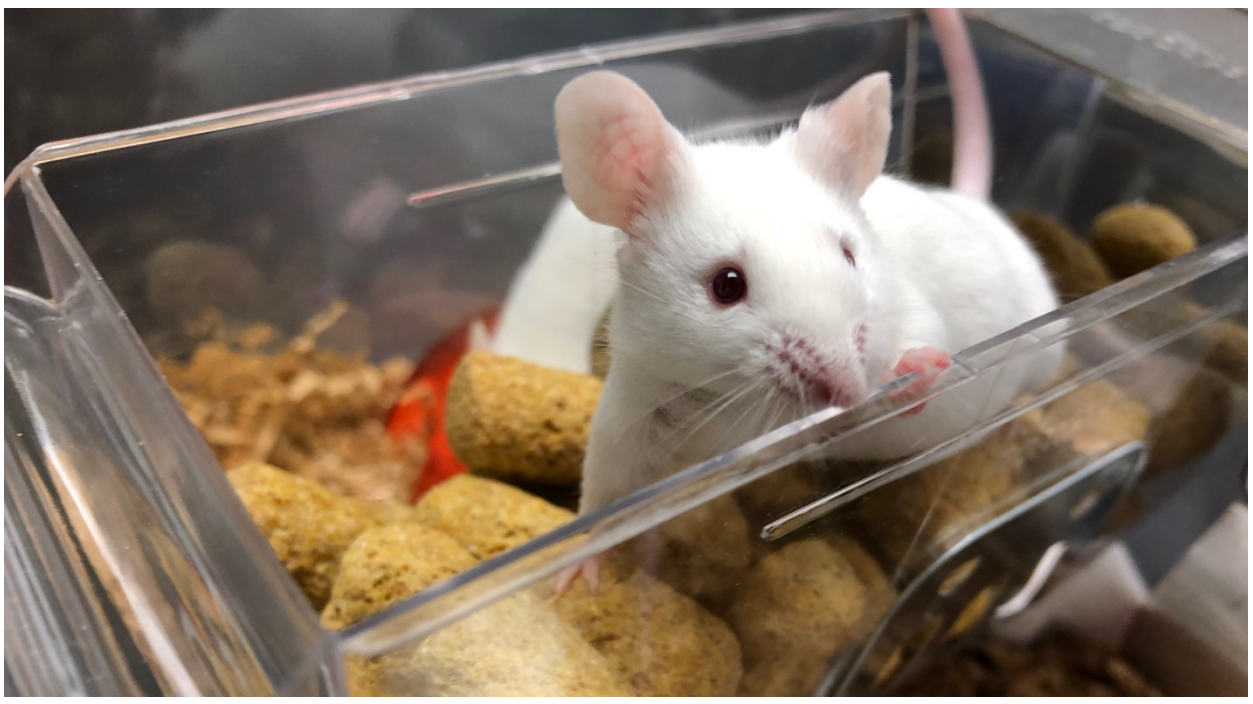
Janet Welter



"I like to remind investigators to take a holistic view of the mouse. It's easy to zero in on the goals of the research and forget that you are working with an entire system." - Dr. Janet Welter

In this issue

Veterinarian Becky Franklin talks about a new potential tool for assessing mouse health: nest building. We are all familiar with monitoring eating, drinking, grimace scoring, weight, grooming, posture, and vocalizations, but using these health assessments can sometimes be tricky and disruptive. Nest building evaluation offers another complementary option.

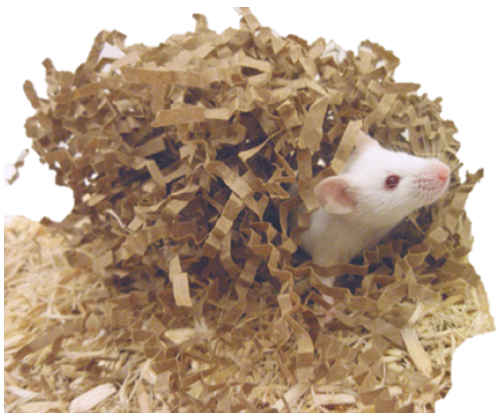
I look at the recently updated AVMA standard for CO_2 euthanasia. The new guidance recommends an increase in flow rate, which could potentially require some flow regulator replacements.

Our six trainers are always available with over-the-phone answers to your mouse handling, behavior, and technique questions. But they also provide hands-on training for many different techniques, too. In this issue, they share some ideas for accessing the brain and collecting epithelial cells.

Get some guidance with the specific nomenclature that many journals require and see if a mouse model might already be available for your research through the resources we list at the end of this newsletter. We also remind you of GEAM, a valuable resource here on campus for saving your scarce and precious mice lines.

NEST BUILDING AS A HEALTH INDICATOR

A Potential New Tool for Assessment



DR. BECKY FRANKLIN

Recent research suggests that evaluating the shreds and shape of a mouse nest can be a useful health assessment tool. Declines in material usage and building activity may reflect a decline in wellbeing.

One study looked at mice nest complexity after surgery, scoring on a scale from zero to five, depending on the shredding of material and the height and shape of the nest. Post-surgical mice nests showed a decrease in material usage and size compared to the nests of mice that had not undergone surgery. A second study added a small amount of measured nesting material to the cage and scored the amount used after 10 minutes.

This observational method isn't without limitations -- pain medications, for one, can impact building skills. One common pain medication, buprenorphine, is known to affect other behaviors, and may have a negative effect on the ability to build a nest.

Becky Franklin

If you set up a nest scoring system, design something quick and easy to use. Calibrate to mouse strain, study objectives, and timing to avoid conflicting or unusable results. Standardize how the test is given and assessed and make sure to test it with different people; they should all arrive at the same score for an animal. Evaluators should know their animal's building abilities before testing as comparison.

To assess materials usage, consider providing nesting material of a different color or type, to make it easier to assess whether or not the new material has been used.

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NEWSLETTER

TRAINERS' TIPS

Brain Access Through Stereotaxic Surgery

DR. SARAH NEWMAN

Gaining access to the brain for study or treatment purposes is challenging. The blood-brain barrier, intended to protect the brain from toxic substances, makes targeted drug delivery difficult. Neurotransmitter manipulations to affect behavior are difficult, if not impossible, without direct delivery to targets within the brain.

You can circumvent these hurdles and deliver manipulations directly into the brain to very specific sites or cell populations through a collective set of procedures called stereotaxic surgery. Stereotaxic procedures vary, depending on the goal: you can inject substances into the brain, implant electrodes to record neural activity, or intentionally modify a certain region to study the effects and possible treatments.

All stereotaxic procedures require an apparatus called a stereotaxic frame, special instruments, and a brain atlas, a map of all the different brain regions for a given species. Using landmarks on the surface of the skull, a surgeon can very specifically measure and target a particular site in the brain for study.

Stereotaxic surgery requires highly qualified training and practice. Contact RARC trainers to schedule stereotaxic surgery education.

Work with an RARC trainer

Get answers to handling and technique questions,
one-on-one instruction, and support tailored to your unique needs.
trainer@rarc.wisc.edu *608-890-0969*

Vaginal Cytology

LUKE BRINKMAN

You can determine a mouse's estrous stage by examining the epithelial cells of its vaginal wall. Follow these steps to collect the cells with minimal stress to the mouse:

First, restrain the mouse along the top of its cage by pulling the base of the tail up into the air. The mouse will grab onto the cage top with its front limbs. You can also place the mouse into a conical tube for added control.

When the hind end is elevated, insert the tip of a pipette containing ~100ul of sterile, double-distilled water into the vaginal opening.

Gently squeeze the pipette to eject a bead of solution into the vaginal canal.

Release the pipette to aspirate the solution back into the pipette.

Repeat these steps four to five times to collect an adequate sampling.

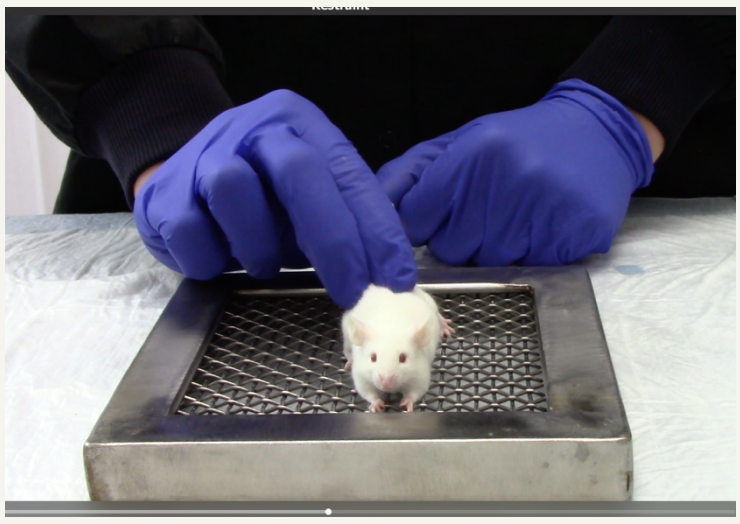
Dispense the solution onto a slide and allow to air dry. Stain the slide using a crystal violet solution and view under a microscope.

Proper Restraint for More Reliability

JENN CARSON

A good restraint, where the mouse's head is entirely immobilized, prevents almost all movement, improving the reliability of experimental results.

An RARC trainer can assess your restraining techniques and give you tips for working with confidence. You can also refresh your skills by watching our restraint technique video at rarc.wisc.edu/training/course/mouse



NEW AVMA GUIDANCE ON CO_2 EUTHANASIA

Flow Rate Is Changed

DR. JANET WELTER

UW-Madison follows the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. In the new 2020 edition, guidance for the use of CO_2 gas as a euthanizing agent for mice and rats changed significantly.

The new guidance specifies a flow rate into a non-precharged chamber at a flow rate displacing 30 to 70% chamber volume/minute (instead of the previous flow rate of 10 to 30%).

New guidance specifies a flow rate into a non-precharged chamber at a flow rate displacing 30 to 70% chamber volume/minute.

Because the new flow rate could be over twice what we previously used, we may need to replace some flow regulators to accommodate the change. RARC staff is checking CO_2 stations in common areas to identify regulators needing replacement. Please contact us if you would like the regulator in your lab checked.

To review the new guidelines, visit www.avma.org/sites/default/files/2020-02/Guidelines-on-Euthanasia-2020.pdf Talk to your research animal veterinarian if you have any questions.

REPORTING BITES AND SCRATCHES

Environment, Health & Safety's Web Page Offers Guidelines and Process

Proper mouse handling can minimize bites and scratches. Review techniques for restraint, blood collection, injections, and ear tagging/notching at rarc.wisc.edu/training/course/mouse to ensure that you are taking the right steps to reduce incidents.

Even with the best precautions, you might be bitten or scratched while working with a mouse. EH&S outlines what you should do when that happens.

Read their guidance at ehs.wisc.edu/animal-bite-or- scratch/

RESOURCES

Saving Mice Lines, Accessing Models and Nomenclature

GEAM

Get local expertise in genome editing design, cryopreservation of mouse embryos and sperm, and the generation of new mouse (and other species) models through the Genome Editing and Animal Models Shared Resource (GEAM). GEAM uses the personnel, facilities and equipment of the campus-wide University of Wisconsin Biotechnology Center to provide services.

Model and Nomenclature Databases

Find an existing model for your research and look up accurate genetic or mouse model nomenclature to meet journal standards through these databases.

Mouse Genome Informatics (MGI) at The Jackson Laboratory
informatics.jax.org/
Maintains a database of mutant, transgenic and other variant mice which have been published. MGI links to the International Mouse Strain Resource (IMSR), a database of mutants in public repositories as mice, gametes, embryos or ES cells.

International Gene Trap Consortium and the Texas Institute for Genomic Medicine
igtc.org and tigm.org
A public library of mutated murine ES cell lines.

International Mouse Phenotyping Consortium
https://www.mousephenotype.org/
International effort by 19 research institutions to identify the function of every protein-coding gene in the mouse genome.

MGI's Phenotypes and Mutants Community Resources
www.informatics.jax.org/mgihome/other/phenoallele_commun_resource.shtml
Provides links to consortia working from the phenotypes of variants and induced mutants back to the mutated gene.