UCSF IACUC Full Committee Meeting Minutes

Committee Name: IACUC Full Committee

Committee Type: IACUC

Meeting Date: 06/04/2019

Chair's Report: Voting Members: [redacted]

Office Staff: [redacted].

• IACUC Chair's Report

[redacted] (LC)

A. Minutes
a. 4/30/2019 Policy Minutes (Handout)- Minutes from 4/30 Policy Meeting were approved
b. 5/7/2019 Full Committee Minutes (Handout)- Minutes from 5/7 Full committee were approved

Director's Report: • IACUC Director's Report

A. Director's Report (Handout)

Job postings:
The position of IACUC Director is now posted and search committee named. [redacted] day at UCSF is June 27.
[redacted] left LARC and is now at [redacted] be leaving.
LARC has posted a position for a Veterinarian level II.
Hunters Point is working to hire a second veterinarian for their program (along with a total of four vet techs).

IACUC Chair: [redacted] is the June 4 meeting

Tropical Rat Mites: LARC will be presenting an update on the Tropical Rat Mite situation that started with Parnassus rodents (non USDA). Pending some additional information, we will follow up on our initial informal report to NIH-OLAW.

Surgery training and oversight:
Program Review as well as the 5/7/19 IACUC meetings discussed surgery outcomes. The 5/7/19 Committee requested a report on surgical complication rates and info on the training resources that would be necessary to have hands-on surgery/anesthesia training for all researchers (we'll need to fine-tune that request --- everyone go through the very basic IACUC/LARC training courses AND in-lab training with a certified trainer for the specific procedures?) [redacted] presented on this at the 5/21 meeting, and will do so at the June 4 meeting as well.

A Program Review Subcommittee met on May 3 and will provide a summary for IACUC member review and signature at the 5/21 and June 4 meetings.

June inspections are coming! But relax, we do not need members to sign up for anything. These are semi-formal inspections that the IACUC staff, as a single annual inspection of low-risk spaces (mostly, in-lab terminal perfusions) and a 3rd inspection to supplement our two official semi-annual IACUC inspections of higher-risk sites (USDA species; Lab housing; Chambers; in-lab Survival Surgery). Hunters Point is no longer on the high-risk list.

NOTES from some recent meetings:

From the May 21, 2019 meeting:

Brief LARC update that some rodent rooms at Parnassus are still under quarantine for Ornithonyssus Tropical Rat Mites

Explained why [redacted] (macaque, mouse, rat) was coming to the Committee after it was reviewed by FCR on April 16 and May 21. The April 16 review granted a one-month approval on May 10, to expire on June 10. The Committee reviewed the Continuation protocol (submitted on May 20) on May 21. The Committee did not find the submitted article on multimodal analgesia in human patients on patient-controlled morphine a compelling case against multimodal analgesia for nonhuman primates on buprenorphine.

June 4, 2019 Subcommittee:

Reviewed [redacted] pilot report on animals with Wernicke's disease, housed in various oxygen (hypoxia to hyperoxia) environments. Hypoxia seems to improve some conditions, but setting endpoints for the model is challenging.

Informed Committee that the June 4 DMR Subcommittee had reviewed a progress report on a PI's work developing a mouse model of Wernicke's disease. The initial report found insufficient MRI or histopathological change when mice go to 30% weight loss, but did not collect sufficient data at 40% weight loss to justify that endpoint for further expanded studies. PI will be allowed to conduct another smaller pilot study to assess whether animals at 40% weight loss show the lesions, and to explain better why it is necessary to see lesions when time-to-illness is already established.

Attending Veterinarian (AV) Report:

• AV Report/LARC Clinical Case Report

A. Tropical Rat Mites Report and Update (Handout)

LARC Director/AV updated the Committee on infestation of tropical rat mites in the mouse/rat rooms at PSB. [redacted] will coordinate fact-finding on the extent of the effects (if any) on NIH-funded reports, the causes of any problems, and IACUC/LARC improvements to minimize future such situations. NIH-OLAW received an initial phone call, and will expect a written follow-up if investigators report significant disruption to funded projects.

IACUC Member Training and Information:

• Committee Information and Training

A. [redacted], Presentation – Surgery Training Updates- Deferred to next Parnassus meeting

B. [redacted] – Cephalopods & Animal Welfare considerations- Deferred to next meeting

C. Upcoming CE opportunities:

• June 20, 2019: PRIM&R Webinar Advanced Noncompliance Scenarios https://www.primr.org/calendar/webinars/2019/noncompliance-scenarios/

• August 23, 2019: NCB AALAS Educational Symposium

• 2019 SCAW IACUC Training Workshop: https://scaw.com/iacuc-training-workshops/

o September 27, 2019: New York City, NY

o November 22, 2019: Chicago, IL

• 2019 IACUC 101 Series: https://iacuc101.org/courses/iacuc-101/

o June 26 - 27, 2019: IACUC 101 and 301 in Providence, RI - Hosted by Brown University

o August 21 - 22, 2019: IACUC 101 and 201 in Minneapolis, MN - Hosted by Medtronics

o November 6, 7, 8, 2019: IACUC 101, 201 and 301 in Houston, TX - Hosted by Rice University

Other Business: • Other Business

A. Standard Procedures for DMR June 2019 List (Handout)- Deferred to next meeting

Committee continued discussion of [redacted], reviewing UCSF veterinarians' correspondence with veterinarians at other universities, including two primate centers, finding that multimodal analgesia is a widespread standard of care for laboratory primates undergoing similar surgeries. Committee weighed concerns about hemostasis for surgeries that penetrate the dura and those that do not. Committee voted for DMR-following-FCR if the vice-chair ([redacted] reviews that the PI has complied with all the requested revisions, and FCR if not. Committee's letter (details below) will include instructions on required animal care (and no allowed data collection) if the protocol expires. Vote: 11 in favor, 1 abstention.

Semi-annual Program Review : Members received the documents in advance of the meeting and signed the letter to the IO. Committee leadership plus the AV will present the semi-annual program review to the IO in June.

Deferred agenda items: Committee CE on cephalopods in laboratories. Review of the surgery training and oversight program (requested update from the Program Evaluation in May, and presented once already at the May 21 meeting).

Protocols Reviewed

During the review process, the members discussed for each protocol, the rationale for involving animals, the appropriateness of the species, the database searches for alternatives, the steps taken to reduce animal numbers, the measures to relieve pain, discomfort or distress, if needed, the appropriateness and adequacy of anesthesia and analgesia, if applicable, and the number of animals to be used.

USDA Covered Species

Project Number: [redacted]

Approval Type: Annual Review

Title: Structural Basis of Amblyopia and Strabismus

PI: [redacted]

Species: Macaque Monkey, Mouse, Rat

Primary Reviewer:

Secondary Reviewer:

Results: **Revisions Requested**

Revisions Requested: Section E.2.2. Explain why the proposed species are the most appropriate
Please provide more detail on why mice versus rats would be used for particular pilot procedures. Explain the criteria you consider in deciding whether to acquire mice or rats for a given experiment.

Section I. Analgesic Agents
For the rodents:
o IACUC recommends using SR-buprenorphine rather than twice daily Buprenorphine HCl. It is acceptable to have both formulations in your protocol for flexibility. The UCSF dose of SR Buprenorphine is typically 1.5 mg/kg for mice.
o Add Meloxicam as an analgesic for mice and rats for all survival surgical procedures.
o Additionally, lidocaine/bupivacaine is indicated for these surgeries as well and should be put back into the protocol.

For NHPs:
o For surgeries that do not penetrate the dura, under “Frequency & Total Duration” administer one dose of meloxicam at time of surgery,1-2x on the day after surgery, and after that, 1-2x/day as needed
o For surgeries that penetrate the dura, add acetaminophen suppository back into the analgesic agents for NHP, once at the time of the Procedure. For those surgeries either continue acetaminophen 3x/day for 1 day on the day after surgery, then as needed OR start meloxicam treatment on the day after surgery

Section J. Management and Monitoring of Adverse Effects of Procedures and Experimental Agents

Macaque:
Subsection J.2:
• -You should remove the statement: “Please note: We will document monitoring of animals after surgery…,” You may change “Yes” to “…”Monitoring notes will cover clinically important information,” if you prefer.

Mice and rats:
Subsection J.3:
-
On your behalf, IACUC has added dehiscence repair as a Standard Procedure for mice and rats in Section F.

Documents

1. Please upload to the “Attachments” listing in RIO (“Documents” section), the version of campus “Guidelines for Food Regulation” and campus “Guidelines for Water Regulation” that you use. The protocol is not complete without these documents

2. By June 15 2019, it will be necessary for you to work with LARC’s primate veterinarians to develop and upload an SOP for all hand-cleaned animal-related items used for your projects, including restraint chairs and slurry-delivery systems. This will assure your regimen addresses the USDA’s concerns from the March inspection.

The SOP will need to set frequencies and methods of sanitization of hand-washed food and restraint equipment, frequencies of sanitization method verification (e.g., annual ATPase validation of your methods), and methods of fully cleaning equipment (e.g., removing all slurry residue after each use) in the days or weeks between sanitization procedures. Veterinarians will work with you to set documentation expectations. The USDA plans to inspect your laboratory and review your procedures in her fall 2019 inspection.

Project Number: [redacted]

Approval Type: Continuation

Title: Ultrasound-Enhanced Transscleral Drug Delivery for Eye Disease

PI: [redacted]

Species: Rabbit

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Progress Report

State the total number of animals you used during the past 3 year cycle.

Section C. Animals
General:
• Provide a table that displays each portion of the study (e.g. ultrasound, diabetes, thiamine, vitrectomy w/glue), includes a brief but complete description of that portion/procedure and the number of rabbits.
• Additionally, provide a diagram/timeline illustrating what intervention(s) each rabbit in the study will receive (i.e.. will each rabbit go through all portions of the study or will rabbits undergo 1 or more portions?), as it is currently unclear. It can also be displayed as a timeline as long as the critical information is included.
• Ensure that the numbers displayed in the C.1 table match the numbers described in C.2.
Specific:
• For ultrasound/normal rabbit portion of the study: clarify what is meant by “normal” or remove the word altogether. Additionally, include the complete calculation you used to arrive at 18 rabbits for this portion of the study.
o Regarding the sentence that begins, “All rabbits will be treated the same, with each rabbit having one non-ultrasound-treated eye…” – if this can be stated for all portions of the study, please move to the beginning of C.2.
• For the diabetic rabbit model:
o Include a brief calculation to accompany the sentence that reads, “a total of 48 rabbits are needed for this portion of the study.” The committee must understand how and why there are 48 animals for this part.
o The sentence that begins, “Then 18 rabbits will be used for the ultrasound treatment portion,” is unclear. If it does not pertain to the diabetic rabbit model, then either move it up to #1 (“ultrasound/normal rabbit portion”).
• For the thiamine portion:
o Please number it as “3”.
o Include a calculation at the end of the paragraph that shows how you have arrive at the total number of rabbits used for this portion of the study.
• For the vitrectomy with glue portion: if the rabbits that are going to be used for this pilot work will not be utilized for any other portion of the study, please explicitly state so.
Section D. Contacts and personnel
The 2 individuals listed on the protocol who are not Dr. Stewart will need to revise their descriptions about training and experience, as it is unclear whether they have the appropriate experience and qualifications to administer anesthesia and perform surgical procedures.
Section G. Procedures Involving Living Animals
Indicate whether you plan to continue with the alloxan model of diabetes induction.

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: Continuation

Title: Investigating axon-glial interactions that control myelination during development

PI: [redacted]

Species: Mouse, Rat

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Progress Report

Replace list of publications with a few sentences summarizing your progress over the past 3 years.

Section G. Procedures Involving Living Animals
Category D animals: Clarify why you propose to administer clemastine by oral gavage.
Section J. Management and Monitoring of Adverse Effects of Procedures and Experimental Agents
• Category C: Re-categorize Shiverer mice from Category (Cat) C to Cat E if you plan to maintain homozygotes for breeding, and provide scientific justification for maintaining these animals to adulthood.
• Provide justification for waiting an hour before euthanizing Shiverer mice who are seizing. For instance: what type of data (if any) might you expect to obtain by observing these animals for an hour as opposed to euthanizing at first sign of seizure?
Section I. Pre-Anesthetics and Anesthetics, Neuromuscular Blocking Drugs, Therapeutics, Analgesics and Experimental AGents
Clarify justification for the use of Avertin for terminal use and confirm that you will follow UCSF IACUC guidelines.

Project Number: [redacted]

Approval Type: Continuation

Title: Early Hypoxia-Ischemia & Activity Dependent Brain Development.

PI: [redacted]

Species: Mouse, Rat

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Progress report

You indicate that you are no longer performing the whisker lesion and monocular deprivation procedures. IACUC staff has removed all mentions of these procedures on your behalf. Please ensure that what we have removed is correct and that the animal numbers are still accurate as a result.

Section D. Personnel and Contacts

We have deleted [redacted] from the protocol as his email address is no longer valid.

Section G. Procedures Involving Living Animals
• Category D: Please create a flow chart or table listing the number of animals (for each species) that will undergo the various procedures/combinations of procedures. This can be incorporated as a supplemental file that you can upload and include in the “Documents” section of RIO.

• Category D mice: “Agents administered through chow” and small paragraph following this phrase: Please clarify and re-write so that the reader understands: (1) exactly which agents (e.g. PLX5622 and/or additional agents?) will be administered through chow; and (2) whether hypoxia ischemia + analyses will be part of *all* listed procedures that follow?

Project Number: [redacted]

Approval Type: New Approval

Title: Characterizing the Innate Immune Response of Mycobacterium Tuberculosis with Single-Cell Resolution

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Section C. Animals

• There seems to be a mathematical discrepancy between the total number of Category D. acquired in the summary able (289) and in the table at the bottom of your narrative (297).
• In the table at the bottom of the narrative, please indicate which animals are bred vs acquired to help reviewers understand how your totals were calculated,
• Please provide a detailed statistical justification explaining your group sizes.
• You explain that females will not be used in experiments, as there are considerable gender differences in the immune response to MTB infection. However, the paper referenced does indeed include both genders (p.1) and clearly describes why both should be used. Therefore, the Committee strongly recommends using males and females and accounting for this variable in your statistical analysis.

Section G. Procedures

• Category Dr. mice infected with MTB: You state that the inhalation exposure device can accommodate up to 20 mice per compartment. However, in the attached biosafety manual, the device description states that no more than 10 mice per basket can be kept. Please reconcile both statements.

Section J. Adverse Effects

• Please separate the adverse effects listed (all pertaining to MTB exposure) into separate row/entries.

UCSF IACUC Subcommittee Meeting Minutes

Committee Name: IACUC SubCommittee/DMR

Committee Type: IACUC

Meeting Date: 06/04/2019

Members Present: IACUC Chair (or Vice Chair): [redacted]

LARC Attending Veterinarian or Designee: [redacted]

IACUC Committee Member as Specified: [redacted]

Chair's Report: Subcommittee: [redacted] (via Zoom Conference Call)

1. Subcommittee Minutes

- 5/7/2019 Subcommittee Minutes (Handout)- Minutes from 5/7 Sub committee were approved

Training and Compliance Report:

2. Training & Compliance Report

- [redacted] Pilot Data Summary (Handout)- Reviewed [redacted] [redacted] pilot report on animals with Wernicke's disease, housed in various oxygen (hypoxia to hyperoxia) environments. Hypoxia seems to improve some conditions, but setting endpoints for the model is challenging.

Protocols Reviewed

The following protocols will be reviewed by Designated Member Review process in accordance with the PHS Policy Section IV.B.3.

USDA Covered Species

Project Number: AN176202-02

Approval Type: Annual Review

Title: Holding Protocol for Animals Assigned to Inactive Protocols or Special Circumstances

PI: [redacted]

Species: Bird, Cat, Dog, Ferret, Fish, Frog, Gerbil, Guinea Pig, Hamster, Macaque Monkey, Mouse, Rabbit, Rat, Salamander, Sheep, Squirrel Monkey, Swine, Vole, Zebrafish

Results: **Revisions Requested**

Revisions Requested: Please provide, in the progress report, how many of each USDA-covered species were used over the past year.

Non-USDA Covered Species

Project Number: [redacted]
Approval Type: Modification
Title: Modeling Pediatric Cancer
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Activation of endogenous stem cells and the myogenic effects of LESW and CRISPRi for improvement of Obesity-Associated Stress Urinary Incontinence in the Zucker rat model.
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Effect of Inhibition of Hepatic Uptake Transporters (OATPs) on Drug Disposition and Metabolism
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: CVRI Zebrafish Facility - Zebrafish husbandry, training, and project development support.
PI: [redacted]
Species: Zebrafish
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Gene therapy for Connexin-26 dysfunction in transgenic mice
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Plasticity and Behavioral Coding in the Rodent Brain

PI: [redacted]

Species: Rat

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Post-transcriptional regulatory pathways that drive cancer metastasis

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: -The Committee suggests scheduling a technical consultation with this company that may formulate these compounds directly in the feed. Please look at the link below for more information:
https://www.researchdiets.com/

-If gavage is necessary, please specify the vehicle used (in Section I.)

-No changes were done to your total of animal numbers. Could you clarify whether new mice will be used? How many will be treated with the new compounds?
Please make changes to Section C. if needed.

Project Number: [redacted]

Approval Type: Modification

Title: In Vivo Evaluation of Experimental Anti-Cancer Therapeutics; UCSF Preclinical Therapeutics Core

PI: [redacted]

Species: Mouse, Rat

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Circuit and functional organization of the rodent auditory system

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Transcriptional control of adipocyte development and energy metabolism

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: In Section C., please provide additional information on your group size calculation and include effect size/variance.

Project Number: [redacted]

Approval Type: Annual Review

Title: The Function of Immune Surveillance in Peripheral Organs and Tissues: Anti-tumor mechanisms of intratumoral stimulatory dendritic cells ; IL-13 and IL-17 dynamics in the asthmatic airway; Manipulating Collectivity and Niches for Developing CD8 Immunity; Mechanisms of peripheral self-tolerance contribute to immune tolerance to cancer; Interrogation of immune responses to fibrolamellar hepatocellular carcinoma; Reinvigorating anti-tumor immunity by reversing macrophage-induced T cell dysfunction; Integrating targeted and immunotherapy to treat genetically heterogeneous cancers; Living Tumor Biopsies to Interrogate Immune Function and Response to Therapy

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Epigenetic regulation of brain tumors

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: The in vivo roles of a ciliogenesis-regulating kinases ICK (Intestinal Cell Kinase) during the embryonic development of the small intestine

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Gladstone Behavioral Assessment Unit

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Genetic Approaches To Understanding Ocular Diseases

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: Add local block (in Section I.) to the anesthetics/analgesics regimen for your mice undergoing the “head mounted goggle” procedure.

Post-Approval Requirements: Please schedule a procedure observation of the first cohort of mice undergoing the new procedure "head mounted goggle surgery". Pleas email [redacted]

Project Number: [redacted]

Approval Type: Annual Review

Title: Brain tumor development and the critical role of the tumor microenvironment

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Mouse models of CNS development and neurological disease

PI: [redacted]

Species: Mouse

Results: **Approved**

UCSF IACUC Full Committee Meeting Minutes

Committee Name: IACUC Full Committee

Committee Type: IACUC

Meeting Date: 06/18/2019

Chair's Report: Voting Members: [redacted]

Office Staff: [redacted]

Guests: [redacted]

• IACUC Chair's Report

A. Minutes
a. 5/21/2019 Full Committee Minutes (Handout)- Minutes from 5/21 Full committee were approved

Director's Report: • IACUC Director's Report

• IACUC Director informed Committee that [redacted] will be interim director for the IACUP office when [redacted] (June 27)

• Informational: Tropical Rat Mites: [redacted] is heading up some work with LARC to identify impacts of Tropical Rat Mites on mouse and rat research projects. Pending some additional information, we will follow up on our initial informal report to NIH-OLAW.

• Informational: Subcommittee met with mouse PI [redacted] to review her pilot findings for her Wernicke Disease model. Agreed that another pilot, with 90 animals, would be appropriate to further refine the model before proceeding to more expansive studies.

• Informational: Director updated the Committee on [redacted] primate protocol. Protocol was reviewed in Full Committee in April and twice in May. A one-month approval granted in May has expired as of June 10. The PI has not resubmitted. The animals are on LARC's Holding Protocol with LARC veterinarians directing their care, and the PIs staff are required to provide specialized implant maintenance. NIH-OLAW has been informed (no non-compliances, so just a courtesy note to OLAW), as have been the PI's department. The UCSF Office of Sponsored Research, the IO, and the funding agency.

Committee member asked how USDA will review this. Director opined that the USDA expects the IACUC to make its own decisions and respects that, but will also look if the IACUC changes its standards on whether that change is based on established veterinary practice and/or science.

Attending Veterinarian (AV) Report: • AV Report/LARC Clinical Case Report

A. Tropical Rat Mites Report and Update

[redacted] updated Committee on tropical rat mite outbreak centered in PSB facility.

• Initial source - most likely wild rodents in interstitial building space
• Contributing causes – lack of coordination among 3 pest control companies (1 for inside building, 1 for outside building, 1 for animal facility), rainy weather, nearby construction
• Control measures – doubled number of rodent bait stations and added more effective bait, cleaned and rodent-proofed interstitial spaces in PSB, rooms quarantined when mites are detected
• Treatment – permethrin nestlets placed in cages in quarantine rooms in PSB, Animal

Towers; Rock Hall treatment is complete (1 room)
• Challenges – Backorder of commercial permethrin nestlets so LARC staff are making them; currently insufficient supply to treat all of PSB at once
• Surveillance - All rooms in PSB have now been tested by PCR; Genentech Hall, SFGH, Neurosciences also screened
• Zoonotic potential – LARC sent some mites to be tested for human pathogens; all negative
• Cost estimate for university – unknown

IACUC Member Training and Information:

• Committee Information and Training

A. [redacted], Presentation – Cephalopods & Animal Welfare considerations- deferred to later meeting due to time constraints

B. Upcoming CE opportunities:

• June 20, 2019: PRIM&R Webinar Advanced Noncompliance Scenarios https://www.primr.org/calendar/webinars/2019/noncompliance-scenarios/

• July 16, 2019: AALAS Webinar Abnormal Repetitive Behaviours: Animal Welfare Significance https://www.aalas.org/store/meeting?productId=9407786

• August 23, 2019: NCB AALAS Educational Symposium

• 2019 SCAW IACUC Training Workshop: https://scaw.com/iacuc-training-workshops/

o September 27, 2019: New York City, NY
o November 22, 2019: Chicago, IL

• 2019 IACUC 101 Series: https://iacuc101.org/courses/iacuc-101/

o June 26 - 27, 2019: IACUC 101 and 301 in Providence, RI - Hosted by Brown University

o August 21 - 22, 2019: IACUC 101 and 201 in Minneapolis, MN - Hosted by Medtronics

o November 6, 7, 8, 2019: IACUC 101, 201 and 301 in Houston, TX - Hosted by Rice University

Other Business:

• Other Business

A. Standard Procedures for DMR June 2019 List (Handout)- A. Informational - Members received list of standard procedures due for renewal this month; will be sent out for DMR

Protocols Reviewed

During the review process, the members discussed for each protocol, the rationale for involving animals, the appropriateness of the species, the database searches for alternatives, the steps taken to reduce animal numbers, the measures to relieve pain, discomfort or distress, if needed, the appropriateness and adequacy of anesthesia and analgesia, if applicable, and the number of animals to be used.

USDA Covered Species

Project Number: [redacted]

Approval Type: Continuation

Title: Understanding social attachment in development and disease; EDGE: Transforming the social

brain in Microtus

PI: [redacted]

Species: Vole

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: -In Section G., Category D. Voles, Acoustic Startle Testing:
-Clarify how often the very loud sounds are delivered and what the total duration of exposure at 130 db would be.

-In Section I., please add DREADDs and Clozapine to your list of Experimental Agents (if still planning on using them).

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: Continuation

Title: Modulation of innate immune responses in abdominal sepsis

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer:

Results: **Revisions Requested**

Revisions Requested: Section I:
Add the following agent(s) in the “experimental agents” listing:
• Fluorescent vascular dye (e.g. AngioSense or AngioSPARK, Perkins Elmer)

Project Number: [redacted]

Approval Type: Continuation

Title: Mehanisms and functions of integrin-mediated TGF-b activation.

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Progress Report
Answer both questions pertaining to the Progress Report and the Unexpected Adverse Events sections.
Section C. Animals

General:
• You mention an “attached spreadsheet,” which we do not see. Please upload to RIO as an attachment.
• For each experiment listed in this section, include animal number subtotals.
• Clarify how transgenic reporter strains fit in with experiments described.
• We require that you provide the approximate number of strains that you are planning to use as this affects your animal numbers. Also, please indicate whether any of these strains have spontaneous phenotypes of concern.

Specific:
• Experiment 12 (A & B): you refer to “section xyz”. Please update with the correct section.
• Please move the second-to-last paragraph (the one that begins: “For the above experiments…”), to the beginning of the section for a proper introduction.
• The final paragraph does not belong in Section C. Please move it to a more appropriate section, such as the Objectives or Procedures (Section G).

Section E. Justifications and Alternatives

Update all literature searches (search dates and years covered)

Section G. Procedures Involving Living Animals

General: You will need to provide additional details so that the committee clearly understands each proposed procedure & to ensure that this section is consistent with Section C.

Specific:
• Exp 1: provide the names of the knockout strains described in Section C.
• Exp 2: specify the strain of transgenic mice used (ITGB8 BAC Tg mice)
• Exp 3: IACUC staff removed unclear sentence on your behalf: “Optimized tobacco exposure measure system, no longer need to measure to determine the effective level of tobacco smoke exposure.”
• Exp 4: for genetic cell-type specific deletion models: discrepancy between description of tamoxifen dosing here and Section 1.5. Reconcile accordingly.
• Exp 8: Active induction of EAE:
o Some additional description about the induction (agents used, timing of injection) must be provided.
o Details about what will subsequently happen to the animals must be provided.
• Exp 11: provide a complete description of this experiment.
• Exp 12: Effects of AvB8 on primary tumor growth:
o All the descriptive sentences related to procedures in Section C must be moved here.
o Cell numbers injected must match details given in Section I.5
o “Immunomodulatory agents,” must be specified here or the “(see section)” needs to be clarified.
o IACUC staff edited the following on your behalf: “(see humane endpoints in Section I)”

Section I. Pre-Anesthetics and Anesthetics, Neuromuscular Blocking Drugs, Therapeutics, Analgesics and Experimental Agents

• Incomplete Freund’s – frequency column: “2 times at days at 3 and 6 wks” — ?? not clear. Revise accordingly.
• Avertin as primary anesthetic – needs justification.

IACUC staff has corrected the following on your behalf:
• Tamoxifen - dosing frequency needs to match Section G
• Ad-Cre-eGFP and Ad-eGFP — are not mentioned elsewhere in protocol — delete
• Monoclonal antibody against avb6 — is not mentioned elsewhere in protocol — delete
• IL17 neutralizing antibodies — not mentioned elsewhere — delete (also delete in J.1)
• Pentobarbital — not mentioned elsewhere — delete
Section J. Management and Monitoring of Adverse Effects of Procedures and Experimental Agents

• IACUC staff has deleted the following on your behalf, as they do not appear anywhere else in protocol:
• ALK +/-; itgb8F/F
• CD11cYFP Col-cre;itgb8F/F
• mt/mG; cd11cYFP col-are itgb8 F/F
• PDGF cre-ER; TGFbr2 F/F
• NG2cre ERT; TGFbr2 F/F
• TCRa -/-

- 30% weight loss for influenza mice – specify the # of animals that lost >20% of weight, how long it took them to recover and how many recovered. Please provide this information in the response to this letter.

Project Number: [redacted]

Approval Type: New Approval

Title: Identification of Novel Gene Regulatory Interactions Driving the Immune Evasion Program Through Transcriptional Activation of CD47 in Cancer Cells

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested:
- Move mice with tumors to Cat D (mice just euthanized for bone marrow are fine in Cat C)
- Remove statement about BCS in Sec G – a little confusing
- Change “life spasms” to “lifespan”

Project Number: [redacted]

Approval Type: Continuation

Title: Metabolic and circadian regulation of immune responses

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested:
Section C. Animals
In your narrative describing experimental groups for Category D. and E. mice, please provide (under each group) the following additional information:
- If both genders are used.
- If experiments are done in duplicate vs triplicate.
- How many ligands/agents are used per group.

Section G. Procedures Involving Living Animals
Under Category E. Mice, Group #5. LPS-induced septic shock at 22C and 30C:
- Please define with more details the concept of “torpor”.
- Describe what criteria are used to differentiate the state of “torpor” from moribundity.

Project Number: [redacted]

Approval Type: Continuation

Title: Extracellular matrix and mammary gland transformation

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested:

Section C. Animals
Category C:

• There appears to be a discrepancy between the number of Category C animals in the supplemental spreadsheet (total = 1980) and section C.1 (total = 5089). Please rectify.

Section E. Justifications and Alternatives
Section E.2.4: this section will need to be re-written, please. See comments below:
• Re-organize this section such that you provide information for each of the 2 types of metastases: (1) surgical resection and (2) late-stage primary tumor.

• For each group (surgical resection animals, late-stage primary tumor animals):
o Specify the expected signs of pain and distress.
o Clarify which animals do/do not receive multimodal analgesia for surgery.

• For any animals that could die despite intensive monitoring (e.g. those that may expire from bladder obstruction caused by the primary cancer), provide the expected percentage mortality. Also, discuss what critical scientific data could be lost by euthanizing animals earlier in the disease process.

• Please provide justification for allowing tumors to reach 2.5cm.

• Also, clarify justification for not providing analgesics and/or anesthetics and clearly specify the procedures/groups in which those agents will not be administered.

UCSF IACUC Subcommittee Meeting Minutes

Committee Name: IACUC SubCommittee/DMR

Committee Type: IACUC

Meeting Date: 06/18/2019

Members Present: IACUC Chair (or Vice Chair): [redacted]

LARC Attending Veterinarian or Designee: [redacted]

IACUC Committee Member as Specified: [redacted]

Chair's Report: 1. Subcommittee Minutes

- 5/21/2019 Subcommittee Minutes (Handout)- Minutes from 5/21 subcommittee were approved

Training and Compliance Report: 2. Training & Compliance Report

- Guest: [redacted] Pilot Data Summary (Handout)- Guest: [redacted] presented results of her pilot study investigating effects of hypoxia/hyperoxia on a mouse model of Wernicke's disease (thiamine deficiency)

- [redacted] Report- BB (Handout)- [redacted] lab self report (Protocol [redacted] rats) Subcommittee reviewed a new PI's self-report of housing rats in a laboratory space not approved for ABSL2 animal housing and not listed on their IACUC protocol. Lab did not document daily checks of lab housed animals or contact IACUC at time of pilot study, as detailed in post-approval requirements of protocol. Subcommittee reviewed lab's corrective actions – met with IACUC, LARC, EHS, facility management to identify appropriate animal housing space and establish all required documentation. Voted to send acknowledgement letter, requiring progress report from next cohort of animals, and for lab members to complete overdue training.

Other Business: 3. Protocol Review Add-ons:

- PI Transfer, [redacted] (Handout)- Approved

Protocols Reviewed

The following protocols will be reviewed by Designated Member Review process in accordance with the PHS Policy Section IV.B.3.

USDA Covered Species

Project Number: [redacted]

Approval Type: Annual Review

Title: Cellular Mechanisms of Vascular Injury (Rabbit)

PI: [redacted]

Species: Rabbit

Results: **Approved**

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: Modification

Title: Maximizing the myelinogenic potential for repair and remyelination.

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Modifications of Mouse Genes to Study the Interaction Between Nutrient Metabolism, Inflammation, and Metabolic Health

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: 13C Labeled Magnetic Resonance Studies of Prostate Cancer in Transgenic Mice

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: In Vivo Evaluation of Experimental Anti-Cancer Treatment with Engineered T cells.

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: Progress Report:
Please provide an answer to the second question- on the health and welfare of Category E. mice.
Section G. Procedures Involving Living Animals
• Experiment 14: The Committee recommends using the lowest possible dose during the pilot experiment. Please contact the IACUC office via email [redacted] or [redacted] prior to beginning the LPS administration.
• Experiment 15: Please provide additional information about the timeline of PLX feeding experiments.
• Experiment 16: Please describe in details the monitoring regimen in place for the GSI experiment. Body weight loss of >15% needs to be justified and these mice must be placed in Category E. Please adjust your total of animal numbers in Section C. accordingly.
Section J. Management and Monitoring of Adverse Effects of Procedures and Experimental Agents
• Please uncheck 15% weight loss as a humane endpoint, assuming that mice will be maintained up to 20% weight loss.

Project Number: [redacted]

Approval Type: Modification

Title: Characterizing and Targeting Tumor Factors Responsible for Vascularization and Recurrence of Glioblastoma

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Cellular Dynamics and Interactions in IgE Responses and Asthma

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Control of skeletal cell differentiation, matrix quality and hearing loss.

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Hyperalgesia and Allodynia in Normal and Transgenic Mice
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Analysis of Homeostatic Synaptic Plasticity in the Rodent Central Nervous System
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Role of BMP signaling in preventing the intellectual disability associated with Fragile X Syndrome
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Role and modulation of innate immune pathways in Staph aureus and E. coli sepsis
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Role of endocytosis in beta adrenergic receptor signaling in cardiomyocytes
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Cellular basis of retinal degenerative diseases
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Lung Transplantation Studies in Mice
PI: [redacted]
Species: Mouse
Results: **Approved**
Post-Approval Requirements: Please schedule a veterinary observation of the new spleen transplant procedure

---

Project Number: [redacted]
Approval Type: Modification
Title: Activation of endogenous stem cells and the myogenic effects of LESW and CRISPRi for improvement of Obesity-Associated Stress Urinary Incontinence in the Zucker rat model.
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Developmental signaling pathways in cancer
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Use of Mouse and Rat Models for Cardiac Development and Regeneration Research
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Analysis of HIV Infection in Humanized Mice

PI: [redacted]

Species: Mouse

Results: **Approved**

UCSF IACUC Subcommittee Meeting Minutes

Committee Name: IACUC SubCommittee/DMR

Committee Type: IACUC

Meeting Date: 06/26/2019

Members Present: IACUC Chair (or Vice Chair):

LARC Attending Veterinarian or Designee: [redacted]

IACUC Committee Member as Specified: [redacted]

Training and Compliance Report: 1. Training & Compliance Report

• [redacted] noncompliance – LARC/IACUC observed rats left not fully recovered from anesthesia in a procedure room. Lab member [redacted] performed surgical procedure (intracranial injection) without shaving or documenting analgesics. All lab members re-read the protocol, attended aseptic technique/surgery refresher training with [redacted] attend July hands-on surgery training course. Subcommittee voted to send a warning letter, requiring follow up with PASSR next month, and weekly IACUC office review of surgery records/outcomes for next 3 months.

• [redacted] noncompliance – LARC observed mice improperly euthanized, and discovered that lab member [redacted] was not performing a secondary method as described in IACUC protocol. Two lab members also performed rodent identification procedures not approved in IACUC protocol. Subcommittee voted to send a warning letter, requiring involved lab members to re-train in euthanasia and genotyping with IACUC staff. IACUC staff will also observe lab members next time they euthanize or genotype mice for study.

Protocols Reviewed

The following protocols will be reviewed by Designated Member Review process in accordance with the PHS Policy Section IV.B.3.

USDA Covered Species

Non-USDA Covered Species

Project Number: [redacted]
Approval Type: Annual Review
Title: Fibrin Mechanisms and Function in Nervous System Pathology
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: NIH R01 Contribution of development and age to breast cancer etiology
PI: [redacted]
Species: Mouse
Results: **Revisions Requested**
Revisions Requested: Modification Justification

Please provide additional information on the tail necrosis occurrence:
– Do you know whether tails are necrosing as a result of self-mutilation or inter-animal aggression?
– Could the necrosis be partly related to handling (degloving) and not related to tail tattoo?
– Have you witnessed any strain differences?
– Please describe what you have done so far to evaluate and address the problem & what the root cause probably is.

Project Number: [redacted]
Approval Type: Annual Review
Title: Stem cell regulation during muscle growth, regeneration and aging
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: The Transport of Neurotransmitters into Synaptic Vesicles
PI: [redacted]
Species: Fish, Frog, Mouse, Rat
Results: **Revisions Requested**

Project Number: [redacted]
Approval Type: Modification
Title: Mechanisms of injury and repair after neonatal stroke
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: The Role of Brg1, Kdm6a, Smpd3, and senescent cells in Pancreatic Development and Pancreatic Cancer
PI: [redacted]
Species: Mouse
Results: **Revisions Requested**
Revisions Requested: Please correct the discrepancy between the number of added Category E. mice in the narrative and in the table at the top of Section C.

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: The Role of Oxygen in Disease and Metabolism
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Genetic control of embryonic salivary gland development and adult stem cells
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Pathogenesis and Therapy of Acute Leukemia
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Study of Kryptolebias marmoratus

PI: [redacted]

Species: Fish

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Glioma Immunotherapy in Sleeping Beauty Transposon-Mediated De Novo Gliomas and other models

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: As you are proposing to perform gavage on an extended period of time, we suggest first consulting with a company such as Bio-serv to see if they can formulate your new agent into chow. As an alternative, could you reduce the gavage period as you mentioned that the expected survival is about 35 days?

Project Number: [redacted]

Approval Type: Modification

Title: Pharmacological Validation of IRE1α for Diabetes Mellitus

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: There seems to be a discrepancy between the number of added mice in the table (200) vs what is described in the narrative (192).

Project Number: [redacted]

Approval Type: Annual Review

Title: The role of developmental pathways in regulating adult lung homeostasis and injury repair

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Cell migration and lineage in the developing brain
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Mouse models to study uterine leiomyomas and infertility
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: GPR56 signaling in brain development, disease and injury
PI: [redacted]
Species: Mouse
Results: **Revisions Requested**
Revisions Requested: You state that the EAE experiment will have a sample size of 5 and no replicates, which contradicts the power analysis you have in Section C. Could you please clarify?

Project Number: [redacted]
Approval Type: Annual Review
Title: Studies on Pancreatic Development, Disease, and Regeneration
PI: [redacted]
Species: Mouse
Results: **Approved**