Committee Name: IACUC Full Committee

Committee Type: IACUC

Meeting Date: 05/07/2019

Chair's Report: Voting Members: [redacted]
Office Staff: [redacted]
Guests: [redacted]

• IACUC Chair's Report

A. Guests from the UCSF Institutional Review Board: [redacted],
B. Minutes
- 4/2/2019 Full Committee Minutes (Handout)- Minutes from 4/2 Full committee were approved

Director's Report: IACUC Director's Report
4/30/19 Program review. Following up on a subcommittee member's request from 5/6/19 program review, the full committee asked IACUC office to provide additional data on scope of program's rodent surgery training needs.
Action item:
IACUC Office will provide report at next meeting on:
a) estimated number of surgical complications via # green cards scanned with health checks.
b) training resources necessary to require hands-on anesthesia and surgery training for all investigators that do surgery.

Attending Veterinarian (AV) Report: AV Report/LARC Clinical Case Report
Update on Tropical Rat Mites Report: PSB mouse and rat rooms. Up to 7 rooms in PSB affected. Mites come in with wild rats. Last fall, Building LEED certification changed outside-of-building pest control to a non-poisonous option, resulting in increased infestation. Recent meeting with inside-of-building and outside-of-building pest control agencies and FM. Outside-of-building company will resume use of poison. No action.

[redacted] and Surgical Records were reviewed
Update. Records are within IACUC requirements. No action.

IACUC Member Training and Information:

UCSF IACUC Full Committee Meeting Minutes

• Committee Information and Training

A. Upcoming CE opportunities

• South San Francisco, CA: IACUC YourWay: From AtoZ May 7, 2019

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

o May 23, 2019: Philadelphia, PA
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: [redacted] (New) “Development of Methods for Precise MR-guided Hyperthermia Delivery for Targeted Cancer Therapies” Reviewers: [redacted] eferred to the 5/21 IACUC Full Committee Meeting

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Project Number: [redacted]
Approval Type: New Approval
Title: Development of polymer-based nasal barrier and drug delivery devices
PI: [redacted]
Species: Rabbit
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]
Results: **Approved**

Project Number: [redacted]
Approval Type: Continuation
Title: Rabbit Studies of Small-Molecule Chloride Channel Activators
PI: [redacted]
Species: Rabbit
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]

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

Results: **Revisions Requested**

Revisions Requested:

Objectives
• There are sentences within the first paragraph that are not entirely understandable to committee members who are not scientists. Please re-write the following sentence so that it can be easily read and comprehended by a non-scientist: “Prior work from our lab had shown that at ocular surface epithelia can produce marked fluid secretion, and we have identified highly potent activators of cystic fibrosis transmembrane conductance regulator (CFTR) that are candidates for first-in-class pro-secretory topical therapy of dry eye.”
o Additionally, you may consider copying the responses from E.2.1 and E.2.2, and including them in the Objectives section as well. The content of the responses is quite easy to read and understand.

• Please update the second paragraph of this section to elaborate on the various experiments you perform(ed) for testing the performance of our CFTR activators in the rabbit model. For instance, in Section G. you mention “new experiments”. Please discuss these new experiments here.

• Describe the chemical composition of your CFTR activators.
Section A. Funding

• Please update this section to reflect any new funding you have been awarded.

• If applicable: upload signed departmental merit review form (if private or departmental funding).
Section C. Animal Numbers

• Clarify why you only use female rabbits, providing scientific justification.
Procedure 1 – Pharmacodynamics: this section is unclear and will need to be thoroughly revised.
• First sentence: “For the “additional requested rabbits…” – this is unclear and has been removed by IACUC staff. No action needed on your part.

• Clarify the following sentence: “For the additional requested rabbits will evaluate pharmacodynamics of our best K-class CFTR activator compound, in 3 different formulations compared to the formulation control (without drug, 4 total treatments).”
o It appears there is a missing word between “rabbits” and “will”
o What is meant by “best”? What is meant by “K-class”? Please re-write sentence.
o Provide justification for the 3 different formulations and explain why/how they differ.
o Please clearly explain what comprises a “formulation”. Is this a compound + a vehicle? Something else?
o We have removed the following parenthetical phrase on your behalf as it is unclear: “(without drug, 4 total treatments)”. No action needed on your part.

• Clarify the following sentence: “The lead compound was selected from our prior work (published in IOVS in 2017), and initial studies done in rabbits.”
o Specify the lead compound and why it was selected.
o “and initial studies done in rabbits” is unclear. Either remove this phrase or re-write it so that it makes sense and adds relevance to the sentence.

• Clarify the following sentence: “Potential vehicles include 0.3%, 0.6%, and/or 0.9% carboxymethylcellulose or 0.5% polysorbate (all of which are standard human ophthalmic vehicles), with or without benzalkonium chloride standard preservative.”
o Are these vehicles the same as the “formulations” that you indicate earlier in the paragraph?
o Will you use all of these vehicles, a few of them, or just one?
o We encourage you to make a table or diagram if it will aid you in explaining the design.

• Clearly state the following:
o outcome being measured
o hypothesis being tested (if no hypothesis is being tested, justify why not)

o experimental unit (eyes or animal)
o experimental design

• Clearly state the sample size for each experimental group.
o In the last sentence of this section you indicate that 16 total rabbits will be used. However the table in C.1 specifies 40 rabbits. Please resolve this discrepancy.

Section E. Justifications and Alternatives

• Update the dates of the most recent literature search as well as the years covered for each of the searches.

• You include an ARVO 2015 meeting. Please remove this or update if you have attended more recent ARVO meetings.

Section G. Procedures Involving Living Animals

• This section will need to be thoroughly revised to clearly describe the various procedures any given rabbit would undergo from the time they enter into your care at the study's outset until the time that the animals are euthanized. Provide a table/timeline of procedures and measurements/observations that a rabbit will undergo in this study, so that the committee fully understands exactly what it is you are proposing to do.

• Paragraph 1:
o The first sentence does not make sense, "…we have activity of our compounds…" Please re-write.
o Please clarify what is meant by: "most promising" in regards to the compounds. Does "promising" equate to "effective"?
o Please explain what comprises a "formulation". Is this a compound + a vehicle? Something else? Describe how you will prepare the formulations.
o Clarify what is meant by "large and sustained" with regard to tear volume.

• Paragraph 2: Clarify both sentences
o Clarify what is meant by, "if possible" in the following sentence. Are there situations when only 1 eye would be treated? Under what circumstance would that occur?
"All rabbits have both eyes treated simultaneously, if possible, to minimize the number of animals used and to reduce the number of times each undergoes measurement."

o Clarify the following sentence and explain how this relates to the experimental design.
"Assignment of eyes to various treatment formulations are made on an on-going basis according to interim observations during the course of the project."
 What is meant by an "on-going basis"?
 You will need to provide complete details about observations in this section (Section G). With regard to observations – discuss the schedule and frequency, the type of observations and the type of information the observations will provide in order to determine which animals will be assigned to the various formulations.
• Please clarify the following sentences: "We will test 3 different Class K formulations and a control simultaneously (4 rabbits each formulation, 16 total), and then use the same rabbits serially after drug washout periods of >24 h. Therefore each rabbit is predicted to undergo general anesthesia 4 times. After that, animals will be euthanized and tissue sharing will be possible should any other investigators require control tissues for analysis."
o The first sentence mentions "new" experiments and this "revised" protocol. IACUC staff has removed this first phrase on your behalf to lessen confusion by the reader. No action needed on your part.
o Specifically, clarify what type(s) of procedure will take place while animals are under general anesthesia (ocular potential differences? Etc.), as well as those for which animals are administered a topical anesthetic. As noted above, please include a visual aid (diagram or timeline of procedures that a rabbit will undergo in this study – can be a supplemental file), so that the committee fully understands your procedures.

• Clearly describe all tests and measurements you will use for your procedures listed in this section, including: Schirmer test, Slit Lamp examination and so forth.

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

I.1. Please list the topical anesthetic in this section.
I.5. You specify the use of Lissamine Green (not mentioned in Section G) and further mention these drops are administered post-op and are used in Procedure 3. Since you only discuss 1 procedure in this protocol and do not have any surgeries listed, it appears that this agent may have been erroneously included in this protocol. Please remove it as well as any other agent (Amiloride? Forskolin?), that should not actually be listed.
o Similar to the point above, for several of the topical perfusates listed, you indicate that the will be infused at 6 mL/minute for 4-6 minutes. However, in section I.9 you state in the last sentence that all routes of administration will be topical.

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

J.1: “Ocular surface perfusion or topical application of novel CFTR activators” – Section 1.9 (see comment above) includes a sentences stating that all routes of admin will be topic. Please address this discrepancy and update accordingly.

J.2: In “frequency” field for “signs of pain…”(monitoring parameter) - you indicate that the rabbit will be evaluated, including weighting during the initial 24 hours post-procedure. “The rabbit will be continued to be monitored…until symptoms of pain have completely subsided.” Discuss why you would not provide pain relief for animals. (If pain relief is not provided, animals will need to be re-categorized as Category E.)

J.5: Similar to the point above, you indicate that “if milder adverse reactions, such as signs of discomfort or milder irritation…were to occur, the animals will be observed closely without medication until resolution.” (If pain relief is not provided, animals will need to be re-categorized as Category E.)

Section M. Physical Restraint of Conscious Animals

You have indicated in Sections E. that you will perform many of the experiments on awake restrained rabbits but have responded “No” to the question in this section. Please address this discrepancy and update the protocol accordingly.

Non-USDA Covered Species

Project Number: [redacted]
Approval Type: New Approval
Title: Genome editing approaches and targeted therapies to treat brain cancer
PI: [redacted]
Species: Mouse
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]
Results: **Approved**

Project Number: [redacted]
Approval Type: New Approval
Title: Myeloid Cell Interactions with Glioma Growth
PI: [redacted]
Species: Mouse
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]
Results: **Approved**

UCSF IACUC Subcommittee Meeting Minutes

Committee Name:	IACUC SubCommittee/DMR
Committee Type:	IACUC
Meeting Date:	05/07/2019
Members Present:	IACUC Chair (or Vice Chair): [redacted] LARC Attending Veterinarian or Designee: IACUC Committee Member as Specified: [redacted]
Chair's Report:	1. Subcommittee Minutes - 4/2/2019 Subcommittee Minutes (Handout)- Minutes from 4/2 Sub committee were approved
Training and Compliance Report:	2. Training & Compliance Report Sohal Surgery Plans– Acknowledgement letter with reminder to submit 6 month update on sx procedure complication rate in mice. [redacted] Surgery/Response– Acknowledgement letter with requirement: PI must provide plan for who in lab will be assigned to manage and triage animal health concerns with pending departure of current lab manager. Committee suggested that he contract LARC for this service. Repeat of noncompliance issues will result in notifying the IO. [redacted] Equipment Rusting– Lab reported they cannot assure that newly rusted areas can be cleaned and repainted within 1 month. Directive for deficiency resolution: All rusted areas must be repaired by June 30 2019. IACUC still expects to receive a long-term plan by June 1. This plan should include how the lab will maintain equipment going forward.

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: MR-guided high frequency focused ultrasound (MRgHIFU) for ablating spinal joints (facet joint and sacroiliac joint).

PI: [redacted]

Species: Swine

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Implantable Bioartificial Pancreas

PI: [redacted]

Species: Swine

Results: **Approved**

Non-USDA Covered Species

Project Number: [redacted]
Approval Type: Annual Review
Title: Bone and Cartilage Crosstalk in Temporomandibular Joint Disease
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Development and regulation of the V-SVZ adult neural stem cell niche
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Administration of Cells, Antibodies, and Soluble Receptors in Mice That Have or Have Not Received a Skin and or Islet Transplant and models of autoimmune disease.
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Synaptic and circuit mechanisms of compensation following loss of cone and rod inputs in the mouse retina
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Oligodendrocyte myelination in development and disease
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Genetic Approaches To Understanding Col4a1-Related Pathologies
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Drugs to combat ER stress-induced dysfunction of AECIIs
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Conventional and gnotobiotic studies of the gut microbiome
PI: [redacted]
Species: Mouse
Results: **Revisions Requested**
Revisions Requested: The Committee grants you approval to conduct a pilot study with 10 mice and a maximum fast duration of 24 hours. Please report to the IACUC once it has been completed.

Project Number: [redacted]
Approval Type: Modification
Title: Brainstem circuits in migraine and pain
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Extracellular Matrix and Pancreatic Ductal Adenocarcinoma
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Role of Telomere Dysfunction in Lung Fibrosis
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Mouse heart development and its transcriptional regulation
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Roles of US9 and MMP12 in HSV-1 immunity and development of anti-HSV therapeutics.
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Engrafting liver tissue constructs in rat
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: Functional genomics approaches to reveal principles of anti-cancer therapy, tumor development and DNA repair in vivo.
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Immunization and Genetic Complementation of Transgenic Mice

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Cell Surface Molecules and Molecular Events Involved in Human Immune Cell Activation and Function.

PI: [redacted]

Species: Mouse

Results: **Approved**

UCSF IACUC Full Committee Meeting Minutes

Committee Name: IACUC Full Committee

Committee Type: IACUC

Meeting Date: 05/21/2019

Chair's Report: Voting Members: [redacted]
Office Staff: [redacted]
Guests: [redacted]

• IACUC Chair's Report

A. Minutes
a. 4/16/2019 Full Committee Minutes (Handout)- Minutes from 4/16 Full committee were approved
b. 4/30/2019 Policy Minutes (Handout)- Minutes from 4/30 were accepted; will vote on final approval at next Parnassus meeting

IACUC Chair's Report

A. Collisson visit: [redacted] visited the IACUC to provide feedback about his lab's recent challenges with protocol approval. Committee discussed evolving standards for protocol reviews, expectation of direct PI involvement in protocol development, and need for RIO technical support to clarify new rodent annual renewal process.

B. IACUC director position updates
a. [redacted] is chairing search committee; interviews start next week
b. [redacted] will be interim IACUC director starting June 28

Director's Report:

IACUC Office Report for 5/21/19

Job postings:
The position of IACUC Director is now posted and search committee named. [redacted] last day at UCSF is June 27.
[redacted] left LARC and is now [redacted], and [redacted] (10+ % LARC) will be leaving. LARC has posted a position for a Veterinarian level II.
[redacted] is working to hire a second veterinarian for their program (along with a total of four vet techs).

IACUC Chair: [redacted] last day as Chair is the June 4 meeting

Surgery training and oversight:
Program Review as well as the 5/7/19 IACUC meetings discussed surgery outcomes. The 5/7/19 Committee has 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?)

A Program Review Subcommittee met on May 3 and will provide a summary for IACUC member review and signature.

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). [redacted] is no longer on the high-risk list.

NOTES from some recent meetings:

From the 4/30/19 Policy meeting:

Much discussion about RIO, as [redacted] is retiring. For years, she has developed RIO functions for LARC, and served as the business analyst who learned the animal program well enough to translate our needs into language programmers would understand. When IACUC passes a new policy eliminating some annual reviews she's the person who knows how a change in that in RIO will impact reminders, cage-card/purchasing approvals, and to ask (for example) what happens if a PI adds DoD funding to a protocol and needs to trigger annual reviews.
[redacted] has been a LARC employee and LARC is not replacing her. [redacted] announced that the IT department IS adding a position to serve RIO functions Kathy has been providing, in addition to the 1.5 FTE programmers for LARC, IACUC, Business Office and EH&S RIO. No action item.

USDA, Newspaper article:
Discussion about the [redacted] requirement of prior notifications of major procedures on USDA-covered animals if LARC is not directly involved.
Action item: Committee voted to continue this requirement as an IACUC requirement, exempting the Manoli voles and the Diep rabbits. IACUC will inform investigators.

Activity/discussion about animal program websites:
Thanks to [redacted] for reviewing some other institutions' websites in prep for this meeting. UCSF currently is less transparent and less pro-active than some others (e.g., [redacted]). Discussion of the pros and cons and risks of transparency, especially of allowing identification (photos, names) of individuals.
Action item: [redacted] to meet with UCSF's public relations folks to review what support they can provide for improving the animal program's public visibility and what support they need to best interact with questions from the press.

Committee CE review of mouse thermoregulatory biology and welfare:
LARC's behavior specialist [redacted] presented some existing data on effects of cage temperatures and nesting material on mouse biology, with reference to performance language in the Guide ("adequate resources for thermoregulation (nesting material, shelter) to avoid cold stress."). She gave a 'state-of-the-art' of LARC's provision of nesting material.
Action Item: Committee requests an update on LARC's use of nesting material at the policy meeting in October, once [redacted] has had a chance to share this information with LARC managers.

Committee also discussed the value of better informing investigators of information such as this --- start brainstorming, please.

From the 5/7 meeting:

Subcommittee:
[redacted] is losing their lab manager, and because of their compliance history, IACUC is asking them for a plan for the lab's animal management, including possible contracting of LARC to provide extra animal health oversight.

Sending a note to the [redacted] to manage the rust on their fish tank shelving while the big longer-term fix with new equipment is in process.

Full Committee:

Committee has requested a report on surgical complication rates and info on training resources (see above)

LARC reported on a Tropical Rat Mite infestation in [redacted]ooms --- will need to review the scope of the issue and assess whether this warrants a report to NIH-OLAW

Committee was updated on [redacted] animals' weights

Attending Veterinarian (AV) Report:

• AV Report/LARC Clinical Case Report

A. Tropical rat mite outbreak – [redacted]urrently has several rooms under quarantine, and LARC is working with 2 pest control companies to control wild rats in interstitial spaces. IACUC will need to report to OLAW if labs slow/halt work due to outbreak.

B. [redacted] weight and surgical records were reviewed and accepted

Training and Compliance Report:

• Training & Compliance Report
A. [redacted] presented an overview of improvements to IACUC program for rodent surgery training/oversight
a. Challenges:
• variability in lab-provided anesthesia/surgery training
• IACUC anesthesia/surgery training courses are optional
b. Program improvements:
• Established a program to certify laboratory-based trainers (pilot project has trained 10 labs)
• Implemented proficiency checklist to objectively evaluate new surgeons
• Training records: trainer/trainee sign off on proficiency and responsibility for follow-up if negative outcomes
• Tracking surgery outcomes using RIO reports of green tags/health checks
• Targeted follow-up of labs with complication rates above benchmark for a given procedure

IACUC Member Training and Information:

• Committee Information and Training

[redacted] gave a presentation on his lab's experience using the 3Rs to improve their research program

B. Upcoming CE opportunities:

• SUBR (States United for Biomedical Research Webinar) & STEM "Using Training to Improve Compliance" June 4
https://register.gotowebinar.com/register/4704095970866646531

• August 23, 2019: NCB AALAS Educational Symposium

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

o May 23, 2019: Philadelphia, PA
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

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: New Approval
Title: Image-guided ultrasound ablation for precision targeting of prostate cancer
PI: [redacted]
Species: Dog
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]
Results: **Approved**

Project Number: [redacted]
Approval Type: New Approval
Title: Development of Methods for Precise MR-guided Hyperthermia Delivery for Targeted Cancer Therapies
PI: [redacted]
Species: Swine
Primary Reviewer: (1) [redacted]
Secondary Reviewer: (1) [redacted]
Results: **Approved**

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: New Approval

Title: Analyzing the stability of nuclear structures in healthy and diseased tissues

PI: [redacted]

Species: Mouse

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Approved**

Project Number: [redacted]

Approval Type: New Approval

Title: CRISPR/dCas9 Activated Expression of Cardiomyocyte Differentiation Factors in CDCs In Myocardial Infarctions

PI: [redacted]

Species: Rat

Primary Reviewer: (1) [redacted]

Secondary Reviewer: (1) [redacted]

Results: **Revisions Requested**

Revisions Requested: Section C. Animals

• Clarify whether guide1 and guide2 are two different CRISPR constructs for the same transcriptional factor. If so, please amend to make it clear that only 1 of the 3 transcriptional factors (TNNT2, GATA4, Mef2c) will be tested in this study. However, if you plan to test all 3 transcriptional factors, then update your numbers accordingly. (Note: see the attached IACUC animal numbers spreadsheet to assist in properly calculating your numbers).

• In light of the number of groups in your study, consider running an ANOVA in lieu of a t-test as it is more appropriate for multiple comparisons.
Section D. Contacts and Personnel

Add intramyocardial injection to “surgery performed” field for each postdoc. (note: IACUC has done this on your behalf. No action needed on your part.)

Section E. Justifications and Alternatives

Section E.2.3. Elaborate on how your proposal minimizes pain and distress. Examples may include administration of analgesics before and following surgery.

Section G. Procedures Involving Living Animals
• Please remove “Acute groups” (CDC experiments), since they also in Section I.9 (as a description to prepare these reagents as non-pharmaceutical agents) and because they do not directly involve living animals.

• For #5 - in vivo imaging system (IVIS) analysis: clarify the first sentence as it is not clear whether this will involve an additional intramyocardial injection.

• State whether rats will be transferred back to CVRI after IVIS measurement or not (as the committee raised the question about whether there might be issues related to quarantine), and the whether the measurement will be performed once or multiple times.

• Specify the frequency & number of imaging sessions that will be performed over the 4 week period.

Post Approval Requirements:

Post-Approval Requirements
Before you schedule your initial surgery, please contact the IACUC office to arrange for surgical procedure observations/guidance by veterinarian, [redacted].

UCSF IACUC Subcommittee Meeting Minutes

Committee Name:	IACUC SubCommittee/DMR
Committee Type:	IACUC
Meeting Date:	05/21/2019
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 - 4/16/2019 Subcommittee Minutes (Handout)- Minutes from 4/16 subcommittee were approved
Training and Compliance Report:	2. Training & Compliance Report - [redacted] self report ([redacted] [redacted] mice) – Subcommittee reviewed PI's report of an implanted mouse inadvertently left head fixed overnight. Lab contacted veterinarian immediately upon discovery; veterinarian assessed animal as healthy after ad lib food/water. Lab established procedure to check all rooms for animals at end of day. Subcommittee voted to send an acknowledgement letter.

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: Development of a Nano-Micro Systems Drug Delivery Device
PI: [redacted]
Species: Rabbit
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Inhibition of Galectin-3 for Therapy of Remodeling After Myocardial Infarction
PI: [redacted]
Species: Swine
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Skin Barrier Protection — Decontamination Intervention Strategy Development Based on Mechanistic Insights of Stratum Corneum Domains and Chemical Reservoir
(Part II In Vivo Guinea Pig Dermato-pharmaco-toxico-kinetics and decontamination Efficiency Evaluation Study)
PI: [redacted]
Species: Guinea Pig
Results: **Approved**

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: Modification

Title: Study of cardiac metabolism in hypertrophic cardiomyopathy

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: -In Section C., there are no changes in your numbers table but you mentioned that a 7th group (non-intense swimming cohort) will be added to all 8 main experiments. Please rectify the numbers and account for the 10% anticipated loss.
-In Section G., can you specify, when you describe the swimming apparatus, how often the water gets changed?

Project Number: [redacted]

Approval Type: Annual Review

Title: Functional characterization of parasite-induced limb deformities

PI: [redacted]

Species: Frog

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: The Role of Growth Factors and Genetic Modifiers in Vascular Disease and Cancer

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Treatment of neurological diseases in rodents using gene therapy

PI: [redacted]

Species: Rat

Results: **Revisions Requested**

Revisions Requested: Section G. Procedures Involving Living Animals
• In the proposed added experiment 5 (nanoparticle-based gene editing), please describe whether you have a control group with a non-formulation Cas9-RNP as the background for the number of genes changes with CED delivery?
• You state that up to 15% of rats could have cannulas misplaced but it does not seem that it has been accounted for into the described group sizes.
• Please clarify whether the volume of Crisper infusion us 20 ul or 15 ul (Section C.)
Section I. Pre-Anesthetics and Anesthetics, Neuromuscular Blocking Drugs, Therapeutics, Analgesics and Experimental Agents
• Please add the PEGylated nanoparticles to your list of existing agents.

Project Number: [redacted]

Approval Type: Modification

Title: Role of endocytosis in beta adrenergic receptor signaling in cardiomyocytes

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: -In Section E., please add the new mouse strains to your literature search.
-In Section I., please add “Nair” to the list of existing agents.
-In Section J., describe the potential adverse effects of the TAC surgery and under humane endpoints, check yes for rectal prolapse.

Post-Approval Requirements: Please schedule a procedure observation (TAC surgery) by contacting the IACUC office via email.

Project Number: [redacted]

Approval Type: Modification

Title: A Drug Discovery Platform for Fast-tracking Adaptations to High Altitude

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: 1) Section C.: for the mCAT mice, you said you are going to use both genders and need 1500 per gender. In that case, this experiment will require 3000 (not 1500) and this total should be reflected in the table.
2) Section D.: add location of previous trainings for Ankur.
3) Section E.: add new lines to your literature search and re-run the search.
4) Other: Please keep sending IACUC staff a weekly update on your studies. . The Committee would like us to keep receiving weekly updates until the end of 2019.

Project Number: [redacted]

Approval Type: Modification

Title: Chemoprevention of carcinogen-induced head and neck squamous cell carcinoma

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: Section G. Procedures Involving Living Animals
• Experiment 10: You state that “an even distribution of male and female mice will be used” but the power analysis in Section C. does not identify the use of both sexes. Please clarify and/or modify the total of animal numbers in Section C.
Section J. Adverse Effects
• Providing wet food once animals are in poor condition is not sufficient, please state that animals will get weighed on a weekly basis.
• Animals in experiment 11 will survive for up to six months. Please provide details on how often these mice will be assessed for tumor development.

Project Number: [redacted]

Approval Type: Modification

Title: Cell Division Modulation During Neocortical Development

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

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/Modify

Title: Dissecting the pancreatic beta cell

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Prothrombin Complex Concentrate for Prolonged Field Care of War Casualties

PI: [redacted]

Species: Mouse, Rat

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: T-Cell Activation, Tolerance, and Memory

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: Aberrant cell growth and translation control in mouse models of human disease and cancer

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Core Facility for Rodent Imaging
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Genetic Programming of Angiogenesis
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review/Modify
Title: A Mouse Strain Rederivation, Cryopreservation, Genotyping and Microinjection Core Facility
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Elucidating the role of NAT1
PI: [redacted]
Species: Mouse
Results: **Revisions Requested**
Revisions Requested: -Section C.: You are adding 4 new mouse lines but the numbers in the table haven't changed. Please modify them accordingly.
In addition, please add the actual numbers of animals that will be used for experiments in section I and II Cat. C animals.

UCSF IACUC Subcommittee Meeting Minutes

Committee Name: IACUC SubCommittee/DMR

Committee Type: IACUC

Meeting Date: 05/28/2019

Members Present: IACUC Chair (or Vice Chair):

LARC Attending Veterinarian or Designee: [redacted]

IACUC Committee Member as Specified: [redacted]

Other Business: ADD ON: [redacted] - 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: Modification

Title: A Placebo-Controlled Study to Evaluate the Efficacy of Local Myocardial Stem Cell Delivery with Bioabsorbable Scaffolds in a Swine Model of Myocardial Infarction.

PI: [redacted]

Species: Swine

Results: **Approved**

Non-USDA Covered Species

Project Number: [redacted]

Approval Type: Modification

Title: Cortical-subcortical interactions in psychiatric disease

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested: Section G. Procedures Involving Living Animals
• Category E. mice: Restraint stress exposure:
o Please specify how long you expect the training phase to be in order to obtain 80% successful avoidance.
o Describe the conditioning process for restraining animals for 2 hours – you may consider trying it in non-implanted animals first and – specify how many will be restrained at the same time and upload an image of the device once it has been developed.
Section J. Management and Monitoring of Adverse Effects of Procedures and Experimental Agents
• Under Adverse Effects for Category E. mice – active avoidance test-, please remove the word “brief” as shocks lasting up to 10 seconds should not be considered brief.
• Under Adverse Effects for Category E. mice – 2-hour physical restraint- please add potential adverse encountered by poor performers unable to achieve 80% avoidance.
Section M. Physical Restraint of Conscious Animals
In the text box asking to describe criterial for removal of animals, please remove N/A as it is inappropriate for an experiment that has the purpose of inducing stress.

Post-Approval Requirements: Post-Approval Requirement
• Restraint Test: The Committee grants you approval for small pilot experiment (no more than 10 mice). Please report back to the IACUC and describe adverse effects encountered (if any) once the experiment has been completed.
• Please schedule a procedure observation of the first animal undergoing the Restraint Test. You can contact IACUC staff Carine Elkhoraibi directly.

Project Number: [redacted]

Approval Type: Modification

Title: Studies of Thermoregulation in mouse

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Molecular Studies of Receptor Function

PI: [redacted]

Species: Alligator, Fish, Mouse, Rat, Salamander, Snake

Results: **Approved**

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

Project Number: [redacted]
Approval Type: Modification
Title: MR studies of Preclinical Models of Multiple Sclerosis
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Oncogenes and Cell Cycle Control
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Prevention of chronic lung allograft rejection
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Modification
Title: Behavior based neuroactive drug discovery in the zebrafish
PI: [redacted]
Species: Zebrafish
Results: **Revisions Requested**

Project Number: [redacted]
Approval Type: Annual Review
Title: Pharmacogenomics of Microtubule Targeting Agents
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Extracellular Vesicles in Acute Lung Injury and Sepsis
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Targeting Inflammation To Reduce Secondary Damage and Improve Neurologic Function After Spinal Cord Injury
PI: [redacted]
Species: Mouse
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Studies on the effect of Icariin-II and low-intensity extracorporeal shock wave therapy on diabetic, obesity-associated and cavernous nerve crush induced erectile dysfunction
PI: [redacted]
Species: Rat
Results: **Approved**

Project Number: [redacted]
Approval Type: Annual Review
Title: Rodent Primary Culture
PI: [redacted]
Species: Mouse, Rat
Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Neuroinflammation, synaptic plasticity and memory: long term outcome after traumatic brain injury

PI: [redacted]

Species: Mouse, Rat

Results: **Revisions Requested**

Revisions Requested: Progress Report
You state that no analgesics will be given post-operatively. However, the references provided do not support this claim as two pertain to morphine use and one regards in vitro use of Buprenorphine. Please address how the post-operative pain/distress will affect the outcomes being studied and re-run the literature search with adequate keywords in Section E.
Section C. Animals
• Clarify whether you will be using a sample size of 10 animals (as stated in your power analysis) or 5 animals (as stated in one of your new calculations.

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: Role of integrins in scleroderma.

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Quantitatively modeling immune responses to cancer

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review

Title: Treatment of Ischemic Heart Disease by Drug, Gene, and Cell Therapy

PI: [redacted]

Species: Mouse, Rat

Results: **Approved**

Project Number: [redacted]

Approval Type: Annual Review/Modify

Title: UCSF Gnotobiotic Core Facility

PI: [redacted]

Species: Mouse

Results: **Approved**

Project Number: [redacted]

Approval Type: Modification

Title: cAMP- and Salt-inducible kinase-mediated transcriptional regulation

PI: [redacted]

Species: Mouse

Results: **Revisions Requested**

Revisions Requested:
Section G. Procedures Involving Living Animals
• Stud 12: Drug-induced hypothermia
o Please provide detailed information on this procedure including duration, monitoring frequency, how the optimal dose will be determined and how body temperature will be assessed. Additionally, please clearly state the hypothesis being tested.
o Clarify whether hypothermia will be induced by Capsaicin or if Capsaicin will be used to treat hypothermia caused by Pentobarbital.
Section I. Agents
• Add Capsaicin and Pentobarbital to your list of non-pharmaceutical grade agents.
Section J. Adverse Effects
• Under Capsaicin and Pentobarbital Sodium, please explain the rationale for euthanizing an animal if the body temperature drops below 28 degrees Celsius instead of warming him/her up.

Project Number: [redacted]

Approval Type: Annual Review

Title: Nano-switches for Optogenetic control of neuronal proteins with ultra-specificity

PI: [redacted]

Species: Mouse

Results: **Approved**