

University of Washington
December 21, 2017 IACUC Meeting Minutes

Members Present:

AB	JLS	LJE (call in)
AS	JM	ML
CH	JS	SH
FRR	JPVH	TB
JFI	KL	

Members Absent: CG MS SL
PB

Opening Business

The IACUC Chair called the meeting to order at 2:31 pm.

Confirmation of a Quorum and Announcement

Quorum was confirmed by JS.

Approval of the IACUC Meeting Minutes

The IACUC Chair called for the approval of the November 16, 2017 meeting minutes.

Moved and seconded: seconded to approve the minutes as written.

Discussion: None

Vote on the Motion: approved with 12 members in favor and 2 abstentions.

Benefit Story

B-cell non-Hodgkin's lymphoma is one of the most common cancers in the United States, and it has a 50% 10-year survival rate. One of the challenges in treating this disease is that drugs that are effective as first-line therapies can be much less effective treating patients who come out of remission. Our benefit story this month comes from the Lieber lab, which is trying to find better treatment options for non-Hodgkin's lymphoma patients who relapse with drug-resistant malignancies. The Lieber lab has identified a protein called CD46 that is strongly upregulated in many cancerous cells. CD46 is normally found at low levels on the surface of most cells, and it serves as self-protection from our body's innate immune system. When CD46 levels rise in cancerous cells, however, it makes these cells resistant to cancer treatments that work by boosting the innate immune system. The Lieber group has systematically tested different laboratory-designed proteins for their ability to bind tightly to CD46 and prevent it from activating a signaling cascade. After initial testing in cultured lymphoma cells, one designer protein, called Ad35K++, was tested further for safety and efficacy in vivo, first in mice and then in non-human primates. After showing considerable promise in these animal studies, Ad35K++ is now in clinical trials over at the Hutch. Ad35K++ treatment has the potential to improve the survival of non-Hodgkin's lymphoma patients who relapse, by suppressing CD46 signaling and allowing the patient's own innate immune system to target and kill cancerous cells.

[Richter et al. 'Preclinical safety, pharmacokinetics, pharmacodynamics, and biodistribution studies with Ad35K++ protein: a novel rituximab cotherapeutic' *Molecular Therapy — Methods & Clinical Development* (2016)]

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Attending Veterinarian's Report – TB

Facility issues:

Humidity: Low humidity reported in our older facilities without humidity control. One case of epistaxis in a NHP reported (12/6/17)

Temperature and lights:

11/22/17: One rodent behavioral space reached 82.3 degrees at 8 am. HVAC responded to the alarm and reduced the temperature by 9:02 am. All mice were fine. The problem was a bad valve, which was ordered and replaced.

11/30/17: This swine room was programmed to have a reverse light cycle. The lights did not go off as were expected for 24 hours. The programming has been modified and DCM is working with all parties to correct the programming for a more permanent fix.

Protocol Monitoring:

There are 18 active protocols on the veterinary monitoring program

Murry heart projects (summary from Sept. to Nov. 14th).

Terminal surgeries: There have been 3 planned terminal surgeries that have proceeded without complications.

Atrial scar project: Two pigs received a survival atrial scar procedure in October and both made it to the planned endpoint.

Myocardial infarct project: This phase of the project is looking at chronic administration of anti-arrhythmic drugs in order to improve survival following engraftment of progenitor cells at the site of the myocardial infarct. Twelve animals have received myocardial infarct surgery. Of those, four animals developed ventricular fibrillation during the procedure. Two were successfully resuscitated and two were not.

Therefore, 10 animals recovered from the myocardial infarct, and four of those ten animals are currently still alive. The other 6 did not survive to the planned experimental endpoint. Four of those six animals developed ventricular fibrillation several weeks post-implantation of engrafted cells. In addition, one animal developed ventricular fibrillation during anesthesia for an MRI and could not be resuscitated and one animal was euthanized due to ventricular fibrillation and an infection that had developed around the telemetry implant.

Adverse event:

Protocol 4374-01: One frog, *Xenopus tropicalis*, had axotomy surgery on 10/31/17 and was found dead on 11/2/17. No necropsy was performed. The investigator thought that survival surgeries were in her protocol, as they are in her grant, but she was mistaken. She is adding them to her protocol. This was the only surgery performed.

Moved and seconded: to send investigator a letter of counsel asking investigator to describe how this will be avoided in the future.

Discussion: Grant was reviewed and survival surgery was not caught. More of an oversight than intentional. Non-Survival surgeries were approved on the protocol.

Vote on the Motion: Approved with 14 members in favor.

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Protocol 2456-06: On 10/17/17, a four-month old singly housed male mouse was found dead with the external portion of the headcap caught in the pellet hopper wiretop. The headcap and cannulization had occurred on 10/5/17 and the animal received a vehicle control. Although the protocol requires weekly checks, the lab contact checks these mice daily. No abnormalities were noted during these checks. Necropsy revealed no evidence of infection and was limited due to significant autolysis.

HBA Subcommittee:

The HBA committee met this month and discussed incidents of morbidity and mortality in USDA species.

OAW Director's Report – STI

Metrics also in the folder. Turnaround time has decreased.

USDA Annual Report in the folder.

Pamphlet available regarding benefits of biomedical research.

Communication from Bob Sikes regarding wildlife jargon used by the USDA also in the folder.

Adverse Events

- **Protocol 3108-01:** ultimate goal is cancer treatment via modifications of hematopoietic stem cells and enhancement of antibody therapy for cancer treatment.

Due to a dosing error animals were administered a higher dose of Doxil (3 mg/kg vs 1 mg/kg) than they were approved for. There were 29 mice total in the study, 22 of which received Doxil (and 7 controls). Ten mice were found dead and remaining mice were euthanized due to ill health and the discovery of the incorrect dosing.

Additionally, it was not apparent that the animals were being monitored daily and weighed in accordance with the protocol so the monitoring procedure was reviewed with the investigator and the research staff.

PI took full responsibility, but the PI gave clearly written instructions to the lab member about the Doxil doses and monitoring, which he did not follow.

Moved and seconded: to send a letter of counsel to the PI and investigator.

Discussion: *None*

Vote on the Motion: approved with 14 members in favor.

IACUC protocol 4315-02: The objectives of this study are to discover new treatments for Graft-vs-Host disease.

Scheduling mistakes when collecting LN biopsies for 4 of the animals. Lymph nodes were harvested 2 days after catheter implantation rather than a week. There were no adverse effects to the animals and the protocol has been updated to clarify 2 days between surgeries for biopsies of this nature. In addition there was further clarifying language regarding the days between surgeries and procedures.

Due to management oversight, this was discovered and once discovered, the group immediately reported. PI took full responsibility, apologized, and ensured that they are following the protocol.

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There was discussion around what constitutes an adverse event, and tradeoffs of longer surgeries versus multiple close-spaced ones and their effects on the animals. Also that there are increased oversight mechanisms that have been put in place recently in addition to HoverBoard making many things very visible that were otherwise not as easy to see on the paper

Moved and seconded: to send a letter of acknowledgment to the Investigator.

Discussion: *None*

Vote on the Motion: approved with 14 members in favor.

IACUC protocol 3235-04: Self-reported. Accidentally overdrew this animal today by about 28mls. He had multiple procedures today (blood draw, bone marrow draw, BAL, laparoscopy (MLNs and spleen), peripheral LN biopsy, upper and lower GI biopsies). He received IV (42ml) and subQ (40ml) fluids. Examined by veterinarian after report of blood draw and no additional follow-up was recommended.

The volumes taken are:

10/26/17	11/06/17	11/06/17
41.0	26.5	2.0
Blood	Blood	Bone Marrow

The investigator is usually very careful not to over draw animals, but had forgotten that they had increased his blood draw on 10/26/17 to a max draw at the last minute and it did not get updated correctly in their own tracking spreadsheet. There was also an error in ARMs for the draw on the 26th. There was a double entry so when workflow alerted to more than a 10% draw they originally thought it was due to the error. Hematocrit didn't drop.

Moved and seconded: to send letter of counsel to the PI group asking them how they are going to approach this in the future when there is a flag (how are they going to train personnel) and acknowledging that they self-reported

Discussion: There was discussion around the frequency of adverse events with primates versus other species. Different types of problems occur with different species. The complexity or protocols and oversight of individual animals versus groups all differ. Also, *there is now increased visibility in HoverBoard, increased oversight, and increased discussion.*

Vote on the Motion: approved with 14 members in favor.

Other Business

3328-05 – Biomarkers of Perinatal Asphyxia

Looking at the effects of perinatal asphyxia.

This study is on the final year (year 10). Infants that are born on this protocol are socialized with infants on the IPRL protocol. This socialization is part of the experiment. There are currently no animals on the IPRL protocol and the PI did put in their protocol that animals from the Breeding colony will be used as social partners. Protocol says 3-5 is preferred for social groups.

One experimental animal has survived and is ready for study.

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One partner infant is available. This infant had failure to thrive about a week after birth. Infant was taken from the mother due to scratches found and is now nursery reared and separated from its mother.

Finding another colony infant (to make a group of 3) is the problem. The proposed infant was previously pulled from its mother to be a social partner and was being nursery reared. Then, following 2 experimental animals that did not survive the experiment, the infant was successfully re-introduced back to its mother.

Which brings up the concern that the infant that was successfully re-introduced to its mother, may have to be used as part of the social group. Should it be removed a second time from its mother?

Since this infant has gone back to its mother, separation when it is older can cause many behavioral consequences.

The research group feels that the size of the social group will affect the result for the study if they are left with only 2 animals rather than 3. These animals are on study for 6 months.

Some important questions raised included:

Does the harm that will be done to the infant and mother justify the benefit of having a 3rd animal in the social group?

Does this endanger the clinical study if the investigator does not get this data? How valuable is the social data specifically? Is it a vital outcome measure in the study?

Moved and seconded: to approve removing the infant from its current dam so that there is a social group of 3.

Further Discussion: None

Vote on the Motion: was neither approved nor rejected with 2 members voting in favor, 5 opposed, and 7 abstentions.

Another meeting will be scheduled for December 28th, 2017 to further discuss this issue.

Semiannual Review – LI

- IACUC Functioning

Historically the Office of Animal Welfare has taken care of the semi-annual report and provided it to the IACUC to read and sign before going to the IO. But this is a report to the IO from the IACUC. Last month and this month OAW has presented data to the IACUC to allow IACUC members to have the opportunity to be more responsible for this report.

An overview of IACUC activity over the last six months was posted this month for review. In summary, everyone is contributing.

Historically, non-standard items have been included in the Semi-annual report. A list of what is required versus what has been supplied in the past was posted for review. Does the IACUC want to continue to include this information in the Semi-Annual reports?

Finally, think about what has occurred in the last 6 months that might be considered a Programmatic deficiency that needs to be corrected.

Discussion: The committee discussed the data and provided guidance to OAW on what to include in the report.

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Standard Operation Procedures / Policies / Guidelines

Environmental Enrichment SOP for Dogs – **TB**

Moved and seconded: to approve the SOP.

Discussion: *any discussion/changes/notes*

Vote on the Motion: approved with 13 members in favor and 1 opposed.

Environmental Enrichment SOP for Ferrets – **TB**

Moved and seconded: to approve the SOP.

Discussion: *any discussion/changes/notes*

Vote on the Motion: approved with 13 members in favor and 1 opposed.

Environmental Enrichment SOP for Swine – **TB**

Moved and seconded: to approve the SOP.

Discussion: *any discussion/changes/notes*

Vote on the Motion: approved with 13 members in favor and 1 opposed.

Care and Maintenance of Ferrets – **TB**

Moved and seconded: to approve the SOP with a change to match the enrichment policy (clean toys every 2 weeks not monthly) and disinfecting with clidox or kenesol.

Discussion: *Will collect data on whether or not the wire cage sides are significantly dirtier when it is cleaned once a month rather than once a week. Will bring back data and report back to the IACUC.*

Vote on the Motion: approved with 14 members in favor.

Neuroscience Studies in Non-human Primates – **JFI**

Moved and seconded: to approve the policy, removing the extra apostrophe.

Discussion: *None*

Vote on the Motion: The motion was approved with 13 members voting in favor and 1 member abstaining.

Annual Renewal Policy Proposal– **AS**

Moved and seconded: to approve the policy which no longer requires an annual review for protocols that do not have USDA species or are not DoD funded.

Discussion: *None*

Vote on the Motion: The motion was approved with 13 members voting in favor and 1 member abstaining.

Other Business (cont.)

EH&S Sharps safety – JC

In the area of sharps, is there a way to reduce the use of needles or provide further safety. Keep an eye out for updated signs.

2018 IACUC Regional Educational Conference – TN

NWABR is February 27, 2018 at the Lynnwood Convention Center.

Preconference activity – Bridging the Gap

New Meeting location in January – JS

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Closing Business:

The Meeting was brought to a close at 4:53 pm. The floor was opened to public comment.

Tabled until next regular meeting in January 2018:

Blood Collection in Laboratory Animals – **JFI**

Combination of 2 policies: Blood with drawls and Blood with drawls with mice and rats.

Euthanasia of Research and Teaching Animals – **JFI**

Concern about combining fish with multiple other species. May consider pulling out the section on fish to its own policy and consider incorporating other species into mice and rats.

Can create a table to make it easier to access specific species.

New lab-managed space requests – JS