

University of Washington  
November 15, 2018 IACUC Meeting Minutes

Members Present:    AB                      JM                      MS  
                              AS                      JS                      SH  
                              CG                      KL                      SL  
                              CH                      KS                      TH (remote)  
                              FRR                     LJE  
                              JE                        ML

Members Absent:    JB                      JPVH

### Opening Business

- The IACUC Chair called the meeting to order at 2:32 pm.

### Confirmation of a Quorum and Announcement

- Quorum was confirmed.

### IACUC Training

- **Kidney-on-a-Chip – EK**
  - EK presented on their work, “Kidneys-on-a-chip”.
    - Can help reduce the number of animals needed
    - Can refine animal use via targeted toxicity testing
    - Cannot replace animal use just yet.

### Protocol Review

- AMEND201801394 (4167-01) – **LJE**
  - LJE concerns: number of craniotomies; is there room for three on a monkey skull?
  - Researcher response:
    - Showed a skull and chamber
    - Diameter of chamber is small compared to skull
    - Previous craniotomies heal relatively quickly and healing confirmed prior to placing subsequent chambers
  - Discussion
    - Time for regrowth of bone
    - History of this animal's craniotomies

Motion was made and seconded: To approve the amendment as written.

Discussion: *None*

Vote: Approved with 14 members voting in favor, 0 against, 2 abstentions.

- PROTO201800085 (2448-12) – **LJE**
  - LJE concerns: Why recapitulate a study done elsewhere; why squirrel monkeys?
  - Researcher response:

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- Squirrel monkeys because group has extensive experience, relevant to this gene transfer model, with the species. Integration of the altered gene into the retina has been demonstrated in this species, not in others. Other species would require full development and proving gene integration, thus many more animals and time.
- Recapitulate because funder asking for demonstrated reproducibility at multiple sites/groups. UW will learn techniques from the other site, they will learn techniques from us.
- LJE concern: Lab is hoping to use PRT (positive reinforcement training) to avoid sedation events, but wants approval of sedation/anesthesia in case this is not successful. Does the lab and WaNPRC have the commitment to PRT, and resources to accomplish it?
- Researcher response:
  - KM from WaNPRC showed the training approach to be taken; progressive steps; equal focus on training the trainer as on training the animals; Goal is to give the animal "choice and control", so they chose voluntarily to present for the testing.
  - Current PRT training is going well.
  - Group has key person dedicated to learn and use PRT
  - Because collaborating institution has developed the model, UW will need to conduct fewer aversive tests to show efficacy, making PRT easier to accomplish

Motion was made: To approve the protocol as written.

- Point of order – there are two other outstanding questions from the committee that will require editing of the protocol, so would recommend sending the protocol to designated member review rather than approving as written.

New Motion was made and seconded: To send the protocol to DMR for approval

Discussion: *None*

Vote: Approved with 16 members voting in favor, 0 against, 0 abstentions.

Discussion ensued about making concerns related to FCR items clear to all members ahead of time.

- They should be in the history as comments in HoverBoard. All members should review ahead of time.
- Member presenting the item at the meeting should enumerate concerns – why and what -- up front in their presentation.

### **Approval of the IACUC Meeting Minutes**

- The IACUC Chair called for the approval of the October 18, 2018 meeting minutes.
  - LJE said she felt they did not reflect the tenor of some discussion. No other changes.

Motion was made and seconded: To approve the minutes as written.

Discussion: *None*

Vote: Approved with 11 members voting in favor, 1 against and 4 abstentions.

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### Benefits Story

- This month's benefit story is on the development of a vaccine that protects against breast cancer, and it comes from Dr. Mary Disis' lab in the UW Center for Translational Medicine in Women's Health.

Triple-negative breast cancers are among the most aggressive, and are associated with high relapse rates and low overall survival. The best outcomes have been seen in patients whose own immune systems have kicked in, sending out tumor-infiltrating lymphocytes to target the cancer. Unfortunately, only a small number of triple-negative breast cancer patients end up making enough of these lymphocytes to successfully fight the disease.

The Disis lab is working to develop vaccines that are specifically directed against proteins made by these breast cancers, in order to boost the natural immune response and drive antigen-specific lymphocytes to the tumor.

Using a mouse model, the research team found that vaccines directed against a protein called HIF-1 $\alpha$  significantly enhanced the influx of lymphocytes, and inhibited tumor growth by 83%. Importantly, there was no evidence that the vaccine triggered autoimmune toxicity.

The HIF-1 $\alpha$  protein is expressed at high levels in the vast majority of triple-negative breast cancers. The anti-HIF-1 $\alpha$  vaccine has the potential to be a powerful weapon in our anti-breast cancer arsenal. Building on the success of research in animals, phase I clinical trials will be the next step for bringing this treatment to patients.

*Cecil, Slota, O'Meara, Curtis, Gad, Dang, Herendeen, Rastetter, & Disis 'Immunization against HIF-1 $\alpha$  Inhibits the Growth of Basal Mammary Tumors and Targets Mammary Stem Cells In Vivo' Clinical Cancer Research 23: 3396-3404, 2017.*

### Attending Veterinarian's Report/OAW Director's Report - KS

- Facility issues:
  - Humidity: No items to report
  - Temperature and lights:
    - On 10/29/2018, ARCF, B148D lights did not turn on as scheduled. Issues was resolved that day.
- Protocol Monitoring:

Twenty-one total protocols. Of the protocols, 12 involve surgery, two restraint (and surgery), one conscious restraint, 2 tumor modeling, 4 miscellaneous (tape skirt, infection, water quality). Seven are inactive right now. 1 protocol has been removed from monitoring due to departure of the PI.

Follow up on Protocol 4417-01 last updated at September 2018 meeting: This protocol was added to protocol monitoring at the request of an IACUC member due to conscious restraint during an echocardiograph procedure. It has been previously reported that during the 5-minute procedure, certain strains of mice appear to tolerate the procedure well (no struggling); however, other strains (FVB) do not. FVB are a more aggressive strain in general and their struggling during this procedure may not be purely a sign of distress. The group has put in a significant change to the IACUC to provide scientific justification to perform it without anesthesia or sedation. The

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amendment also clarifies this echocardiography procedure including a description of some acclimation procedures, release of the mice if struggling and return to vivarium until the following day and placing imaged mice in a separate cage so they don't update mice that are still to be imaged. Vet Services will continue to monitor during this procedure including use of an ultrasonic vocalization (USV) detector to see if mice vocalize during this procedure which may or may not be an indicator of distress. That said, one UW PI has used this detector and couldn't detect any USV during fear conditioning. The amendment is currently in committee review.

- *Question re: 4417-01 on Vet Monitoring: Is there PRT for mice?*
  - *Member answers: ML stated that PRT can be challenging in mice compared to other species and that rats are more amendable to it than mice.*
- No Harm Benefit Subcommittee meeting this month.
- Submitted Concern:

A question was submitted to the Concerns email regarding the make-up of the IACUC members. The Chair responded with information that our IACUC meets regulatory requirements, is properly constituted and membership is voluntary.
- Adverse Events:

#1 - On the morning of October 17th approximately 33 sablefish (100% mortality) and 60 coho salmon (85% mortality) died due to a power failure that effected both the seawater and the oxygen supply to the tank water at the NOAA marine station. The likely cause was due to a fault in one of the main breaker panels for the pumps resulting in a power failure. This power failure lead to no circulating water in the tank and no oxygen supplied to the water. A low flow alarm call went out to 4 people, however they either did not get the actual alerts on their phones (due to the power failure) or failed to acknowledge the alerts until hours later. This is the first such incident involving the alarm system. Corrective and prevention measures taken:

  1. The pump power leads and breaker have been replaced as well as new pumps installed.
  2. The air blower system (that supplies added air to the tanks) will be transferred to a separate breaker from the pumps, so oxygen will be supplied if water is temporarily cut off.
  3. More responders have been added to the alarm call list and retrained on how the current alarm system works and how to acknowledge the alarms.
  4. Install a redundant alarm system in the facility (on a different breaker panel) that will monitor water flow as well as water temperature.
  5. Alarm systems will be tested to ensure functionality

**This will be reported to OLAW.**

- *Questions and discussion re: fish deaths when pumps failed*
  - *Will there be retraining, reevaluation of procedures to ensure response when an alarm is received?*
    - *Not a UW facility, so power of UW IACUC unclear*
  - *IACUC would like more detail on how the alarm works and responsibilities to respond*

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- *IACUC should be cognizant of these issues if use of this facility is proposed in the future*

#2 - Flooding of 71 cages at SLU 3.1 on 10/27/18 due to issues with the Automatic Watering System (AWS) resulting in deaths of 1 adult and several litters of mouse pups. At this location, Facilities Management is provided by a vendor under contract with the School of Medicine. On 10/22 there was a low water level alarm and when that issue was addressed a small leak was noted in 1 of the 2 AWS pumps. On the afternoon of Friday, 10/26, without notification to any DCM staff or the vendor supervisor, a vendor Engineer shut off the water supply and the water outlet valves to Pump # 1 when Pump # 2 was running. Shortly after that, the AWS automatically switched to Pump #1 causing a large drop in system pressure and the system alarmed out to both DCM and the Engineers. The Engineers were not familiar with the alarm in question and erroneously checked a different system but did not contact DCM to question the alarm. 12 hours later when the system switched back to Pump #2, the 12 hour pressure loss resulted in leakage through some of the rodent cage water valves, randomly flooding 71 cages. Pump #1 valves were later reopened after their closure was discovered while investigating the cause of the cage floods. The vendor Engineers have been instructed on the importance of informing DCM about all AWS issues and to get approval before any system modifications are made. DCM is in the process of re-evaluating alarming of and alarm response to this system as well as looking into improvements in the specificity of RO system alarms to prevent misinterpretation in the future.

**This will be reported to OLAW.**

- *Questions and discussion re: flooded cages at SLU 3.1*
  - *Timing of when leaks were discovered*
    - *Clarified was per expectation, when next Animal tech crew arrived in the morning*
  - *IACUC wants to register its deep concern about the contracted engineering support at this leased facility*
    - *UW School of Medicine is the lessee; Should start with the SOM facilities head*
    - *IACUC chair and AV to follow up*
- **PI follow-up to adverse event reported at the October IACUC meeting**

In response to the IACUC's Letter of Reprimand for improper euthanasia, the PI responded with a list of corrective actions that have been taken to prevent reoccurrence. The actions include a discussion of the issue with every member of the laboratory; a review of lab personnel training records to ensure that all are fully compliant and current with training requirements; the individual involved has undergone retraining in euthanasia procedures by AUTS; decided that all lab members will now use cervical dislocation as the secondary method for euthanizing mice; and the lab will review their euthanasia procedures annually at a laboratory meeting and maintain a record of attendees.
- *No further action on response to previous letter of reprimand*

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### **WaNPRC ABC Supervisory Veterinarian's Report - TH**

- Facilities items: No items to report.
- Adverse events:

On November 9, 2018 at 6:55 am veterinary services was notified that a 2 year old, female pigtail macaque had her right arm woven through the metal mesh of an indoor enclosure. The animal was promptly sedated and the mesh was cut to free the arm. Radiographs revealed a fracture of the humerus at the location of the proximal growth plate. The animal was started on non-steroid anti-inflammatories, opioid pain relievers, and the arm placed in a sling. The animal moved to a single animal cage and kept under video monitoring and ongoing pain management and supportive care until consultations with other veterinarians and an assessment of the response to anti-inflammatories. The arm remained in a sling with no change in swelling noted on subsequent exams and no movement of the fingers on the affected side occurred.

After discussions with the AV, the assistant director, and clinical veterinarians, euthanasia was considered the most humane option and performed the morning of the 11/13.

**The incident has been reported to OLAW and USDA.**

### **Standard Operation Procedures / Policies / Guidelines – KS**

- Training VVC Designee SOP
- Review and Approval of Protocol Amendments
- Monoclonal Antibody Production via Ascites in Mice
- Permissible Weight Loss in Research Animals
  - *This policy needs work. **Withdraw from slate.***
- Use of Complete Freund's Adjuvant (CFA) and other Adjuvants in Research Animals
  - *Rename to add back in "Polyclonal Antibody Production"*
- Genotyping of Laboratory Mice
- Tumor Growth Monitoring and Endpoint Criteria in Research Animals
- Radio or Audiovisual Use in Animal Rooms
- Rodent Cage Sanitation Frequency

Motion was made and seconded: To approve all as written except as noted above.

Discussion: *None*

Vote: Approved with 16 members voting in favor, 0 against, 0 abstentions.

### **Other Business**

- **Semi-Annual Report – LI**
  - LI will post in December meeting documents the suggestions made in the previous semi-annual report. Please review. Let LI know any data or other information you need to evaluate progress on the suggestions. IACUC will discuss progress at the December meeting, and any new suggestions.

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- **Neuroscience NHP Repair Implant Longevity Subcommittee Report – FRR**
  - Subcommittee has decided initial focus is eye coils. They have identified desired information and are identifying potential data sources for that. Students may be available to do data analysis.
    - FRR trained the IACUC on how an eye coil works and is implanted.
  
- **Feedback on Daily Packets – AS**
  - AS reviewed that to use the new 'in review' reports, you must already be logged into HoverBoard.
  - Discussion: Some members have seen the daily packets as more work
    - OAW will review to ensure no one member is receiving an unfair share of assigned reviews, considering full protocols versus annual renewals and amendments.
  - Members like the new reports.
  - Daily packets are good for the researchers.

The Chair reminded members to send any suggested items for an IACUC meeting to OAW no later than 2:30 pm the preceding Thursday. Include details of what and why. The planning group can then properly assess the proposed items.

**Closing Business:**

The Meeting was brought to a close at 4:49 pm. The floor was opened to public comment.