

University of Washington  
April 18, 2019 IACUC Meeting Minutes

Members Present:    AB                    JE                    KS                    SL  
                          CG                    JPVH                LJE                    TH (remote)  
                          CH                    JS                    \*MB  
                          FRR                KG                    ML

Members Absent:    AS                    JB                    JM                    KL  
                          MS                    SJH                  SRH

\*MB alternate for AS

**Opening Business**

- The IACUC Chair called the meeting to order at 2:30 pm.

**Confirmation of a Quorum and Announcement**

- Quorum was confirmed by KC.

**Protocol Review**

- PROTO201900020 (4465-01) – AS
  - Reason for FCR: Protocol is a new model of aggression for UW and the potential for animals enrolled in these studies to experience pain/distress.  
The goals of this protocol are to understand what brain regions control aggression motivation and the molecular mechanisms underlying this behavior using a mouse model. The initiation of aggression (like starting a fight in response to a threat) and the seeking out of aggression (like choosing to participate in sports such as boxing or mixed-martial arts) are controlled by different parts of the brain.  
This protocol primarily uses two behavioral procedures that the group has previously developed: (1) PTSD-like behavior will be modeled in mice using chronic social defeat stress. In this procedure, mice are paired and allowed to naturally engage in antagonist interaction. After multiple pairings these mice exhibit a constellation of symptoms that are similar to depression and PTSD: anhedonia, social avoidance, and increased general anxiety. (2) To measure the effects of PTSD-like behavior on aggression, mice will also be trained for operant self-administration of aggression, where they can choose to lever press for access to attack a smaller subordinate intruder mouse. Notably, during both procedures, research staff are always present and observing the mice. The procedures are halted at the first sign of injury to either mouse.
  - *PI gave a brief history behind their aggression research that led to the current research focused on PTSD. The IACUC then discussed the issues that may result for the subordinate mouse and the precautions the group is taking to reduce the physical stress as much as possible. The IACUC also discussed and received clarification from the PI on the use of analgesia in the protocol, the look of animals after certain experiments, the frequency of injury, and the study design.*

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Motion was made and seconded: to approve the protocol as written.

Further Discussion: *None*

Vote: Approved with 13 in favor, 1 opposed, none abstaining.

• AMEND201801034 (4266-02) – **JFI**

- Reason for FCR: All 40 animal in the experiment are included in USDA Pain Category E. The goal of this protocol is to use a non-human primate model to develop a vaccine that can protect against both the regular, seasonal strains of influenza and also provide an added level of protection against different strains of influenza, including bird or swine flu, which could cause a pandemic potential in the human population.

The purpose of this experiment is to determine immunogenicity and protective efficacy of two candidate DNA vaccines (UFlu-1, UFlu-2). In a previous experiment these candidate vaccines (UFlu-1 and UFlu-2) protected mice from both a pandemic and seasonal influenza strain. The experimental endpoint of this study assesses the impact of a vaccine in ameliorating or preventing the natural course of an influenza infection. As such, no medications or interventions that reduce symptoms of influenza or antivirals that can interfere with influenza replication or its natural course of disease should be administered.

- *The IACUC discussed the reason for prospectively categorizing these animals as possible Category E, alternative medications that could be used, the monitoring of the animals while on study, the symptoms that the animals experience, and the length of time the animals are singly housed.*

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

Further Discussion: *None*

Vote: Approved with 14 in favor, none opposed, none abstaining.

**Member left at 3:13pm**

**Other Business**

- Primate Zoonoses: Perceived vs. real risk and what this means for animal welfare – LJE
  - *IACUC members and an invited expert presented on the levels of risk associated with various zoonoses between humans and primates, and focused on whether or not unседated animal handling (via positive reinforcement training) is possible with animals that have various infections. The IACUC discussed the risk experienced and perceived by people in various roles, and the IACUC's role in deciding safe handling methods. Positive reinforcement training is being pursued as possible. Ultimately, the precautions that should be taken are determined by Occupational Health and Safety.*

**Approval of the IACUC Meeting Minutes**

- The IACUC Chair called for the approval of the March 21, 2019 meeting minutes. *There were suggested edits to the minutes. Due to these suggested changes, the meeting minutes will be revised and revisited for approval at the next meeting.*

## Benefit Story

This month's benefit story comes from Eva Corey's lab and it's about building a better mouse model to treat prostate cancer. Prostate cancer is responsible for over 30,000 deaths a year in the United States. One of the major challenges for treatment is the heterogeneity of mutations that lead to tumors. Different types of prostate tumors respond differently to different cancer treatments. A better understanding of the different types of prostate tumors will help doctors choose the best treatment option for their patients.

The Corey lab is heading up an international consortium of researchers who are working to develop a collection of mice that have been transplanted with 108 distinct prostate cancers derived from human patients. A crucial improvement is the use of immuno-deficient mice whose bodies do not reject the transplanted cancer tissue. This allows researchers to test the effects of different cancer treatments on different types of tumors in a far more clinically relevant setting than was previously achieved by testing with tumor cell lines grown in petri dishes. Results from mice engrafted with different patient-derived tumors show clear differences in their response to androgen deprivation and chemotherapy, two common treatments for prostate cancer.

These xenografted mice provide a critical platform for understanding prostate cancer biology, and for developing and testing new anti-cancer therapies. By helping doctors to tailor prostate cancer treatments based on the genetic profile of their patient's tumor, Dr. Corey's research holds great promise to speed the delivery of effective treatments that can cure prostate cancer.

'Movember GAP1 PDX project: An international collection of serially transplantable prostate cancer patient-derived xenograft (PDX) models' Navone et al. *The Prostate* **78**: 1262-1282 (2018)

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

- IACUC metrics- see meeting documents
- Reminder: If you are the assigned reviewer on a submission, please add comments/questions within the 7 days period before the DMR assignment occurs and if you are the assigned DMR, please complete your review/approval in a timely manner. Also, all IACUC members are encouraged to review and add comments/questions to any submission. If you have reviewed it (even if you added a reviewer note), please remember to add a private comment so OAW has a sense of how many IACUC members are reviewing submissions.
- HBAS: The sub-committee finished assessing which capture/trapping methods listed on various protocols would be considered prolonged restraint based on our IACUC definition. There is a summary of that assessment in the meeting supporting documents section. HBAS will next be reviewing “Other” procedures to see which, if any, may include prolonged restraint.
- Facility issues:
  - ARCF HVAC in cage wash area: Airflow direction in this area has been a problem in the past. That has been corrected but now there is increased airflow through the tunnel washer that is impacting its ability to consistently reach sanitation temperature. Non-USDA rodent caging is run through the tunnel washer and is always autoclaved prior to use so there is no

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- animal health or rodent biosecurity issue associated with this problem. Estimate at least 2 weeks to fix.
- Follow up on Facility issues identified on inspections: See supporting documents Facility Issues Summary and Details. Some items have been completed since these documents were generated. Larger repairs continued to be delayed.
  - Protocol Monitoring:
    - Twenty-one total protocols. Of the protocols, 13 involve surgery, two restraint (and sx), one conscious restraint, 1 tumor modeling, 4 miscellaneous (tape skirt, infection, water quality). Seven are inactive right now. Added 1 protocol at request of the IACUC at the last meeting. Nothing to report this month.
  - Adverse Events:
    - Follow up from last meeting: On protocol #2225-06, an NHP underwent surgery and died during the recovery period. On the morning of the surgery it was found that the animal had not been fasted due to a miscommunication. The veterinary and surgical teams agreed to delay the procedure for over 1 hour (i.e., an abbreviated fast) and then proceeded, in accordance with the WaNPRC fasting SOP in effect at that time. The surgery was uneventful, but the animal went into respiratory arrest during the recovery period which led to the need for CPR and re-intubation. During CPR, the animal was seen to vomit, and ingesta was aspirated, based on observation of ingesta in the endotracheal tube. The animal was revived and appeared to be recovering but arrested again later and died. Based on the clinical course (timeline), laryngospasm is postulated as the cause of death and the aspiration of food may have been a contributing factor.  
**Corrective Actions:** WaNPRC fasting SOP is being revised to include if an animal is not fasted appropriately, the research procedure will be rescheduled. Any exceptions to proceeding with research procedures must be approved by the Attending Veterinarian or Associate Director, Department of Primate Resources.

**Reported to USDA and OLAW.**

*The IACUC discussed the animal's previous surgical history and received explanation of "laryngospasms".*

- There was an incident of diversion of a controlled substance at the Primate Center that led to one NHP receiving less than optimum dosing of an opioid analgesic during clinical treatment. After the diversion was discovered the drug vial was analyzed and the drug was found to have been diluted. The animal did receive other pain relievers and did not appear clinically painful during that time and recovered uneventfully. The employee involved in the incident has been terminated from employment. This drug has been transferred to a central safe with limited access and is not in the lock box at the individual facilities. If an animal needs the medication, aliquots are taken out to do the treatments.

**Reported to DEA, USDA and OLAW.**

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- Follow up from last month: In the past several months, there have been several mortality reports where mice were found dead in a cage without food. In some of cases, it's not clear how long they were without food and whether the lack of food was the specific cause of death. The cases have occurred in the same facility but in a couple of different rooms and involved different lab groups so the exact cause of the lack of food in these cages is not clear cut. It doesn't appear to be an issue with visualizing the food levels in the cage. These incidents seem to occur over weekends when fewer staff are working but they still need to do daily checks on all cages in the facility. Vet Services and DCM facility managers have discussed with husbandry staff, the importance of filling feed hoppers with enough food and checking for adequate amounts of food in the hopper on daily checks. In the last month, there has been 1 new report of a cage found without food in this same facility. In this case, a research group member who weaned some mice did not add food to the cage. The weaning was done prior to a weekend and on following Monday, one of two mice were found dead. It is not clear if lack of food was the cause of death in this case. The research group acknowledges the mistake and understands the importance of double-checking that feed is present when weaning cages. DCM will continue to closely monitor these types of incidents and identify contributing factor(s).

*Some IACUC members wondered whether staffing might be a factor. The AV will report back next meeting should this continue to be an issue.*

- Back in January 2019, it was reported to the IACUC that a rack in the ARCF had a disconnected water line that led to mortalities. Another incident occurred in March in the same room but a different rack location. Some mice were affected and treated but no mortalities occurred. Vet Services, DCM management and husbandry staff have been looking into the cause of these 2 occurrences and determined that at least one cause may be the top of rack jarring the water supply line quick disconnect connection at the wall, which in turn causes the line to dislodge and no water goes into the rack.  
**Corrective action:** ATs have been moving the racks away from the walls several inches and locking the rack wheels in place to prevent the racks from getting too close to the water lines on the wall. ATs have been trained to look along the wall behind the rack to ensure that the water line quick disconnect is still connected to the supply line on the wall. DCM is also working on possible fixes with the rack vendor or physical plant personnel to modify the connection of the rack to the automated water supply on the wall.
- In a centrally managed zebrafish facility, 263 zebrafish were found dead in a system that houses about 5500 fish. System maintenance was done the previous afternoon where crumbled and broken smaller sized activated carbon was used to fill system filters instead of larger sized pelleted carbon. Because the filter pore size was larger than the size of the crumbled carbon, the carbon was not contained within the filter and was distributed throughout the recirculating system. All disposable filters were immediately changed or replaced and plans were initiated to siphon these particulates from the system. The next day there were an additional 11 mortalities on the same system. These deaths were believed to be associated with an observed low level gas super saturation traced back to a three-way valve that failed to close completely and allowed air entrainment into the rack supply line from the back-up pump water supply line. The cause of the mortality is most likely

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mechanical asphyxiation associated with exposure to fine carbon dust dissolved in the water, in addition to the low level gas super saturation.

**Corrective actions:** Staff that performed system maintenance have been re-trained. Also, the back-up pump was removed from the system and that pump supply line was capped. Plans are being made to determine how best to remove/repair the inadequate sealing three-way valve.

**Will be reported to OLAW.**

- Non-compliance:

- **Protocol non-compliance on 4356-01:**

During surgical certification of a lab member, it was noted that several aspects of the rodent head plate placement procedure were not being performed by lab members as described in the protocol. These included no usage of a local analgesic at the incision site, incorrect timing of administration of first dose of systemic analgesia, no prophylactic use of antibiotic (although it is generally not required for this type of procedure) and use of a different type of glue to secure the plate. It was also noted that the duration of post-operative analgesia was unclear for this procedure. It is unclear whether these issues led to increased pain or distress to these animals but the lab group was not following their protocol.

**Corrective action:** Acquire and use local analgesic and amend the protocol to change prophylactic antibiotic use to optional, clarify the analgesic regimen and clarify type of surgical glue to be used.

**Reported to OLAW**

Motion was made and seconded: to send a letter of counsel.

Discussion: *Letter of counsel was chosen over reprimand because it is not known if there was any added pain or distress to the animals and the protocol was not clear. The PI was very responsive as soon as he heard of the report.*

Vote: Approved with 13 in favor, none opposed, none abstaining.

- From Arizona - **TH**

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

### **IACUC Training**

- How OAW handles Annual Reviews – **KS**

- *The AV gave a quick presentation on how Annual Reviews are done, including pre-review within OAW, veterinary review, and the IACUC's review. The AV emphasized where to find related concerns and husbandry exceptions for protocols and reminded members to review these during each annual review.*

### **Closing Business:**

The Meeting was brought to a close at 5:01 pm. The floor was opened to public comment.