

University of Washington
August 15th, 2019 IACUC Meeting Minutes

Members Present:	AB	JM	MK (remote)	TH (remote)
	AS	JPVH	ML	*CB
	CG	JS	SJH	
	CH	KG	SL	
	FRR	KS	SRH (remote)	

Members Absent: JE KL JB

*CB alternate for JE

Opening Business

- The IACUC Chair called the meeting to order at 2:34 pm.

Confirmation of a Quorum and Announcement

- Quorum was confirmed by JS.

IACUC Training

- Singly housed rodents without SSRs – **KS**
 - *KS gave a training on SSRs and husbandry exceptions. IACUC doesn't have responsibility around whether a Special Service Request (SSR) is in place for any husbandry exception. So when an IACUC visitor notes a lot of singly housed animals from a specific PI, then they can look to see if there's a SSR in the room to explain that singly housing. But if there is no SSR, they should note the protocol number and OAW can check to see if there's an IACUC approved husbandry exception..*

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the July 18, 2019 meeting minutes.
Motion was made and seconded: to approve the minutes as written.
Discussion: None
Vote: Approved with 15 members voting in favor, 0 against and 2 abstentions.

Benefit Story

- This month's Benefit Story comes from the Oberst lab, and it's about developing a new kind of treatment for solid tumors that boosts the body's own immune system response to help fight off cancer. Using mouse models, the Oberst group has discovered that they can trigger a robust immune response targeting tumor cells when they inject dying cells into the center of a tumorous mass. The dying cells send out a signal that acts like a beacon for resident immune cells to come charging in to the tumor to clean up the mess.

Because of the way the immune system works, the immune cells that enter the tumor mass in response to the dying cells end up programmed to destroy the previously thriving tumor cells. The dying cells do not need to be cancerous themselves to trigger this response. Once programmed to destroy the local tumor cells, the

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activated immune cells can move throughout the body to systemically attack any tumor cells that have metastasized.

Once the Oberst research team had identified the signaling pathway that was responsible for programming the tumor-targeted immune cells, they set out to find a way to turn it on without having to inject dying cells into a tumor mass. They determined that they could elicit the same anti-tumor immune response using a gene therapy-like approach, where genetically engineered virus is injected into the tumor to trigger the death of a sub-population of tumor cells. These dying tumor cells then send out the call for resident immune cells to come and destroy both thriving and dying tumor cells.

Although more testing is needed before this treatment can be translated to a clinical setting, anti-tumor immunotherapy holds promise for expanding the arsenal of weapons that can be deployed in the fight against cancer.

Snyder AG, Hubbard NW, Messmer MN, Kofman SB, Hagan CE, Orozco SL, Chiang K, Daniels BP, Baker D, Oberst A. Intratumoral activation of the necroptotic pathway components RIPK1 and RIPK3 potentiates antitumor immunity. *Sci Immunol.* 4: eaaw2004 (2019).

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

- Congratulations to 3 of our clinical veterinarians who just passed the American College of Laboratory Animal Medicine (ACLAM) board exam and are now certified as veterinary specialists in lab animal medicine. There are 6 ACLAM boarded vets in DCM, 3 in WaNPRC and 1 in OAW.
- HBAS: Subcommittee finished the assessment of "Other" procedures listed on various protocols to determine if they would be considered prolonged restraint based on our IACUC definition. See supporting documents for a summary.
- IACUC metrics- see meeting documents
- Facility issues: None
- 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.
 - Update on 3235-04, Cell and Gene Therapy for HIV Cure. In 1 of the current studies, 4 primates received an infusion of a high number of modified CAR-T cells. High numbers of CAR-T cells can induce what is called cytokine release syndrome (also called a cytokine storm) which is a massive systemic inflammatory response that can be triggered by a variety of factors such as infections and certain drugs and can be fatal. So these animals were treated with an immunosuppressive drug after the infusion to try to block that reaction. The next day, 2 of the 4 animals developed respiratory difficulties that did not improve despite treatment and supportive care, and they were euthanized. The remaining 2 animals were put on additional immunomodulating drugs to block a specific cytokine that appears to be a key mediator of this syndrome and were closely monitored. 1 additional animal developed similar clinical signs 2 days later and also had to be euthanized. The remaining animal has

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done very well and remains healthy. The research group (including the PI), WaNPRC veterinarians including the Associate Director and attending veterinarian met to discuss the situation and strategies for prevention of similar occurrences. To decrease the risk of a cytokine storm in future studies, the research group will modify the mixture of cells and lower the number of cells infused, and place the animals prophylactically on immunomodulating drugs.

- Follow up from March 2019 meeting:
 - There have been no additional incidences of mortality associated with mice being found without feed in the cages. DCM has done re-training of animal techs with emphasis on checking for feed levels during daily cage checks. The AUTS group is also developing on-line training to cover topics such as checking for feed and water which will be included as part of facility orientations as well as used for re-training purposes.

- Adverse Events:
 - 3057-01: A cohort of ten mice received an IP injection with either vehicle or compound suspended in vehicle. Within 30 minutes of the injection, the mice were noted by the investigator to be lethargic, however, they recovered and appeared normal. The next morning, seven mice were found dead by the animal technician– four of five vehicle injected mice and three of five compound injected mice. The three surviving mice were lethargic and poorly-responsive so the investigator elected to euthanize. After reviewing the records, the investigator determined that the experimental solutions were inadvertently diluted directly into vehicle rather than into saline. As a result, these mice received a highly concentrated, alkaline vehicle fraction and that is believed to be the cause of the morbidity/mortality based on histopathology. On discovering this miscalculation, the investigator promptly reported the mistake to VS and said that they will make sure that this oversight does not happen in the future.

Reported to OLAW.

Motion was made and seconded: to send a letter of Acknowledgement to the group.

Discussion: *There is concern regarding the personnel who did not dilute the compound properly. The letter of acknowledgement will ask the group to describe the corrective actions that have been taken.*

Vote: Approved with 16 members voting in favor, 1 against and 0 abstentions.

- 4450-01: Two female mice with litters of different aged pups were co-housed in a cage. The mother of the older litter (15 day old pups) was removed by the research group for set up in a breeder cage. So only 1 dam was in the cage with 2 litters. 2 days later, around 7:00 pm, the remaining dam was found dead in cage by the research group, with all pups reportedly alive. The female's body was removed, a foster dam was not able to be found for the pups, and Veterinary Services was not notified of the dead animal. The following morning, husbandry staff found the cage and reported it to Veterinary Services. At that time, all 12/12 of the younger (11 days old) pups were found dead. 4/4 of the older (17 day old) were alive, but hunched, and immediately given dietary gel and soft food. A member of the research group elected to euthanize them later that morning.

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Corrective Action: An in-person meeting was held with the two research scientists most immediately involved with the animals. At the meeting, it was re-iterated that sick and dead animal reports must be submitted immediately, and the on-call veterinarian paged after hours, especially in cases of orphaned pups with no mother. It was also emphasized mice pups should be weaned around 21 days of age, and that if early weaning is necessary, an IACUC amendment should be submitted in consultation with Veterinary Services. Additionally, the IACUC policy on the number of animals maintained in a breeding cage was reviewed, and sent electronically to the group members. The group members present at the meeting agreed to share these recommendations with the rest of their team members.

Reported to OLAW.

There were multiple things that went wrong in this situation, and it seems that the group did not think through the consequences of the choices they made. The group has not had other issues with mortality but has had other issues.

Motion was made and seconded: to send a letter of reprimand to the group.

Discussion: None

Vote: Approved with 14 members voting in favor, 3 against and 0 abstentions.

- DCM AT was delivering 3 rodent shipping boxes of newly arrived rats from the 6th floor to the T-wing on the same cart as some water bottles that required autoclaving. As per DCM standard practice, the entire contents of the cart was covered with a blue transport drape and then the cart went down in the elevator to the T-Wing animal facility. Upon arrival at the T-wing autoclave area, the AT was interrupted by a researcher and left the room to provide assistance. Upon returning to the wash area, the AT rolled the cart into the autoclave and started it. The AT quickly realized that the rats were still on the cart and shut down the autoclave but the animals were dead.

Corrective Action: In response to this incident, the following changes in procedure will be implemented by DCM. Animals will be moved on a designated “Animal Only” cart by DCM personnel between 6th floor and T-wing, incoming animals will be delivered and received in the T-wing and no longer on the 6th floor, increased signage will be posted and training implemented for aborting autoclave loads, and all individuals working in cage washes will be retrained to check the carts and remove any extra drapes prior to placing a cart in the autoclave. The animal technician involved received final counseling with a performance plan.

Reported to OLAW.

This individual has been working at the UW for 15 years and was devastated by the incident. They have met with their supervisors and HR about this incident. They have also been directed to the Compassion Fatigue program for additional help.

A statement describing the incident, corrective actions being taken, and expressing regret for the deaths of these animals has been drafted by the UW communication team and they are determining the best place to post the statement.

Member left at 3:45

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Motion was made and seconded: to send a letter of concern to DCM, asking them to reply with updates on their corrective action plan.

Discussion: *The letter should include an acknowledgement regarding the individual's work dedication and encourage them to reach out to the Compassion Fatigue program.*

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

- WaNPRC ABC Supervisory Veterinarian's Report - **TH**
 - Facilities items: On July 19th, ABC Facilities was alerted that the upstairs misters, which cool some of the outdoor enclosures, were leaking. Facilities responded immediately and replaced the nozzles for this section of misters.
 - Adverse events: No adverse events to report.

Other Business

- Letter of Commendation – **JS**
 - *During a site visit, the IACUC member saw that the animals in a particular tech's room were calm and most were successfully co-housed. The tech also works to challenge the animals intellectually and provide them enrichment. This shows that the animal tech is giving extra effort to ensure the highest care and wellbeing of the animals.*

Motion was made and seconded: to send a letter of commendation to the animal tech.

Discussion: *none*

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

- Rodent Environmental Enrichment SOPs– **KS**
 - *DCM would like to add to the SOPs that the cardboard tubes will be discarded every 2 weeks or once heavily soiled.*

Motion was made and seconded: to update the EE SOPs with change noted above for mice, rats, gerbils, guinea pigs, and hamsters.

Discussion: *None*

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

Closing Business:

The Meeting was brought to a close at 3:55 pm. The floor was opened to public comment.