

University of Washington
March 21, 2019 IACUC Meeting Minutes

Members Present:	AB	JPVH	ML
	AS	JS	MS
	CH	KG	SRH (remote)
	FRR	KL (entered at 3:09 pm)	SL
	JE	KS	TH (remote)
	JM	LJE	
Members Absent:	JB	CG	SJH

Opening Business

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

Confirmation of a Quorum and Announcement

- Quorum was confirmed by KC.

Protocol Review

- PROTO201800108 (4459-01) – **JFI**
 - Reason for FCR: Discuss the harm vs benefit of this new protocol on which animals are categorized as pain category E.
 - The objective of this proposal is to study the neuroprotective effects of therapeutic hypothermia with and without human neural stem cell therapy in a rat model of neonatal hypoxic ischemic injury (HII). HII remains a devastating and common injury, and the only current evidence-based treatment option is whole body hypothermia, which has become standard of care. However, hypothermia is ineffective in severe HII, illustrating the need for a more targeted treatment modality. Under this protocol, local analgesics are provided at the time of surgery, but the animals receive no systemic or post-operative analgesia because analgesics may have neuroprotective or neurotoxic properties that would confound the results. Thus, all experimental animals on this protocol are categorized as Pain Category E.

The IACUC discussed the addition of buprenorphine to the protocol and the decision to use at the time of treatment.

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

Discussion: *any discussion/changes/notes*

Vote: Approved with 16 members voting in favor.

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- TR201900015 (4165-02) – **KSH**
 - Reason for FCR: Concern regarding the number of sedation events.
 - Zika virus is a mosquito-borne virus that's found in Africa and Asia that prior to 2007 had only been documented and reported in 14 cases. Infected travelers have now introduced Zika virus to at least 20 countries. A precipitous increase in a birth defect called microcephaly (meaning small head) occurred simultaneous to the Zika virus epidemic and is strongly linked to the viral infection. The goals of the project are to establish the following:
 1. Determine the mechanism of fetal brain injury in order to design therapeutics to minimize injury.
 2. Determine the spectrum of fetal injury beyond the brain (e.g. eye, hearing)
 3. Test therapeutics and vaccines to block maternal-fetal transmission of Zika virus.

The PI added the following comment to her protocol today, which states "In consultation with veterinary staff, I would like to add language to my protocol that if there are veterinary concerns with the number of sedations, then we won't sedate the animal until cleared by veterinary staff."

The IACUC discussed the number of sedation events, as well as the use of positive reinforcement training (PRT) that is describe in the protocol, with an understanding that there needs to be an alternate option to PRT in the event an animal does not train well. There was also discussion in regards to the chosen species for this project.

Motion was made and seconded: to approve the triennial with the folding conditional statement incorporated into the protocol:

"In consultation with veterinary staff, I would like to add language to my protocol that if there are veterinary concerns with the number of sedations, then we won't sedate the animal until cleared by veterinary staff".

Discussion: None

Vote: Approved with 15 members voting in favor, and 1 against.

- AMEND201801558 (3328-07) – **AS**
 - Reason for FCR: Intensity of the new model being proposed.
 - The goal of this protocol is to evaluate treatments for neonatal brain injury. In particular, the group studies perinatal asphyxia, which is defined as a critical lack of oxygen and blood flow to the fetal brain during labor and delivery. Treatment options for perinatal asphyxia are limited.

To simulate neonatal brain injury, ferret kits will be administered an agent to induce an inflammatory response and then undergo a survival surgery. Kits receive one dose of systemic analgesia just prior to surgery, and one dose of local analgesic during the surgery. To simulate adult brain injury, kits will experience a traumatic brain injury produced by CHIMERA (which is a piece of equipment that allows for a precisely controlled closed head impact to be delivered). Animals will undergo up to 5 exposures to traumatic brain injury,

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spaced one day or up to 1-2 weeks apart. Animals will be anesthetized during this procedure and will receive systemic analgesia following each exposure. Behavioral testing will be performed at several time points throughout the study to evaluate various motor and gait characteristics and memory.

MEMBER ENTERED AT 3:09PM

The IACUC discussed concerns regarding some of the behavioral tests being done with the ferrets and the adult CHIMERA optimizations, as well as the enrichment exception that is in the protocol. Additionally, there was clarification given in regards to the purpose of the “Ligation Repair” surgery that is proposed in the amendment.

Motion was made and seconded: to send the amendment to DMR with the following changes:
Put on Vet monitoring for the Morris water maze and the CHIMERA optimization.
Remove environmental enrichment husbandry exemption on exp. 4.
Better description of Artery Ligation repair surgery and limit to the duration that this can occur after surgery.
Optimization of CHIMERA called out as a separate experiment.
Modification or removal of experiment 5

Discussion: None

Vote: Approved with 17 members voting in favor.

- PROTO201800096 (4458-01) – AS
 - Reason for FCR: Harm Benefit considerations of this new protocol proposing use of animals in surgical training, when this surgery program has used non-animal alternatives for the past four years.
 - The goal of this protocol is to provide a realistic training environment for surgeons and surgical residents in a variety of surgical procedures, techniques and new technology, to increase their surgical skill level prior to using these techniques in the operating room on humans. Due to a lack of funding pigs have not been used by this surgical program since 2014, however new sources of funding have become available.
 - Pigs on this protocol will be deeply anesthetized and then undergo a terminal surgery. The particular procedures that are performed during the terminal surgery vary based on student need, but include laparoscopic abdominal surgeries, open abdominal surgeries, video-assisted thoracic surgeries, open thoracic surgeries and neurosurgeries that involve either the cranium or spinal column. Animals are euthanized at the end of the terminal surgery. Blood or tissue samples may also be collected just prior to or after euthanasia for analysis.

The IACUC discussed the pros and cons of the use of animals for surgical training compared to the use of inanimate models. The PI had indicated that the use of animals was a standard practice in the past and is beginning to come back due to the lack of experience residents feel they have prior to entering the operating room; data to support this was not presented, nor were data that show that inanimate models result in less competent surgeons.

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The IACUC also discussed the purpose of this protocol in training advanced, experienced surgical residents specifically in laparoscopic abdominal surgeries as these are not surgeries that are done regularly.

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

Discussion: *None*

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

- AMEND201900139 (2225-06) – **KSH**
 - Reason for FCR: research group wants to make the changes within the next couple weeks.
 - This research group is evaluating the potential of human embryonic stem cell-derived/induced pluripotent stem cell-derived cardiomyocytes (hESC/iPSC-CM) as a new treatment to restore heart function in patients with heart disease. They use non-human primate models to study the efficacy and side effects of their cell product and investigate a clinically relevant cell delivery method. Immunosuppressive regimens necessary for the cell product are studied in an allogeneic transplant model in non-human primates that either receive a myocardial infarction or are un-infarcted.
 - Modifications requested in this Amendment:
 - Experiment 005. Allogeneic Transplant Study
 1. Change the immunosuppression regimen to be tested, as they would like to test low immunosuppression because the rejection of the wildtype cells in non-immunosuppressed animals was mild.
 2. Add an option not to perform myocardial infarction, as the primary goal of the experiment is to assess engraftment of the cells under different immunosuppression regimens and not efficacy. The change is proposed to simplify the experiment to accelerate the study.
 3. Add an option to not implant the venous catheter/telemetry system, when it is not necessary for drug administration or blood draw, which depends on the selected immunosuppressive regimens.
 - Experiments 001-005:
 4. Add description of defibrillation procedure

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

Discussion: *None*

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

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the February 21, 2019 meeting minutes.
 - Motion was made and seconded: to approve the minutes as written.
 - Discussion: *None*
 - Vote: Approved with 15 members voting in favor and 2 abstentions.

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

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- Adoption of 1 dog – This dog was a member of the canine myotubular myopathy (XLMTM) colony and she was adopted by a family that includes a young boy with human myotubular myopathy. The family previously adopted another XLMTM dog.
- HBAS: The sub-committee started assessing which capture/trapping methods listed on various protocols would be considered prolonged restraint based on our IACUC definition. That assessment is on-going and will be shared with the full committee when completed.
- IACUC metrics- see meeting documents
- Facility issues:
 - Humidity:
 - With the unseasonably cold winter in February, low humidity has been seen in several facilities. There were a few cases of bloody noses in non-human primates. Also, there was one cage of 14 day old mouse pups where some had ringtail (tail constrictions) which can be due to low humidity. Humidity in the room was 15-20% but in the cage itself, it would probably be higher. Ringtail is rarely seen in rodent facilities even when there is low humidity.
 - Temperature and lights:
 - 2 separate lighting malfunctions at SLU. One was due to a lighting system programming change over to Daylight Savings Time and the other due to a wiring disconnection. Both issues were discovered and fixed within 24 hours.
- Protocol Monitoring:
 - Twenty total protocols. Of the protocols, 13 involve surgery, two restraint (and sx), 1 tumor modeling, 4 miscellaneous (tape skirt, infection, water quality). Seven are inactive right now.
 - One protocol was added at the request of the IACUC at last month's meeting. Two protocols have now been removed from monitoring. One of them (4265-01) involved aseptic technique during surgery and there have been no issues noted with recent surgeries done by the group. The other (4417-01) involved the use of conscious restraint during mouse echocardiograms. Duration of the procedure is less than 5 minutes. Monitoring during the procedure for ultrasonic vocalizations (which can be an indicator of stress) showed no vocalization occurred as well as the mice were not seen to be struggling. In addition, the research group is breeding their mice onto a calmer background strain and thus, these mice will probably be less stressed during the procedure.
- Adverse Events:
 - From August 2018; Protocol 3042-12: At Western Fisheries, 10/20 juvenile rainbow trout in one of 16 tanks were found dead. Fish were on study but the cause of the mortality was believed to be due to a clog in the inflow valve which led to no water inflow into that tank. Dissolved oxygen was likely low in the tank and is the presumptive cause of mortality.
Corrective actions taken: The group plans to scrub inflow pipe, and clear inflow valves and lines prior to experiments in the future. Also to avoid future clogs new valves have been

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installed where clogs have been noted, and "Y" filters have been ordered to provide a pre-filtration step for inflow lines. Recommend Letter of Acknowledgment

This was self-reported.

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

Discussion: *None*

Vote: Approved with 17 members voting in favor.

- There was a non-human primate that unfortunately died during recovery from surgery. We are still awaiting the histopathology report so more information will be provided at the next meeting when we have that information.
- 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. Root cause analysis is on-going and DCM management has been re-training animal technicians on assessing food levels during daily checks. I will follow up with more information as we investigate this issue further.
- Non-compliance:
 - Protocol 3278-01: Mice were dosed via a route of administration that was not listed on the protocol. 6 out of 8 mice that were dosed either died or were euthanized due to poor condition. Histopathology lesions may support an anaphylactoid response, but the literature describes that compound being dosed via that route without issues. The group member mistakenly thought they could dose via that route and the lab has no plans to change their protocol to dose this compound via another route.

Will report to OLAW. Letter of Acknowledgement.

This was self-reported.

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

Discussion: *discussion/changes/notes*

Vote: Approved with 17 members voting in favor.

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

Standard Operation Procedures / Policies / Guidelines

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- Number of Mice Maintained in a Breeding Cage – **KS**
 - *Removed some background information from policy and put on FAQ.*
 - *Make sure the FAQ and policy are consistent.*

Motion was made and seconded: to approve the policy with the removal of the redundancy regarding posting responsibility.

Discussion: *None*

Vote: Approved with 17 members voting in favor.

Other Business

- Update on Pain/Distress Guidance from Other Institutions – **AS**
- List of Criteria that automatically route a protocol/amendment to FCR – **LJE**
 - *The IACUC discussed the pros and cons of having set criteria for FCR's.*

Closing Business:

The Meeting was brought to a close at 4:52 pm. The floor was opened to public comment.