University of Washington
MAY 18, 2023 IACUC Meeting Minutes

Members Present:		ES	KG	MRB
	AB	GL		
	AP	JFI	MB	SP
	CC	JPVH	MK - 2:41	
		JS		
	DT			
Members Absent:		DM		
	MRK	GS		
	AW	MS		

Opening Business

- The Floor was opened for public comment at 2:30 pm.
- The IACUC Chair called the meeting to order at 2:39 pm.

Confirmation of a Quorum and Announcement

- Quorum was confirmed by ZR.

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the April 20, 2023 meeting minutes.
  Motion was made and seconded: to approve the minutes as written.
  Further Discussion: *none*
  Vote: Approved with 10 members voting in favor, 0 against and 2 abstentions.

Benefit Story

This month's benefit story highlights two of the three Rs, Replacement and Reduction, in the development of new tools for the treatment of brain diseases.

Although it isn't obvious looking at it, the brain is made up of a multitude of different subtypes of neurons. Many brain diseases are the result of one subtype of neuron becoming dysfunctional. For example, Parkinson's disease is caused by the death of dopaminergic neurons in a part of the brain called the substantia nigra, while ALS is caused by degeneration of motor neurons in a different part of the brain. It would be great if gene therapies could be developed to selectively target subtypes of neurons that are at risk in these and other brain diseases.

A critical element to the success of this plan is the identification of stretches of genetic code that are uniquely turned on in specific subtypes of cells in specific parts of the human brain. Researchers at the UW Primate Center have now teamed up with the Allen Institute for Brain Science to do just that. They began their experiments in mice and identified multiple stretches of

human DNA sequence that preferentially activate specific subtypes of neurons whose dysfunction in humans is thought to play a role in epilepsy, schizophrenia and Alzheimer's disease. After narrowing down their candidates from 20 to 5 DNA sequences by testing in mice, the researchers were ready to test the specificity in primates, both human and non-human.

In the next phase of the experiment, researchers injected these 5 DNA sequences into three monkeys and confirmed that they worked as they did in mice. While this cross-species validation was extremely important, further testing on an increased sample size was needed.

To reduce the number of monkeys used, the researchers turned to our UW Primate Center's Tissue Distribution Program. Although the name may sound a little cold, this program is an amazing resource that maximizes what we can learn from each individual animal by sharing all the different parts of the body with different research teams, not unlike organ donation programs for humans. By performing additional follow-up studies in long-term cultures of brain slices obtained from the Primate Center's Tissue Distribution Program, the researchers were able to minimize the number of animals needed to test candidate DNA sequences prior to testing in human brain. In the final phase of the experiment, the most promising DNA sequences were tested in long-term cultures of brain tissue obtained from human patients undergoing surgery to treat epilepsy or cancer. The DNA sequences that showed high specificity for the target subtype of neuron in human tissue can now be used to develop new treatments for a variety of brain diseases.

Mich et al. 'Functional enhancer elements drive subclass-selective expression from mouse to primate neocortex' Cell Rep. (2021)

Attending Veterinarian's Report – CC

· I have checked with the leadership at all sites and have no reportable facility events for the committee at this time.

Update on Protocol Monitoring: We now have a total of 25 protocols with ongoing enhanced monitoring. Of these 25 protocols, 9 protocols are actively performing the procedure for which they are on monitoring. All of the PIs continue to work closely with the veterinarians and the procedures are all going well at this time without any unexpected complications.

OAW Director's Report – JFI

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IACUC metrics – The metrics are posted under Supporting Documents in the meeting folder

Training Updates – A new lesson has been published called "ABSL-2: Dirty Cage Handling and Bagging". It is required training for all new ABSL-2 researchers. This lesson has been added to the course "Animal Facility Online Learning Course with ABSL-2." We published a Navigator News article earlier this month that links to the lesson so that researchers that have previously completed facility orientations get the new messaging. The lesson was created to address handling dirty cages before they reach the cage wash, to help ensure the safety of cage wash staff. The lesson was deployed with facility signs to ensure consistent messaging and visuals.

We also made available new videos that talked about the Refined Mouse Handing workshop that UW hosted with the "Three Rs Consortium" on March 1st. We had representatives from multiple institutions from the Seattle region learn about the research that has shown this to be a less stressful way of handling mice.

Responses to Letters & Other Follow up –

In March an adverse event was reported to the IACUC in which a nonhuman primate sustained an injury to the cerebral tissue during placement of a recording device. The IACUC voted to send a letter of reprimand, including requesting additional detail about the PI's training process for new lab members, documentation methods for training, and objective measurements that can be implemented to prevent a similar occurrence. The PI responded to each of these specific requests. They described a 3-step process for training that begins with shadowing, followed by performing procedures while supervised and with verbal instruction, and then performing procedures while supervised but without verbal instruction unless necessary. Once the individual can perform the procedure without requiring correction, they are considered proficient. Training will be documented and made available during site visits if requested. For objective measurements, the distance between the top of the recording chamber and the surface of the underlying tissue will be measured and the cannula must be retracted to above this point prior to positioning. This has been added to a checklist that is affixed to the experimental set-up.

No additional action asked for by the Committee.

In February a noncompliance was reported to the IACUC in which an investigator had mice that were up to 3 years of age, which is significantly beyond the age approved in the protocol, and they had also not been monitoring their mice as described in the protocol. The IACUC voted to send the PI a letter of reprimand, with specific request for them to describe corrective actions that are being taken to prevent recurrence. The PI responded describing that they (the PI) had sustained a serious injury in late 2021 that left them unable to perform the planned experiments or monitor their colony, and that they were in regular phone contact with DCM staff to ensure their animals were monitored and treated appropriately. The PI described their corrective actions as including hiring a new lab manager, and amending their protocol to cover the unexpected event where no lab staff are available to monitor the colony.

Questions/Discussion: *The IACUC discussed that it was a very long period that the mice were not monitored by the research team; discussed that the PI did not adequately acknowledge the significance of the noncompliance, their responsibility for monitoring the animals, or provide a convincing corrective action plan; Could we put protocol on monitoring? There are no animals actively on protocol; Would a Liaison collaboration be helpful? There has been communication with Liaison; discussed age endpoints, OAW will review the protocol and ask for additional clarification around age endpoints if needed; Were able to find another lab who could utilize the animals in research*

Motion was made and seconded: to send a Follow-up letter to PI
Further Discussion: s*uggest that they continue working with their OAW liaison*
Vote: Approved with 14 members voting in favor, 0 against and 0 abstentions.

Noncompliance –
2153-08
In January 2023, 8 mice were enrolled in an experiment to determine if certain kappa opioid receptor antagonists are long lasting, which is key to understanding the clinical utility of these antagonists (like naltrexone) in the treatment of substance use disorders. As part of the January experiment, all mice received daily IP injections of the kappa opioid agonist nalfurafine for 7 days, with assays performed before and after to evaluate effect. At the planned experimental endpoint, the mice were euthanized. Though the general sequence of events in this study was approved on the protocol, the specific drug being evaluated in this group of mice (nalfurafine) was not approved for use on this study.

In April 2023, when the group became aware of this oversight, they immediately submitted an amendment to add this group to the study. As additional corrective actions, the research group has refined their experiment preparation process to include a second check of the protocol by the lab manager. When getting ready to start an experiment, the individual conducting the experiment will now notify the lab manager, identifying specifically where in the protocol their experiment is described, and the lab manager will confirm that the study is described in the protocol. Additionally, during amendment writing, all investigators will now be asked to review the experiments they intend to perform to ensure that the full scope of the study is captured within the amendment.
This has been reported to OLAW.

Questions/Discussion: *How big is this protocol? Very large; discussed ways of making the protocol easier to follow, such as splitting it into multiple protocols or approving drugs by class if appropriate rather than specific compounds; suggest they continue working with OAW liaison;*

; animal impact was low; discussed a possible double-check mechanism, and that group has already instituted a second check by the lab manager.

Motion was made and seconded: to send a Letter of Counsel.
Further Discussion: *include suggestions about how to prevent this moving forward - e.g., confirming that there's a double-check by the lab manager.*
Vote: Approved with 14 members voting in favor, 0 against, 0 abstentions.

4216-01

During a site visit on 4/18, the IACUC site visitors discussed surgical practices with a lab member that had been performing cranial surgeries in mice (specifically cannula placement in the cerebral cortex). During that discussion, it became apparent that the surgeon was not performing the procedure as outlined in the protocol – including instrument sterilization, proper shaving and skin preparation, administration of local anesthetic, and provision of post-operative analgesia. The PI was contacted and voluntarily suspended any further surgeries until the situation could be fully evaluated. Upon investigation, it was confirmed that this individual had been initially trained internationally and had performed this same surgery for a number of years before coming to the UW. The individual participated in the required UW classes for animal handling, surgery 1, and surgery 2. Unfortunately, they did not complete the required surgery certification step prior to performing independent surgery. It was determined that a total of 30 surgeries had been performed by this individual since early 2022. It was also noted that record-keeping was sparse so it was difficult to confirm treatments provided and to verify proper post-operative monitoring.

The PI is taking this non-compliance very seriously. As stated, surgeries have been temporarily suspended. The surgeon is retaking all surgery training courses and will obtain certification before performing independent surgery. The lab has worked with OAW to create analgesic and post-operative monitoring documentation to ensure adequate recordkeeping. The PI has created a surgery check-list to be used by the surgeon and reviewed by the PI for every surgery.

CLATR (previously AUTS) has also evaluated our training program and made some changes regarding surgical training communication. Specifically, we will be emailing attendees (and their PI) after completion of surgery 2 class reminding them that they need to obtain certification prior to performing surgery. We will also be sending another reminder 10 months after completion of the course reminding them of the 12-month time limit for surgery certification.

This event has been reported to OLAW.

Discussion/Questions: *discussed whether any negative impact to animals- no reports of infections or complications and the animals made it to endpoint; there is no record of administration of analgesics post-operatively; IACUC members expressed discomfort with this individual performing surgery; individual had been performing the surgery internationally prior to coming to this institution, and received appropriate training in the lab; discussed actions available to the IACUC with regard to suspending a protocol or activity, or suspending an*

individual's ability to work with animals; PI appeared to not understand the requirement for certification; individual is currently required to retake all training and then become certified prior to performing independent survival surgery, and a veterinary resident is assigned to work with this group; discussed gathering additional information and then determining if additional IACUC action is needed.

Motion was made and seconded: to send a Letter of Reprimand.
Further Discussion: *IACUC members asked, what is the control environment or method of PI oversight that allowed someone to perform this surgery for an extended period without certification and out of alignment with the protocol?; What are the corrective actions- what will be done to prevent this from happening in the future?; Discussed that recordkeeping was inconsistent*
Vote: Approved with 14 members voting in favor, 0 against, 0 abstentions.

Standard Operating Procedures / Policies / Guidelines

- Standard procedures for gerbils, hamsters, mice, and rats– **AS**

Motion was made and seconded: to approve the procedures as written.
Further Discussion: *none*
Vote: Approved with 13 members voting in favor, 0 against, 1 abstention.

Policy Review

- Prolonged Restraint Policy– **CC**

Motion was made and seconded: to approve the policy as written.
Further Discussion: *none*
Vote: Approved with 12 members voting in favor, 0 against, 1 abstention.

- Adhesions Policy– **CC**

Motion was made and seconded: to approve the policy as written.
Further Discussion: *none*
Vote: Approved with 14 members voting in favor, 0 against, 0 abstentions.

- Audiovisual Use in the Vivarium– **CC**

Motion was made and seconded: to approve the policy as written.
Further Discussion: *none*
Vote: Approved with 14 members voting in favor, 0 against, 0 abstentions.

- Protocol Review Policy– **CC**

Motion was made and seconded: to approve the policy as written.
Further Discussion: *none*
Vote: Approved with 14 members voting in favor, 0 against, 0 abstentions.

IACUC Training

Environmental Enrichment SOPs:

- Environmental enrichment for Mice & Rats
- Environmental enrichment for Birds
- Environmental enrichment for Rabbits

Facility Biological Monitoring Program (FBM) - SP

Purpose: Validate the efficacy of sanitation procedures

- ATP Testing (any equipment that comes in contact with live animals and gets hand washed)

Questions:

- *Lab members aren't present and there's no one to ask? person hosting the visit should be aware of activities, and if not leave a note for Zak to follow up*
- *How often do you test, and swabs/item? Annual test and minimum of 6 samples; if they find issues it's more frequently*
- *All sanitization protocols are vet-approved*
- *As part of this process, they post sanitization SOPs (not required, but recommended)*
- *There is an exception in the plan so they aren't testing all induction chambers, for ex.*
- *What about body weight scales and beakers? Haven't come across those specifically, will consult veterinarian*
- *Most people use Clidox and alcohol (standard)*
- *Retention requirement on records? All via email, if they have from last year (started in 2019)*
- *Many labs aren't aware of this program- trying to find a way to advertise it and keep it realistic*
- *There is an email you can give for reference*

Semi-annual Report – BE

Need to break into smaller groups and then present findings at the next meeting; at July meeting there will be full semi-annual report for review

ACTION: Look for email from Bob and ensure that you get into groups as soon as possible.

Closing Business:
The Meeting was brought to a close at 4:06 pm.