

University of Washington
February 21, 2019 IACUC Meeting Minutes

Members Present: AB JE *KZ
 AS JPVH MS
 CG JS SH (remote)
 CH KG SL
 FRR KS TH (remote)

Members Absent: JB LJE JM
 KL SJH

*KZ alternate for ML

Opening Business

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

Confirmation of a Quorum and Announcement

- Quorum was confirmed by KC.

Protocol Review

- AMEND201801509 (3235-06) – **JFI**
 - Reason for FCR: The member who called for FCR would like the committee to “discuss whether the investigators' desire to "maximize the use of these valuable SHIV+, cART treated animals with this new experiment"... outweighs the harms to these monkeys.”
 - The initial objectives of the relevant study were to determine the impact of allogeneic transplantation on the HIV reservoir, investigate the components of an allogeneic transplant and their impact on HIV eradication as described in the Berlin patient, and create a comprehensive “map” of the HIV reservoir as it is impacted by allogeneic transplantation.
The group has determined that Group 3 studies, investigating MHC-Matched Allogeneic Transplantation, were unsuccessful due to unanticipated post-transplant toxicities, and they have discontinued that line of study. However, 4 animals are already on-study and have been infected with SHIV and are currently receiving combined antiretroviral therapy. The group is requesting to enroll these 4 animals in a new study investigating Autologous CCR-5 edited CD4CART-cell transplantation.

The IACUC discussed the amendment and noted that the original protocol on which these animals were enrolled was much more invasive than the new study and that there is a decrease in overall total sampling in the proposed experiment. Since this experiment does not compare two groups, this number of animals is useful -- a power analysis is no longer necessary.

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

Discussion: None further

Vote: Approved with 15 members in favor, none opposed and none abstaining.

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- AMEND201900099 (4382-01) – **AS**

- Reason for FCR: The intensity of the new model being proposed and the requested number of animals in Category E.

- The goal of this protocol is to study 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. Work currently approved on the protocol is aimed at developing models of neonatal brain injury so that they can gain a better understanding of the underlying mechanisms that contribute to this type of brain injury, as well as evaluating new therapies to treat this condition and improve neurodevelopmental outcomes.

The proposed pilot project being added with this amendment will extend on this work by studying the effects of early neonatal brain injury on adult onset brain injury (e.g., concussion, stroke). There is currently no preclinical data on the relationship between neonatal and adult onset brain injury. The proposed pilot project seeks to address this question.

The IACUC discussed with the researcher the type of traumatic injury, its immediate effects, and the reason for repetitive injury. The rats on this project, approximately 2-3 months after neonatal brain injury, will experience a traumatic brain injury produced by CHIMERA (a piece of equipment that allows for a precisely controlled closed head impact to be delivered). The expected mortality rate following the chimera impact is 3-5% as based on other similar studies. The injury will be repeated 3 times in order to recapitulate the concussion model.

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

Discussion: None further

Vote: Approved with 15 members in favor, none opposed and none abstaining

- PROTO201800109 (4454-01) – **KSH**

- Reason for FCR: This protocol proposes up to 16 planned surgeries and up to 5 chamber placements.

- The proposed studies will:

- 1) Explore the neural underpinnings of complex sensorimotor learning behaviors including learning to control a brain-machine interface, and
- 2) Design and test brain-machine interfaces that leverage neuroplasticity to restore and repair neurological function.

The experiments record and manipulate neural activity across multiple sites in the brains of non-human primates as they learn sensorimotor tasks including controlling sensorimotor brain-machine interfaces. Learning occurs across multiple brain areas, spans several time-scales (minutes to days), and occurs both during practice and during sleep.

Therefore the group studies activity with semi-chronic and chronic recordings in multiple brain areas, and both while the animals perform the behaviors and during rest (e.g. sleep). These lines of investigation will both shed light on how our brain learns complex motor behaviors, and will lead to the next-generation of brain-machine interfaces that can restore skilled motor control to people with paralysis.

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The IACUC discussed with the researcher the total number of surgeries, disposition of any animals that might not accept all planned implants and any effect of this on the research. The protocol is designed to incrementally add surgeries and there are contingency plans based on the outcomes of procedures. If an animal is not doing well, it can be removed from study at any point. It was suggested that it may be appropriate to put this protocol on Vet Monitoring. Vet Monitoring means a vet will be assigned to the protocol and monitor all critical procedures (i.e. surgeries). All protocols on Vet Monitoring are discussed at the monthly AV Meeting. If concerns or problems arise, the IACUC will be made aware and the protocol amended as needed.

Motion was made and seconded: to approve the amendment as written and to put the protocol on vet monitoring.

Discussion: None further

Vote: Approved with 15 members in favor, none opposed and none abstaining.

General Discussion

- Discussion on fluid restriction in rodents to inform discussion on 3 amendments that have severe fluid restriction included in them –**KS**
 - The committee has seen a lot of food restriction, but not so much for fluid restrictions. Similar to food restriction, fluid restriction is being used as a motivator to learn a complex behavioral task. The animals need to be trained to do a behavioral task repeatedly and consistently. Adult mice, in general, drink 4-7 mL per day. Adult rats, in general, drink 80-110 mL/kg. When fluid intake decreases, food intake also decreases. In these studies, mice can be restricted down to 1 mL of water per day, outside of the fluid reward obtained during the behavioral tests. Animals are monitored for dehydration and weighed daily to ensure that they do not show clinical signs of dehydration or lose more than 15-20% of their pre-study body weight. If any animals go beyond 20%, they are immediately put on ad lib access. Both mice and rats adjust to the fluid restriction after a few days. The literature shows that it is actually better to keep the animals on the restriction, then to go off and on, since they do acclimate. Research animals that are on a food or fluid restriction are actually healthier than those that are given ad lib access to food and water.

- AMEND201900011 (4265-01) – **KSH**
 - Reason for FCR: “The unusually long proposed duration of up to 24 hours, and chronic nature of the water restriction for behavior testing procedures.”
 - The goals of this protocol are to explore the use of stimulation of the mammalian brain and spinal cord as a therapy for overcoming motor deficits and directly re-animating limb function following central nervous system injury. The group obtained IACUC approval to water restrict animals for up to 24 hours via an Amendment to the protocol in January 2015. The triennial review was approved in July 2017 and the resulting descriptions for food and water restriction for these two behavior procedures were unclear. This Amendment is to clarify the food and water restrictions for these two behavior tests.

The IACUC discussed with the researcher the length of the fluid restriction and any adverse effects on the animals. No adverse effects are expected, based on numerous

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other studies that have used this technique. In fact, positive effects have been shown from moderate food restriction.

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

Discussion: *none further*

Vote: Approved with 15 members in favor, none opposed and none abstaining

- AMEND201801494 (4450-01) – **AS**
 - Reason for FCR: Extent of Fluid Restriction
 - This amendment adds several new experiments to the protocol (Expts 008- 013). The aim of these experiments is to study how highly targeted neural populations are impacted by various stressors, drugs, cytokines, hormones and diet, each of which is used to model different maladaptive states, such as addiction or anxiety. In particular, these experiments propose to use two techniques – head fixed calcium imaging and head fixed optogenetics – to gain a better understanding of how neuronal activity contributes to behavioral responding. Both of these procedures allow the group to image deep brain structures of awake mice while they are performing various operant or classical conditioning tasks (e.g., pressing a lever to receive a reward). As just discussed, mice enrolled in these studies will be fluid restricted as part of these behavioral assays in order to motivate the mice to seek physiological rewards.

The IACUC discussed with the researchers the phasing in and total magnitude of fluid restriction, and social versus single housing of the animals.

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

Discussion: *None further*

Vote: Approved with 15 members in favor, none opposed and none abstaining

- AMEND201801575 (4452-01) – **MN**
 - Reason for FCR: Extent of fluid restriction.
 - *The IACUC again discussed with the researchers the total magnitude of fluid restriction, and social versus single housing of the animals. This protocol is similar to the 4450-01 protocol.*

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

Discussion: *None further.*

Vote: Approved with 15 members in favor, none opposed and none abstaining

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the January 17, 2019 meeting minutes.

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

Discussion: *None*

Vote: Approved with 12 members voting in favor, none opposed, and 3 abstaining.

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

- Adopting out 3 rats.
- IACUC metrics- see meeting documents
- As previously mentioned, HBAS finished its evaluation of existing Hoverboard “Physical Restraint” procedures to determine which of those procedures are prolonged restraint using the definitions in the IACUC policy. In the meeting supporting documents, there is the HBAS summary of prolonged restraint. Capture and Trapping will be reviewed soon.
- Facility issues:
 - Humidity: Low humidity (which is not unusual in the winter months) has been noted in one primate area that does not have central humidification. There have been a few instances of epistaxis (nose bleed).
 - Temperature and lights
- 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. No updates to report.
- Adverse Events: None to report.
- Non-compliance:
 - Protocol non-compliance: Self-reported. It involved the collection of bats in field study outside of the US. The protocol listed particular bat genera for either collection of pregnant females or non-pregnant adults. Some genera were cross-listed on the protocol. The researcher inadvertently collected 4 pregnant individuals of a genus that was listed on the protocol but not for the collection of pregnant females. Their action did not violate any permits and that total collection of bats was well under what was approved on the protocol. The researcher has completed work covered under this protocol and the protocol has been closed.
Corrective action: In future field work, they will have a field-durable, easy-to-read list of IACUC approved genera accessible to them.
As collection was outside of US, it is not reportable to USDA.

Will be reported to OLAW.

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

Discussion: *This was a graduate student. Should send letter to the PI and emphasize the importance of communication.*

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

Discussion: *None*

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Vote: Approved with 15 members in favor, none opposed and none abstaining.

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

Follow-up from last month's presentation on Vet Services:

- Veterinary Services staffing numbers:
 - DCM – 6 Clinical/Residents, 11 Clinical Veterinarians (not 100% time), 7 Veterinary Technicians
 - WaNPRC – 8 Clinical Veterinarians, 12 Veterinary Technicians
- The IACUC will send a letter of appreciation to the staff of WaNPRC, DCM and Lab-Managed staff that ensured proper animal care during the snow storms that came through Seattle.

Standard Operation Procedures / Policies / Guidelines - KS

- Food and Water Restriction in Non-Rodent USDA Species

Motion was made and seconded: to approve the policy with the change of adding specific definitions of fluid regulation and fluid restriction.

Discussion: None

Vote: Approved with 15 members in favor, none opposed and none abstaining.

- GNAC Husbandry Exception (re-approval)
 - *Minor changes: Increase inspection of housing racks, yearly rack cleanings, light cycle updated to 14:10 that is standard within the facility.*
 - *Exception renewal: Animals that are housed in isolators and are bacteria-free. Although bedding is changed at least weekly, the cages, wire-tops, and water bottles will only be changed on an "as needed" basis until the end of the cage use or if made necessary by a physical flaw or excessive buildup of non-removable waste.*

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

Discussion: None

Vote: Approved with 15 members in favor, none opposed and none abstaining

- Care and Maintenance of Ferrets SOP
- Quarantine SOP

Motion was made and seconded: to approve both the above SOPs as written.

Discussion: None

Vote: Approved with 15 members in favor, none opposed and none abstaining

Other Business

- Discussion of deferred semi-annual corrective actions - **LI**

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- Review of the facility items that had TBD for their completion dates. Going forward, these will be given tentative dates, depending on the type of work, and will be replaced once a finalized date is received from Facility Services.
- Due to uncertain funding, there have been repeated extensions of some of the facility issues, for instance the room that the WaNPRC cage wash is in, and there is no assurance new items identified will be able to be fixed.

The IACUC discussed the importance of correcting facility deficiencies and the impact of failing to do so on animals, people, research and the overall program.

Motion was made and seconded: to send a letter of concern to the IO about the lack of Institutional Support.

Vote: Approved with 15 members in favor, none opposed and none abstaining

- WaNPRC Common Use Drug Formulary – **CH**

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

Vote: Approved with 15 members in favor, none opposed and none abstaining

Closing Business:

The Meeting was brought to a close at 4:32 pm. The floor was opened to public comment.