

Members Present:	AB	JB	MG
	AS	JPVH	ML
	CG (Public)	JS	MT
	CH	JFI	SL

Members Absent:	AF	JM	MB
	CG	JM	NK
	CJ	KL	PB
			TB

Opening Business

The IACUC Chair called the meeting to order at 2:37pm.

Approval of the IACUC Meeting Minutes

The IACUC Chair called for the approval of the February 18, 2016 IACUC meeting minutes.

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

Discussion: None

Vote on the Motion: The meeting minutes were approved with 10 members voting in favor and two abstentions.

The Benefits of Research – JS

‘Concurrent erythropoietin and hypothermia treatment improve outcomes in a term nonhuman primate model of perinatal asphyxia’ Traudt CM, McPherson RJ, Bauer LA, Richards TL, Burbacher TM, McAdams RM, and Juul SE. *Developmental Neuroscience* (2013) 35:491-503.

Protocol Review

- Dr. Murry, 2225-06, V50 “Non-human Primate iPSC Derived Cardiomyocyte Grafts Evaluation in Myocardial Infarction”

JFI presented the Significant Change to the Committee. A member of the group was present to answer any questions.

Background: This group studies stem cell therapy for the treatment of cardiac infarction (aka heart attack). They transplant stem cell derived cardiomyocytes into the infarcted heart of NHPs. Their goal is to develop a therapy for use in clinical trials.

The purpose of this significant change is to modify their approved survival surgeries to add laparotomy as an alternate method of obtaining vascular access for their catheter-based surgeries. The reason for full committee review is that the group has a cell injection surgery

scheduled for March 22nd (next Tuesday), and they would like to have this modification in place for that surgery, in case it is needed.

In section A, I thought the group did a good job of considering the potential harm associated with the procedures on this study, discussing the steps they take to mitigate that harm, and weighing that against the benefit of their work.

To summarize the requesting modification – With this significant change, the group is requesting to modify their catheter-based infarct and cell injection surgeries to allow for alternate vascular access if the femoral artery is deemed to be too small for catheterization at the time of surgery. Currently, the group is doing a cut-down to the femoral artery and placing an arterial sheath, through which the required instrumentation is advanced in order to perform the cardiac infarction or the cell injection. While this has been generally successful, the group has experienced situations where the femoral artery was found to be too small to accommodate the arterial sheath without damage to the vessel. This has resulted in post-op complications or inability to proceed with the surgery. The group is requesting the option to extend the surgical incision proximally in order to access alternate larger vessels (external iliac artery, common iliac artery, abdominal aorta) via the peritoneal cavity. The arterial sheath placement and the remainder of the surgery would then proceed as currently approved.

Note that the group is currently approved to use this technique during terminal surgeries (V37, VVC), and have done this once without complication. Also, there is a significant change currently in pre-review to increase the maximum size of animals on this protocols to hopefully avoid this complication in the future.

Motion: A motion was made and seconded to approve the Significant Change as written.

Discussion: None

Vote on the Motion: The Significant Change was approved unanimously with 12 members voting in favor.

- Dr. Fetz 2326-08 V.114, V.115, V.116 “Brain-computer interface for primates”

JFI explained that there were three significant changes related to repair surgeries. She provided background on the protocol, and then presented the Significant Changes one at a time.

Per the UW IACUC policy entitled “Guidelines for Non-Human Primate Neuroscience Studies”, decisions regarding requests for additional repair surgeries must be made at convened meetings of the IACUC. Policy states that relevant protocols can and should include provision for one or two repair surgeries, and these requests must include justification of the need for that specific animal to continue in the study, as well as complete medical history.

Background: This group is researching the use of a brain-computer interface to establish artificial connections within the central nervous system. They record signals from one area of the brain, and then deliver signals to our areas of the brain, spinal cord, or muscles. They are investigating mechanisms of cortical plasticity and developing methods for inducing and controlling plasticity, with the goal of supporting development of neurorehabilitation treatments for brain injury and stroke.

JFI commented that she thought the group did a good job of summarizing the goals and significance of this project, and addressing the potential harm, and steps taken to mitigate that harm.

➤ V.114, Animal Z08111

The group is requesting 2 repair surgeries for this animal because he currently requires repair to his Halo head restraint implant, and that surgery is scheduled for April 25th. The group is requesting a 2nd repair to have available in case of unforeseen issues with his implants.

This animal is a 7-year old male pig-tail who received his first surgeries on this protocol in 2012 to implant a Utah array. The group reports that he is reliably producing useful data and performs his task well, and that the brain implant is still capable of producing data as long as the Halo is in place. The group reports some minor incidences of inflammation around the pin margins, which they treat with antibiotics and regular cleaning of the area.

Surgical history:

- 2 repair surgeries related to nerve block catheters in 2013
- one repair surgery for his Halo implant about 1 year ago

Clinical history:

- Appears to be healthy
- History of +MRSA culture, but appears to be asymptomatic
- Some issues with nerve catheter surgical sites in 2013 that resolved with treatment and/or removal of the implant

Current implants:

- Cortical implant
- "Halo"-type implant (presently only the skull plates are implanted; pins have been temporarily removed)

Motion: A motion was made and seconded to approve the Significant Change as written.

Discussion: None

Vote on the Motion: The Significant Change was approved unanimously with 12 members voting in favor.

➤ V.115, Animal A14231

Requesting 1 repair surgery for this animal. This is a 4 year old male rhesus who received his first surgeries on this protocol in April of 2015. He had a surgery in January of this year for subcutaneous routing of wires related to his VNS (Vagus Nerve Stimulation) implant, and had a recent repair surgery to remove the generator and connect new wires to the electrode. The animal is currently healing, and then the studies will resume. The group reports that this animal carries a unique combination of implants and is well-trained in a complex motor behavior task, and is very valuable to their research.

Surgical history:

- Unremarkable – one repair

Clinical history:

- Appears to be healthy
- Only minor local inflammation after January surgery that resolved with treatment

Current implants:

- Cortical implant
- Left vagus nerve cuff (connected generator has been removed); stimulation is now delivered with external stimulators

Motion: A motion was made and seconded to approve the Significant Change as written.

Discussion: None

Vote on the Motion: The Significant Change was approved unanimously with 12 members voting in favor.

➤ V.116, Animal Z08216

Requesting 1 repair surgery for this animal. This is a 7 year old male pig-tail who received his first surgery on this protocol in December 2015. He had a repair surgery in February to externalize some connectors that had been placed in January, because during that initial surgery, space limitation didn't allow for exposure of all of the connectors without inhibiting skin healing. Skin was sutured over some of the connectors, and after the skin was healed, the connectors were then exposed with that repair surgery. The group reports that, since then, the animal has provided a wealth of information, is in excellent health, and is very well trained in a fairly complicated motor-behavior task.

Surgical history:

- One minor repair surgery in February

Clinical history:

- Animal appears to be generally healthy
- Noted a small, chronic wound/lesion on his back that seems to have come and gone with MRSA decolonization and antibiotic treatment, but he's been bright and alert throughout
- Minor trauma back in 2014 related to social reintroduction
- Few comments about low BCS that resolved with nutritional support, but no evidence of weight issues in the last year or so

Current implants:

- Cortical implant
- "Halo"-type implant

Motion: A motion was made and seconded to approve the Significant Change as written.

Discussion: None

Vote on the Motion: The Significant Change was approved unanimously with 12 members voting in favor.

- Dr. Hajjar, 4230-01, V.167 "Linking Innate and Adaptive Immunity"

The PI has requested quick turn-around on this significant change request in order to meet an OSP/sponsor deadline.

The significant change request is to increase animal numbers for experiments already approved on the protocol for a new grant that just got approved.

The group is studying the role of the microbiome and gut microbiota in cystic fibrosis (CF). The gene mutated in CF is CFTR (cystic fibrosis transmembrane conductance regulator), and they use CFTR KO mice in these studies. These have to be bred by heterozygous crosses because the KO are sterile. Furthermore, the KO develop intestinal obstructions so they are maintained on laxative water after weaning that greatly reduces this complication. When you breed het by het you would expect to have 25% KO. However, they found that only ~5% of the mice that are weaned are KO.

They recently rederived the CFTR heterozygous mice germfree, so they are totally sterile and live in a bubble to keep them sterile. So now they have both regular SPF and GF mice that allows them to dissociate the role of the microbiota from the CFTR gene itself in GI disease. It is not known whether it is mutated CFTR or altered microbiota that plays a larger role in inflammation in CF.

In the first set of experiments, they are requesting mice as tissue donors, where no procedures are performed on the live mice. They will do euthanasia followed by histology, live cell imaging by flow cytometry, and whole tissue or cell RNA and protein extractions, so 3 different sets of tissue donors per group. The groups consist of WT and KO mice and either GF or SPF. They will also study M and F mice at 4 different ages. Based on only 5% of the mice being KO that results in needing 2702 mice being born to achieve those numbers of KO which should yield an excess of WT mice as controls.

The second set of experiments consist of performing fecal microbiota transplants, where feces are given orally to the sterile mice and then changes that develop in the mouse are examined at 2 timepoints after colonization. They want to test 5 different fecal samples from human infants with CF or control non-CF infants. They will also use their SPF mice for a set of donor fecal samples (both CF and WT). They propose to again use M and F (3 each) germfree CF or WT recipients. They would need 7,430 mice to be born to get 396 KO mice to study all the fecal samples using all 3 assays described above if only 5% of the germfree mice weaned are KO. But if their hypothesis that the microbiota are important to increasing inflammation in CF then they would predict that greater than 5% would be KO in which case they would need fewer mice born. If they find they get the expected 25% KO weaned in the isolator, then 1,440 mice would have to be born, although to achieve adequate WT mice too may require additional mice. The point is that they would reduce the amount of breeding based on the proportions of KO that are born if they find they are born at greater than 5%.

Motion: A motion was made and seconded to approve the Significant Change as written.

Discussion: It was confirmed that there were no new procedures associated with the request.

Vote on the Motion: The Significant Change was approved unanimously with 12 members voting in favor.

Attending Veterinarian's Report

Facility issues:

- **Humidity:** Humidity has been low in several centralized and decentralized animal facilities.
- **Temperature and lights:** In one decentralized rodent facility, temperature varied greater than 4 degrees on February 9, 2016. Facility Services was contacted and the temperatures have been stable since. This facility is also being vacated as part of the moves into the T-wing.

Protocol Monitoring: There are 16 protocols on the veterinary monitoring program. One protocol has been added to veterinary monitoring. Protocol 2326-08 has been added by the attending veterinarian to monitor surgical technique following a clinical complication which may or may not be related to surgical technique.

OAW Director's Report – Summary slide in folder

The Committee was reminded that the Deficiencies at a Glance spreadsheet was in the meeting folder for review.

Responses to previous non-compliance:

- 4262-01 - The PI responded as required and the response was summarized for the Committee.
- 2077-14 - The PI responded as required and the response was summarized for the Committee.
- 4092-01 - The PI responded as required and the response was summarized for the Committee.

Adverse Event

One mouse was found dead on a sticky trap used to capture insects. Traps are not used in housing rooms and sticky traps are not used for rodents. It is unknown how the trap was moved to the room. Pest control has been contacted about placement of the traps to make sure that they are not placed accidentally in the room. This event has been reported to OLAW.

IACUC SOPs and Policies:

- Use of Antibiotics in Laboratory Animals – ML summarized key points of the policy and explained that there were no changes to be made to the content of the policy. It was proposed that the policy title be changed to Antibiotic Use in Laboratory Animals.

Motion: A motion was made and seconded to approve the change to title of the policy.

Discussion: None

Vote on the Motion: The motion passed unanimously with 12 members voting in favor.

IACUC Training

- Prophylactic antibiotics in protocols – ML gave examples of when prophylactic antibiotics are used in surgery.
- Process for asking veterinarians questions during protocol. - If during review, IACUC members have veterinary questions, they can put comments in top box (administrative section) of Catalyst and the reviewer will forward the questions to the veterinarians or questions can be sent to the veterinarians directly.. Vets don't mind at all, its what they are there for. If questions are sent directly to the vets & you want it held for a reply, also put it in the top box.
- Process for reviewing CTC questions before they are sent to the PI. The Committee was reminded that general questions not directed to the PI can be put in the top box (administrative section) of Catalyst. All questions are reviewed by the teams & admin staff to be sure that the questions are clear for the PI. This process will be different with the Hoverboard system. JS asked CTC members to make sure that they are well written. OAW staff will correct clerical errors.

Harm Benefit Analysis Subcommittee Update – The Harm-Benefit Subcommittee held its monthly meeting. Eight protocols were evaluated due to the risk of the animals having seizures, either because the laboratories are studying epilepsy, or seizures are a possible side effect of other procedures. Two cases of clinical complications which could be related to experimental procedures were also discussed. One of these cases was serious enough that the Attending Vet put the protocol on vet monitoring while the case is being investigated.

eIACUC See slides – GL updated the IACUC on the status of the eIACUC solution. Procedure SOPs will need to be approved by the IACUC. The Committee was ok with sending through the normal CTC process.

Other Business:

CTC DMR – How do we know when it's okay to approve? When a protocol is ready to approve, an email is sent to the DMR listing what has been done and questions that have been addressed, typically in an attachment. 'Do you approve?' is the prompt.

Closing Business:

The Meeting was brought to a close at 3:34 pm. The floor was opened to public comment.