University of Washington
July 21, 2022 IACUC Meeting Minutes

Members Present:	AB	DM	KG	MRB
	AC	ES	KM	MRK
	AP	JFI	MB	SRH
	CC	JS	ME	
			MK – 2:58PM	

Members Absent:

AW
GS
JM
JPVH

Opening Business

- The Floor was opened for public comment at 2:32pm.
- The IACUC Chair called the meeting to order at 2:43pm.

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 June 23, 2022 meeting minutes.
  Motion was made and seconded: to approve the minutes as written.
  Further Discussion:
  Vote: Approved with 12 members voting in favor, 0 against and 3 abstentions.

Benefit Story – JS

This month's benefit story comes from three UW research teams who worked together to identify a distinct brain circuit that mediates the rewarding component of opioids that is thought to underlie addiction.

Opioids are powerful drugs that can effectively control debilitating pain and allow people to lead productive lives. As we are all aware, however, there is also the potential for abuse.

Ideally, we would like to identify ways to manage pain that do not lead to addiction. A necessary first step is to determine whether it is even possible to achieve one without the other. It might be, if separate signaling pathways are involved. If a unique brain circuit is responsible for the rewarding elements of opioids, and this circuit is distinct from the one controlling pain sensation, then it might be possible to selectively tap into the pain suppression pathway without triggering activity in the reward circuit that could lead to addiction.

Using cutting-edge techniques in mice, the UW research teams were able to selectively manipulate very specific subsets of brain cells and look at the effects on behavior. Activating a particular population of neurons triggered the release of endogenous opioids—endorphins—and

increased the consumption of sugar water, which was used as a read-out for how rewarding, or potentially addicting, activation of that circuit might be. This effect was blocked by genetically knocking out opioid receptors throughout the body. This blockade of reward could be reversed by using gene therapy techniques to restore opioid receptors to a particular type of neuron in a particular part of the brain. Critically, the selective re-expression of opioid receptors in this one part of the brain did not restore the ability of an exogenous opioid, morphine, to relieve pain.

These results suggest that the researchers have identified a brain circuit that is specifically involved in the addictive properties of opioids, distinct from pain relief. This holds promise for the development of treatments that can selectively activate the pain-relieving circuit without triggering addiction. Although we often focus on biomedical stories with more immediate relevance to human health, basic research like this provides the critical foundation for translational studies that can take findings into the clinic.

Castro et al., An endogenous opioid circuit determines state-dependent reward consumption *Nature* 598: 646-651 (2021)

Attending Veterinarian's Report – CC

- I have no reportable animal events for the committee this month (for either the Seattle or Arizona sites).
- I have no reportable facility events for the committee this month (for either the Seattle or Arizona sites).

- **Update on Protocol Monitoring**
  - There were no new protocols added to vet monitoring this month. A mouse protocol was removed from monitoring after review by the AV and veterinary team. Thus, we have a total of 21 protocols with ongoing enhanced monitoring. Of these 21 studies, we continue have only 5 protocols actively performing the procedure for which they are on monitoring.
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- **Other announcements**
  - There has been a complaint submitted to OLAW, and OLAW has asked the IACUC to complete an investigation regarding the allegations made and to report back to OLAW. We are putting a team together to respond to the OLAW request. If there are any IACUC members that would like to be included in this team please reach out directly to Jane after this meeting. The investigation may be somewhat time consuming and does require a timely response back to OLAW so please consider your other obligations before volunteering.
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OAW Director's Report – JFI

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

Responses to Letters & Other Follow up –

- **Non-compliances --**

4190-01 - It was self-reported on June 21st that on June 7th 5 mice were injected IP with an agent, called DMXAA, that was not approved on the protocol. 4 of the 5 mice died within 8 hours of the injection, which was an unexpected outcome. The 5th mouse was euthanized. The group was attempting to perform a follow-up experiment with the same conditions reported in a previous publication from their group, but after the fact they realized that the DMXAA injections were actually approved on a different PI's protocol. The original experiment was a collaboration performed by a jointly-mentored graduate student, and prior to initiating the recent study the PI did not confirm which PI's protocol covered this work. Unfortunately, the PI does not know the reason for the high mortality compared to their prior experience with this agent. It is possible that the new batch of DMXAA was miscalculated, but the batch was prepared from powder on the day of the experiment and the entire batch was used, so that could not be verified. The group has no plans to perform additional DMXAA injections in the near future, but they are in communication with their OAW liaison about adding this work to their protocol. The PI was apologetic and acknowledged that he should have reviewed the protocol more carefully before initiating the experiment. Moving forward, to avoid confusion with collaborations, the PI will also no longer perform experiments that are not on their own protocol. In other words, the experiment will either be on their own protocol, or the animals will be transferred to the care of the collaborating lab.

This has been reported to OLAW.

There is no record of previous reportable events with this group.

Motion was made and seconded: to send a letter of counsel to PI

Further Discussion: include language to make sure this doesn't happen again

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

4266-01 – A group self-reported on July 13th that on July 6th and 7th one cage of mice (5 mice) was used for training procedures without the mice first being transferred to the training protocol. These animals were assigned to an experimental protocol, and they had completed an experiment on the protocol (a vaccination study), but tissues were not needed so the group intended to donate the animals to the training protocol. One cage of mice was used over 2 days for training a member of the lab on ABSL3 procedures, including cage changes, handling with forceps (which involves picking the animal up by the tail to move between cages, a weight container, or a restraint device), weighing, IP injection of dye followed by CO2 euthanasia, and IP injection of anesthetic agent followed by intranasal administration of saline and anesthetic recovery. All mice were euthanized over that 2 day period following the training procedures. The instructor, who is a member of DCM, did ask the group member which protocol the animals were assigned to and whether they were approved to be used for training. The group member indicated that they were on a training protocol, but it was realized after-the-fact that training procedures are not actually approved on this protocol.

For corrective actions, the group is planning to add training animals to their protocol. The OAW liaison for this group discussed with the DCM instructor ways to loop them in earlier in the process of adding ABSL3 work to experimental protocols so that they can more proactively confirm what is approved on the protocols and what training may be needed. They also discussed potentially ensuring as part of the review process that training animals are added to all protocols that involve ABSL3 activity.

This has been reported to OLAW.

Motion was made and seconded: to send a letter of acknowledgment to PI
Further Discussion:
Vote: Approved with 16 members voting in favor, 0 against, 0 abstentions.

IACUC Training - CC

PowerPoint presentation on Valley Fever

Drug Mix Refresher – AB

-Have seen expired drug mixes on recent site visit

-Use by date of 30 days recommended by Vet Services. Site visitors are encouraged to direct research teams to VS to discuss.

-VS is encouraged to clarify drug mix expiration policy and work with the IACUC to disseminate this information throughout the community.

Semiannual Report - BE

Physical IACUC Training Room – CC

This should be finalized and operational for practice inspections within 1 – 2 months

Closing Business:

The Meeting was brought to a close at 3:18pm.