University of Washington
November 19th, 2020 IACUC Meeting Minutes

Members Present:	AB	JA	KS
	AW	JM	MB
	CM	JPVH	ML
	FRR	JS	SRH
	GS	KG	SL
		KAG	
Members Absent:	DM	MK	

Opening Business

- The IACUC Chair called the meeting to order at 2:32 pm.

Confirmation of a Quorum and Announcement

- Quorum was confirmed by AW.

Approval of the IACUC Meeting Minutes

- The IACUC Chair called for the approval of the October 15th, 2020 meeting minutes.
  Motion was made and seconded: to approve the minutes as written.
  Further Discussion: *None.*
  Vote: Approved with 16 members voting in favor, 0 against and 0 abstentions.

Benefit Story - JS

- I am again going to focus this month's benefit story on local efforts to develop a Covid vaccine. First, I want to update you about the Fuller lab's novel RNA-based vaccine, which I told you about in August. This is the Moderna vaccine, which was reported earlier this week to be 94.5% effective in Phase 3 clinical trials that ran in parallel with the monkey research. [C*orrection: the Fuller lab vaccine is not the same as the Moderna vaccine*.] This is tremendously exciting news.

  I think most of you are aware, though, that the global goal is to identify a variety of vaccines with different properties, and so the need for further vaccine testing continues.

  Neil King's lab, working in collaboration with many fellow UW researchers, has very recently reported their findings on a different kind of vaccine in the journal Cell. The King group began by generating a computer model that predicts the 3-dimensional shape of the part of the SARS-CoV-2 virus where it binds to ACE2, the naturally occurring cell-surface protein that serves as an entry receptor for the virus. This allowed the researchers to predict the part of SARS-CoV-2 where antibody binding could most effectively block binding to ACE2, and thus block entry of the virus into cells.

  The key concept here is that exposure to the isolated protein binding domain, which on its own does not cause disease, triggers the production of antibodies that will attach to the

binding domain and prevent infection by the virus upon exposure. In vitro studies showed that simultaneously presenting multiple copies of the binding domain was much more effective at triggering antibody production than individual binding domains. This led the researchers to create so-called 'nanobodies' that are composed of aggregates of recombinant SARS-CoV-2 binding domain protein.

When these nanobodies were injected intramuscularly into mice, they rapidly elicited antibodies at levels that matched or exceeded the levels found in humans with COVID. Seven weeks after immunization, ***all*** the mice injected with the nanobodies were ***completely protected*** from detectable virus replication in the lungs and nasal tissue, and high antibody titers persisted undiminished out to 24 weeks.

Follow up studies in mice with humanized immune systems provided additional confidence that the nanobodies would work in people, but a final experiment tested the ability of the nanobodies to elicit antibodies in a single non-human primate. Eight weeks after immunization, the monkey's serum contained high levels of antibodies that could inhibit binding of virus to ACE2 in an in vitro assay. I do want to emphasize that there was no virus challenge for the monkey, and also that **none** of the monkeys at the UW primate center have tested positive for COVID.

The benefits of nanobody vaccines include their track record for safety and their potency, which means a little can go a long way. Nanobody vaccines are also amenable to large-scale manufacturing, which is particularly important during a global pandemic. I am excited to see how this new nanobody vaccine performs in clinical trials.

Walls et al., '*Elicitation of Potent Neutralizing Antibody Responses by Designed Protein Nanoparticle Vaccines for SARS-CoV-2*' Cell 183: 1-16 (2020)

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

- As of November 1, 2020, Joe Giffels, the Associate Vice Provost for Research Administration and Integrity, is the Institutional Official.

- Adoptions – 3 dogs and 2 rats have been adopted out in the last month.

- COVID impacts update: There is no change in conducting animal research or providing hands-on training/facility orientations in light of the Governor's new restrictions. Animal care and veterinary staffing has continued been adequate.

- Training program updates: New weaning and sexing of mice on-line lesson is now available.

- IACUC metrics- see meeting documents

- Facility issues:
    - 3.1 lighting: Mid-afternoon the lights in animal rooms set to the 7am ON -9 pm OFF schedule went to dark cycle. This change activated alarms and was quickly identified and reported to the facility staff and the lighting vendor. An investigation by the vendor found

that the issue was due to a manual change in a shared lighting control template. Unaware that this control template was shared, a supervisor in another facility unclicked a box to adjust the monitoring parameters and accidentally removed controls for the 3.1 facility. Vendor technicians changed the template back to appropriate controls and approximately 3 hours later, the lights in those animal rooms came back on their appropriate cycle. Corrective Action: Lighting control templates will no longer be shared between facilities. *An IACUC member asked if faculty that had animals in the room were notified about this issue, and the Attending Vet is not aware if they were notified by DCM.*

- Protocol Monitoring:
  - Seventeen total protocols. Of the protocols, nine involve surgery, one restraint (and sx), 2 tumor modeling, 6 miscellaneous (tape skirt, infection, water quality, prolonged anesthesia). Ten are inactive right now. Placed one protocol involving a new mouse surgery technique on inactive status as the lab as no plans to do this surgery until after the pandemic ends.

  - Ferret CHIMERA pilot study update: The lab performed a pilot study to look at the feasibility and parameters needed to develop a model of traumatic brain injury (TBI) in young ferrets using the CHIMERA (Closed-Head Impact Model of Engineered Rotational Acceleration) method. The initial study was performed in August 2019 with 10 animals receiving three exposures, one every 24h, and then analyzing the behavioral and brain tissue changes. The lab has recently finished analyzing the data and met with the AV to discuss the results and future plans. The pilot study has given the lab a better understanding of the tolerable impact energies in adolescent ferrets and showed that behavioral and histological changes are seen with three successive impacts. While the data on the initial study is promising, additional studies will be needed to further refine this model. The group has no plans to do follow up studies involving multiple CHIMERA exposures to induce TBI and these experiments will be removed from the protocol during its triennial review in January 2021. Before any new pilot studies are performed, the lab will discuss them with the AV and those studies will need to be reviewed and approved. The IACUC will be updated if and when additional studies are planned.

- Adverse Events:
  - DCM: A cage of 5 experimentally naïve, adult mice were found dead in the cage on a Sunday. The red "engagement indication" dot on the rack was mostly covered, but the cage was not appropriately seated in the rack, thus inhibiting reliable access to water from the lixit. The last time the cage was handled by husbandry staff was to refill the food hopper on Thursday, and the investigative group had not touched the cage since that time. The mice had visual health checks on Friday and Saturday, but were not reported sick, and the improperly seated cage was not noticed. Corrective Action: The animal technicians that missed the improperly engaged cage were notified, and the husbandry staff was retrained to identify cages not completely engaged.
    Reported to OLAW.

  - 4249-01: Two 8-week old mice presented for severe dehydration. The cage was found disengaged from the rack. Despite fluid therapy, one mouse died and the other mouse was euthanized later that day. The last cage change was performed 10 days prior and the lab group did not perform any experimental manipulations on this cage of mice, however they did report that lab members sometimes move the cages around to make more room on the

rack. The animal technician who reported the sick mice also checked this cage on the two previous days. Corrective Action: Lab members were reminded to make sure to double-check that cages were engaged on the rack. All DCM husbandry staff are in the process of being re-trained in performing daily cage checks.
Reported to OLAW.

The IACUC discussed these 2 adverse events focusing on how to detect when a cage is not fully engaging in the rack as well as prevention of these types of events. Currently there are no automated remote monitoring systems that can detect when a cage is not fully seated in the rack. Older cages that have been washed and autoclaved repeatedly do not always easily slide in and thus, someone may think the cage in fully seated when it is not. Daily cage checks by husbandry staff are observational and it is not always easy to detect whether the indicator dot is visible when the cage is mostly, but not fully, in the slot on the rack. It has been suggested to DCM that daily checks include a push on the cage to ensure it is engaged in the rack. As part of a corrective action plan, there are online animal use training lessons that the IACUC could require as part of the retraining for both researchers and DCM husbandry staff. As part of a general prevention plan, the annual DCM refresher training can be updated to utilize a rotating group of lessons to increase awareness and hopefully prevent the types of adverse events that have occurred.

Motion was made and seconded: to send two Letters of Counsel to both DCM staff and the lab members containing retraining requirements, including the specific online training lesson, and suggesting the addition of a physical push to each cage as part of the daily cage checks.
Further Discussion: *None.*
Vote: Approved with 15 members voting in favor, 0 against and 1 abstention.

- Non-compliance:
  - 2448-12 – An OAW liaison recently discovered that the lab which works with squirrel monkeys did not following their approved protocol regarding the interval between successive intraocular injections. In late May/June, two animals received 2 successive injections 1 week apart rather than the approved 3-4 weeks between injections. No animal welfare issues have been noted and the monkeys have continued on study. Corrective Action: The lab has been reminded to ensure adherence to the protocol and that the protocol should be amended and reviewed by the IACUC if they plan to do successive injections at less than 3-4 weeks intervals.
    Reported to OLAW and USDA.

    Motion was made and seconded: to send a Letter of Counsel.
    Further Discussion: *None.*
    Vote: Approved with 16 members voting in favor, 0 against and 0 abstentions.

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

Protocol Review

- Standard Procedures Review – **KS**
  The AV reviewed over the changes to the standard procedures.

  Motion was made and seconded: to approve the new standard procedures as written.
  Further Discussion: *None.*
  Vote: Approved with 16 members voting in favor, 0 against, 0 abstentions.

Standard Operation Procedures / Policies / Guidelines

- IACUC Protocol Requirements Policy – **KS**
  The AV went over the revision adding oversight over cephalopods resulting from feedback from the last AAALAC visit.

  Motion was made and seconded: to approve the policy as written.
  Further Discussion: *None.*
  Vote: Approved with 16 members voting in favor, 0 against, 0 abstentions.

Other Business

- Semiannual Report due in January - **BE**

Closing Business:

The Meeting was brought to a close at 3:30 pm. The floor was opened to public comment.