INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, July 19, 2017
Time: 10:00 AM – 12:00 PM

Location: Foege N-130A

Members Present:
1. Thea Brabb, Comparative Medicine *(Animal Containment Expert)*
2. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
3. Richard Grant, Washington National Primate Research Center
4. Kevin Hybiske, Allergy and Infectious Diseases
5. David Koelle, Allergy and Infectious Diseases
6. Scott Meschke, Environmental & Occupational Health Sciences
7. Matthew R. Parsek, Microbiology
8. David Scarsella, Pacific Northwest Diabetes Research Institute (*Community Member*)
9. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer, Animal Containment Expert, Acting IBC Chair*)

Commonly Used Abbreviations
IBC: Institutional Biosafety Committee
BSO: Biological Safety Officer
BUA: Biological Use Authorization
BSL: biosafety level
PI: Principal Investigator
IACUC: Institutional Animal Care and Use Committee
NIH: National Institutes of Health
DURC: Dual Use Research of Concern
SOP: standard operating procedure

1. **CALL TO ORDER:** The acting Institutional Biosafety Committee (IBC) Chair called the meeting to order at 10:14 am. A quorum was present.

2. **REMINDER:** The acting IBC Chair reminded attendees that any notes that they retain are subject to public disclosure. A statement was also made about conflict of interest and voting on research proposals as described in the IBC Charter. This includes sharing a grant or a familial relationship.

3. **APPROVAL OF MINUTES:**
   - The acting IBC Chair sought a motion to approve the minutes from the June 21, 2017 meeting.
   - A member made a motion to approve the June 21, 2017 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the June 21, 2017 meeting minutes.

4. **OLD BUSINESS**
   - At the April IBC meeting, Dr. Fuller's BUA was approved pending biosafety officer review of the IACUC protocol & discussing animal housing room assignments with Comparative Medicine. The IACUC protocol was reviewed by the biosafety officer and the letter was sent.
   - At the April meeting, Dr. Hybiske's BUA was approved pending receipt of NIH approval for Chlamydia strains falling under section III-A of the NIH guidelines. The NIH approval was received. Dr. Hybiske needs to submit some SOPs and confirm that he has set up additional practices as required by the NIH.
   - At the May meeting, Dr. Hampe's BUA was approved pending completion of the IACUC protocol. The IACUC protocol was submitted reviewed by the biosafety officer and the letter was sent out.
   - At the June IBC meeting, Dr. Parsek's BUA was approved pending the lab inspection. The lab inspection will be scheduled.
   - At the June IBC meeting, Dr. Rathod's BUA was approved pending some lab inspection corrections. These corrections were made and the BUA letter was sent out.
   - At the June IBC meeting, Dr. Young's BUA was approved pending correction of the BUA application. This was completed and the letter was sent out.

5. **DURC UPDATE**
   - The DURC IRE (Dual Use Research of Concern Institutional Review Entity reviewed an application for Dr. Ronald Kwon, whose BUA renewal will be discussed later at this meeting.
   - The agent involved is Botulinum neurotoxin. The research involves injecting Botulinum toxin B to inhibit cholinergic nerve function and to examine effects on skeletal function. The lab does not modify the botulinum neurotoxin in any way. The DURC IRE reviewed the application by email.
   - The DURC IRE determined that none of the experimental effects of concern apply to this research, that the research does not meet the DURC definition, and that a risk mitigation plan is not warranted. A quorum of members voted to approve the application.
   - The acting IBC Chair sought a motion to endorse the DURC IRE's recommendation to approve the DURC application.
   - A member made a motion to approve the DURC application. Another member seconded the motion.
   - The committee voted unanimously to approve the DURC application for Dr. Ronald Kwon.

6. **BIOSAFETY OFFICER (BSO) REPORT***:* The Biosafety Officer Report includes (1) projects involving recombinant or synthetic nucleic acids covered under section III-E and III-F of the *NIH Guidelines,* (2) proposals involving non-recombinant biohazardous agents requiring BSL-1 and BSL-2 containment, and (3) administrative updates, such as room additions.

   a. Biosafety Officer Report
      - Dr. Gao, Dr. Chiu, Dr. Glass, and Dr. Stempien-Otero each renewed a BUA involving human cells.
      - Dr. Waterston, Dr. DePaolo, Dr. Theberge, and Dr. Grant each added a new room to their respective approvals.
      - Dr. Dunham, Dr. Murry, Dr. Trapnell, Dr. Gray, and Dr. Stevens each added a new cell sorting facility to their respective approvals.
      - Dr. Chen, Dr. Brentnall, Dr. Pan, and Dr. Vaughan each renewed a BUA involving human and non-human primate blood and cell lines.
      - Dr. Hajjar received a new BUA approval for human feces and *Mycobacterium bovis* used in mice.
      - Dr. Fontana received a new BUA approval for *Plasmodium chabaudii* used in mice.
      - Dr. Wang added human cells in mice to her BUA approval. She had previously been approved for human cells in vitro only.
      - Some lab areas in the Washington National Primate Research Center Western facility were rearranged and converted from ABSL-2 to ABSL-2 with ABSL-3 practices areas. Several BUA letters from Drs. Klatt, Fuller, and Hu were updated to reflect this change. No new agents were approved.
      - The acting IBC Chair sought a motion to approve this month's Biosafety Officer Report.
      - A member made a motion to approve this month's Biosafety Officer Report. Another member seconded the motion.
      - <u>The Committee unanimously voted to approve this month's Biosafety Officer Report.</u>

7. **INDIVIDUAL PROJECT REVIEWS**

   1. Baker, David, change, *Institute for Protein Design and affiliate investigators: (Baker Lab, King Lab, iGEM Lab)*
      - The assigned IBC Primary Reviewer presented the Primary Review.
      - This is a change request to add lentiviral vectors and human cells for in vitro use and cell sorting.
      - The lab inspection is pending. The required trainings have been completed.
      - The draft BUA letter was shown.
      - The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Baker.
      - <u>The Committee voted unanimously to approve the draft BUA for Dr. Baker, pending the lab inspection.</u>

   2. Chen, Eleanor, change, *Druggable pathways in rhabdomyosarcoma*
      - The assigned IBC Primary Reviewer presented the Primary Review.
      - This is a change request to include myxoma virus (a pox virus of rabbits) as an additional viral delivery agent. The goal is to introduce the CRISPR/Cas9 gene targeted vectors against tumor-specific essential genes into MYXV to enhance

tumor cell killing. This will involve transfection of the vector and culture in human cells in vitro. In addition, the virus will be given in vivo to mice that have implanted human tumor cells.

- An IBC member asked if the virus was zoonotic and known to be infectious to humans. The virus does not infect humans in nature, but has been known to infect human primary fibroblasts in a laboratory cell culture situation. BSL-2 containment is used for this virus.
- A lab inspection was not required for this change. All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Chen.
- The Committee voted unanimously to approve the draft BUA for Dr. Chen.

3. Fowler, Douglas, renewal, *Large-Scale Phenotyping of Tumor Suppressor Variants in Human Cells*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab studies the effects of mutations on cell function.
- A third generation lentiviral vector containing oncogenic inserts is used in vitro. Human cells and recombinant plasmids are also used.
- The lab was inspected and no deficiencies were found. The required trainings have all been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Fowler.
- The Committee voted unanimously to approve the draft BUA for Dr. Fowler.

4. Frevert, Charles, new, *Proteoglycans and Influenza Infection: Gene-targeted mouse models to study versican*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a new BUA from an established investigator. The lab studies how a family of proteins called proteoglycans regulate the ability of the immune system to detect, eliminate, and recover from viral lung infections.
- In this project, the lab will culture influenza virus and inoculate mice with influenza virus.
- The influenza virus used on this project is a mouse adapted strain, influenza A/PR/8/34. BSL-2/ABSL-2 containment will be used.
- Influenza vaccination prior to initiation of work with influenza virus is offered to personnel having direct contact with influenza virus, and those caring for infected animals or handling bedding or other waste of infected animals.
- A formal lab inspection was not required because all of the rooms on this project have been recently inspected. The biosafety officer met with the lab to review lab procedures. All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Frevert.
- The Committee voted unanimously, with one abstention, to approve the draft BUA for Dr. Frevert.

5. Hajjar, Lynn, renewal, *Linking Innate and Adaptive Immunity*

- The assigned IBC Primary Reviewer presented the Primary Review.

- This is a renewal of an existing BUA. The investigator is interested in innate immunity in the gut, and utilizes murine models to study this.
- This project involves working with mice infected with bacterial pathogens. These pathogens include *Bordetella pertussis*, *Pseudomonas aeruginosa*, *E. coli*, *Staphylococcus aureus*, and Salmonella enterica serovar Typhimurium.
- No new recombinant strains of these will be created, however existing recombinant strains of bacteria will be used.
- The lab was inspected and no deficiencies were found. All required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Hajjar.
- The Committee voted unanimously to approve the draft BUA for Dr. Hajjar.

6. Hoppins, Suzanne, renewal, *Mitochondrial Behavior*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The lab studies the behavior of mitochondria, including the mechanisms of mitochondrial movement on microtubules and the mechanism of mitochondrial fusion using biochemical and cell biology techniques.
- Replication deficient ecotropic gammaretroviral vectors are used in vitro. Human and non-human primate cells are also used.
- The lab was inspected and all deficiencies have now been corrected. The required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Hoppins.
- The Committee voted unanimously to approve the draft BUA for Dr. Hoppins.

7. Hu, Shiu-Lok, change, *Macaque model to validate the significance of a V1/V2-based vaccine toward protection against HIV-1 infection.*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request. The investigator is requesting to add AAV with a green fluorescent protein insert. The AAV will be used in a macaque model.
- The AAV was approved at ABSL-2 because all work with macaques must be conducted at a minimum of ABSL-2 because macaques are known to occasionally carry herpes B virus.
- A lab inspection was not required for this change because the laboratory has been inspected in the past 12 months. All required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Hu.
- The Committee voted unanimously to approve the draft BUA for Dr. Hu.

8. Kwon, Ronald, renewal, *Neuromuscular Regulation of Bone in Zebrafish*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a 3-year renewal. The PI studies skeletal muscle development pathways using a zebrafish model.
- The PI will use botulinum neurotoxin to paralyze fish and then manipulate them genetically using morpholinos, CRISPR/Cas9, and various viruses including AAV and herpes simplex virus (HSV) amplicons.

- The HSV amplicons will be received from the Neumeier lab at UW. Some of their approaches include transplanting murine cells into zebrafish, and the murine cells will also be manipulated using these approaches. The genes introduced using vectors include fluorescent proteins and "skeletal proteins" but no oncogenes. A variety of genetic knockout zebrafish will be used.
- The approval is contingent on replication-competent virus (RCV) testing. RCV testing must be conducted on each lot of HSV amplicon to be used, and each specific lot must be certified as RCV-negative.
- The room where mouse cell culture is performed at BSL-1 should be listed on the BUA letter.
- Dr. Kwon still needs to submit the IACUC 3-year renewal, which will be reviewed by the biosafety officer.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Kwon, contingent upon RCV testing results, revising the BUA application to list the BSL-1 room, and biosafety officer review of the IACUC protocol.
- The Committee voted unanimously to approve the draft BUA for Dr. Kwon, contingent upon RCV testing results, revising the BUA application to list the BSL-1 room, and biosafety officer review of the IACUC protocol.

9. Ladiges, Warren, change, *Anti-cancer gene expression platform*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change to add the use of lentiviral vectors in vitro and injection of filter-sterilized cell culture supernatant into mice.
- Third generation lentiviral vectors will be used.
- A lab inspection was not required for this change. All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Ladiges.
- The Committee voted unanimously to approve the draft BUA for Dr. Ladiges.

10. Monnat, Raymond, renewal, *Small Molecule Protection of Bone Marrow Hematopoietic Stem Cells*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a renewal of an existing BUA. The investigator studies hematopoiesis as it relates to leukemia.
- Human cells and third generation lentiviral vectors containing known oncogenes are used in vitro on the project.
- The laboratory inspection identified a number of issues that need to be addressed. The biosafety officer is working with the Monnat lab to correct these issues. The BUA letter will not be issued until the lab satisfies the lab inspection requirements.
- All required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Monnat. The Committee voted unanimously to approve the draft BUA for Dr. Monnat, pending a satisfactory lab inspection.

11. Pepper, Marion, change, *The Differentiation and Protective Function of CD4+ memory T cells*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request to add a recombinant strain of Plasmodium falciparum that expresses green fluorescent protein and luciferase.
- The parasite will be grown in vitro to measure efficacy of immune factors, such as antibodies, in restricting parasite growth.
- A lab inspection was not required for this change. All required trainings have been previously completed.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Pepper.
- The Committee voted unanimously to approve the draft BUA for Dr. Pepper.

12. Theberge, Ashleigh, change, *Studying cell signaling and cell-microenvironment interactions with new analytical tools*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a change request. The investigator is requesting to add several new strains of bacteria and fungi. Some of the strains have been modified to express green fluorescent protein and red fluorescent protein.
- The strains being added include *Aspergillus flavus, A. fumigatus, Fusarium solani, P. aeruginosa, Geomyces destructans, Trichophyton equinum, T. tonsurans, T. rubrum, Microsporum canis,* and *Penicillium marneffei*.
- The draft BUA letter was shown.
- The lab was inspected and no deficiencies were noted. All required trainings have been completed.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Theberge.
- The Committee voted unanimously to approve the draft BUA for Dr. Theberge.

13. Ware, Carol, renewal, *Human ES Cell Core*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This is a renewal BUA for the Human Embryonic Stem Cell Core. The core maintains cultures of stem cells (embryonic & induced pluripotent), cultures human/murine/non- human primate cells (primary and cell lines), and transduces human/murine cell lines with integrating viral vectors (e.g. AAV, Sendai, lentivirus, foamy virus).
- All viral vectors are engineered to be replication incompetent.
- Cells, including those with recombinant DNA, are also transplanted into mice. The introduction of some known oncogenes into vectors is reported.
- On the BUA application, question 53 was completed incorrectly.
- Dr. Ware still needs to submit the IACUC 3-year renewal, which will be reviewed by the biosafety officer.
- The draft BUA letter was shown.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Ware, pending correction of the BUA application and biosafety officer review of the IACUC protocol.
- The Committee voted unanimously to approve the draft BUA for Dr. Ware, pending correction of the BUA application and biosafety officer review of the IACUC renewal.

SUBCOMMITTEE REPORTS:

14. Gale, Michael, change, *The Host Response to Virus Infection*

- Three members of the IBC served as the Subcommittee Reviewers to conduct a preliminary review of this proposal to work with Junin virus. One of the Subcommittee Reviewers presented the Subcommittee Report.
- The Gale Lab in Immunology studies the immune response to viral infection. They seek authorization to study the effects of small molecules that activate the RIG-I innate immune pathway on infection and spread of non-vaccine strains of Junin virus in cell culture. This is a preliminary review for proposed work with this agent. It is a CDC Select Agent which would require additional approvals beyond the IBC.
- Junin is an arenavirus that is the causative agent of Argentine hemorrhagic fever. It is endemic to Argentina, where it is maintained in a rodent reservoir and transmitted to humans via aerosolized rodent excreta. Person-to-person transmission is rare but has been observed.
- A vaccine (Candid #1) is available in Argentina. The vaccine strain is approved by BMBL at BSL-2. Previously, other strains of Junin could only be studied at BSL-4; however, it has been, "reclassified to BSL-3, provided that all at-risk personnel are immunized and the laboratory is equipped with HEPA-filtered exhaust." The UW BSL-3 facility includes the necessary engineering controls.
- The Attending Physician for UW Medicine inquired with the CDC and USAMRIID regarding vaccine availability. At this time, there is no vaccine available in the United States. However, the CDC has provided information for vaccination at a facility in Argentina. The CDC stated that the vaccine cannot be shipped to the US; therefore, personnel requiring the vaccine would need to travel to Argentina. Both the CDC and USAMRIID work with the Junin virus in a BSL-4 facility.
- The UW does not have a BSL-4 laboratory facility and research requiring BSL-4 cannot be approved for work at UW. Dr. Gale has the following options:
    - Contract the work out to another BSL-4 laboratory that can safely accommodate the work.
    - Modify research plans to use a different virus strain that can be safely handled at BSL-2 or BSL-3.
    - Laboratory staff and other UW employees requiring the vaccine could travel to Argentina to be vaccinated in order to perform the work at BSL-3. However, this option will not be feasible if other staff need to be vaccinated (e.g., biosafety staff, facility staff, etc.). If the PI would like to move forward with this option, it would require further review, discussion, and consideration.
- The acting IBC chair made a motion to send a formal memo from the IBC & EH&S stating these options. Another member seconded the motion.
- <u>The Committee voted unanimously to send Dr. Gale a formal memo explaining the options for research involving Junin virus.</u>

15. Maloney, David, new, *A Phase 2 Multicenter Study of Axicabtagene Ciloleucel in Subjects with Relapse/Refractory Indolent Non-Hodgkin Lymphoma (INHL)*

- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a new BUA application for a multicenter trial of an autologous cell therapy for CD19-targeting T cells. The participant's T-cells are obtained, activated, and transduced with a retrovirus that expresses a transmembrane protein. Participants will be infused

with their own cells that have been transduced with the CAR-encoding gammaretrovirus.

- The protocol has been reviewed by the Recombinant DNA Advisory Committee, which determined that an in-depth review was not warranted.
- The subcommittee reviewed the consent forms and found that they adequately explained potential harms and risks relating to biosafety issues.
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Maloney. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Maloney.

FOR YOUR INFORMATION:

- An NIH reportable incident occurred. Due to time constraints, this will be discussed in full at the August IBC meeting.

ISSUES FROM THE FLOOR & PUBLIC COMMENTS:
There were no issues from the floor, and no public comments.

MEETING ADJOURNED AT APPROXIMATELY 11:20 a.m.