INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, October 17, 2018
Time: 10:00 AM – 12:00 PM

Location: Foege N-130A

Members Present:
1. Thea Brabb, Comparative Medicine *(Animal Containment Expert)*
2. H.D. "Toby" Bradshaw, Biology *(Plant Expert)*
3. Richard Grant, Washington National Primate Research Center
4. Garry Hamilton (*Community Member*)
5. Kevin Hybiske, Allergy and Infectious Diseases
6. David Koelle, Allergy and Infectious Diseases
7. Scott Meschke, Environmental & Occupational Health Sciences
8. Jason Smith, Microbiology (*IBC Vice Chair*)
9. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer, Animal Containment Expert*)
10. Paul Swenson, Seattle-King Co. Dept. of Public Health (*Community Member*)

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 Institutional Biosafety Committee (IBC) Chair called the meeting to order at 10:01 a.m. A quorum was present.

2. **REMINDER:** The 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 IBC Chair sought a motion to approve the minutes from the September 19, 2018 meeting.
   - A member made a motion to approve the September 19, 2018 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the September 19, 2018 meeting minutes. There was one abstention from a member who was unable to attend the September IBC meeting.

4. **OLD BUSINESS:**
   - At the August meeting, Dr. Beliveau's BUA was approved pending a lab inspection upon the investigator's arrival.
   - At the September meeting, Dr. Greenberg's BUA was approved pending the removal of murine AAV from the BUA letter. The BUA has been sent.
   - At the September meeting, Dr. Greninger's BUA was approved pending a successful lab inspection. This is still pending.
   - At the September meeting, Dr. Najafian's BUA was approved pending a successful lab inspection. This has been completed, and the BUA has been sent.
   - At the September meeting, Dr. Oberst's BUA was approved pending a BUA revision. This has been made, and the BUA has been sent.
   - At the September meeting, Dr. Poolos's BUA was approved pending training. This has been completed, and the BUA has been sent.
   - At the September meeting, Dr. Tang's BUA was approved pending a successful lab inspection. This has been completed, and the BUA has been sent.

5. **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. Furlong renewed a BUA for *Effects-Related Biomarkers of Environmental Neurotoxic Exposures,* using E. coli, non-pathogenic strains in vitro.
      - Dr. Mulligan removed the use of recombinant or synthetic DNA/RNA (including siRNA) in rats for his BUA titled *Mediators Involved in Direct Lung Ischemia Reperfusion Injury of Lung.*
      - Dr. Schwartz's labs moved to a new location. A change was made to reflect the new lab spaces for his BUAs for *Neuro-Endocrine Control of Energy Balance [in mice and rats].*
      - Dr. Sullivan added the use of non-human primate tissue confined to designated areas of each room for her BUA *Cellular and Molecular Mechanisms of Synaptic Transmission.*

- Dr. Kim updated the BUA *IKKBeta Mediated Impairment of Endothelial Nitric Oxide Production* to list a lab move.
- Dr. Meschke added a new BSL 2 lab space and new cell lines for in vitro work to the BUA *Detection and Characterization of Pathogens in Environmental Media.*
- Dr. Tian received a new BUA for use of human blood, tissue, body fluids, and cell lines in vitro for *Preoperative nicotinamide riboside supplementation in elective LVAD patients: Myocardial metabolism and redox state effects.*
- Dr. Kwon's lab moved locations, and all BSL 2 in vitro work was removed from the BUA *Neuromuscular Regulation of Bone in Zebrafish.*
- Dr. Soge's BUA for *Recharge Center CORE Laboratory Testing: DNA and RNA Amplification of STIs* was renewed, allowing in vitro use of chlamydia trachomatis, mycoplasma genitalium, Neisseria gonorrhoeae, and trichomonas vaginalis.
- Dr. Matute-Bellow renewed the BUA for *Inhibition of the Fas/FasL system in experimental acute lung injury,* using staphylococcus aureus in mice. This project also uses non-viral recombinant or synthetic DNA/RNA and human blood, tissue, body fluids, and cell lines in vitro.
- Dr. Hebert renewed use of human blood, tissue, body fluids, and cell lines in vitro for the BUA *Obstetric-Fetal Pharmacology Research Unit Lab.*
- Dr. Himmelfarb renewed the BUA *Kidney Research Institute Laboratory for Measuring Assays Related to Kidney Disease and its Complications,* using human blood, body fluids, and cell lines in vitro.
- Dr. Yeung received a new BUA for *Modulation Of Drug Transport At The Renal Proximal Tubule By Uermic Solutes - Implications In Chronic Kidney Disease,* using human blood, tissue, body fluids, and cell lines in vitro.
- Dr. Mao added new rooms to their BUA *Mechanism of BCRP* for in vitro work with human blood, tissue, body fluids, and cell lines.
- Dr. Ingalls received a new BUA for the project *Analyzing metabolites from marine microorganisms.* This uses Alteromonas macleodii, Ruegeria pomeroyi, and Vibrio fischeri in vitro.
- Dr. Wurfel renewed the BUA for *Human Innate Immune Variation.* This approves in vitro use of Acinetobacter baumannii, human blood, tissue, body fluids, and cell lines, and recombinant or synthetic DNA/RNA (non-viral).
- Dr. Davis was approved for in vitro use of human blood, tissue, body fluids, cell lines, and human induced pluripotent (iPS) stem cells with the BUA *Investigating the role of GBA in the propagation of Lewy bodies in Parkinson's disease (PD).*
- The 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>

6. **DURC REPORT:** The Dual Use Research of Concern Institutional Review Entity (DURC IRE) did not meet this month because there were no applications to review.

7. **INDIVIDUAL PROJECT REVIEWS**

   a. Hallstrand, Teal, renewal, *Asthma and Translational Research Core*
   - The assigned IBC Primary Reviewer presented the Primary Review.

- This research analyses human airway lining fluid, leukocytes isolated from peripheral human blood, and primary cell cultures from umbilical cord blood and tracheal samples. Ex vivo, epithelial cell culture models of allergen-induced and respiratory virus-induced, human rhinovirus, and epithelial dysfunction are used, often by co-culture model with leukocytes.
- Lentiviral vector use containing shRNA transduction to silence gene expression of PLA2GIO in epithelial cell lines or primary cells in vitro is the most important biohazard.
- The lab was inspected and no deficiencies were identified.
- 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. Hallstrand.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Hallstrand.</u>

b. Rasmussen, Jeffrey, new, *Interplay between skin and axons*

- The assigned IBC Secondary Reviewer presented the Primary Review.
- This project uses zebrafish to understand the cellular and molecular mechanisms involved in somatosensory axon development, repair, and regeneration. The lab engineers plasmids in E. coli K12 strains and generates transgenic zebrafish using microinjection of these plasmids in embryos.
- The lab has not yet been set up. The biosafety officer will inspect the lab once the investigator moves to the new location and the lab is ready.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- The IBC Secondary Reviewer made a motion to approve the draft BUA for Dr. Rasmussen pending a successful lab inspection.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Rasmussen pending a successful lab inspection.</u>

c. Stuber, Garret, new, *Neural Circuits for Motivation and Reward*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This project's goal is to genetically manipulate neural circuits in mouse brains to identify regions that control specific behaviors associated with psychiatric disorders in humans. Viral vectors derived from adeno-associated virus, pseudorabies virus, and envAG-deleted rabies virus are used to transduce non-oncogenic constructs into mouse brains in vivo, as well as in mouse and human cell lines in vitro. E. coli K12 strains will be routinely cloned.
- Tissue fixatives used to perfuse the mouse brains and tetrodotoxin are the greatest biohazards used.
- This lab is only breeding mice, and is not creating transgenic mice. The staff do not need to be vaccinated for rabies virus because they are using an attenuated strain at BSL 2.
- The lab has not yet been set up. The biosafety officer will inspect the lab once the investigator moves to the new location and the lab is ready.
- 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. Stuber pending a successful lab inspection and changing of the BUA letter.
- The Committee voted unanimously to approve the draft BUA for Dr. Stuber pending a successful lab inspection and changing animal use space on the BUA letter. There was one abstention from a member who arrived late to the discussion.

8. SUBCOMMITTEE REPORTS:

d. Green, Damian, new, *An Open-Label Phase 1/2 Study of JCARH125, BCMAtargeted Chimeric Antigen Receptor (CAR) T Cells, in Subjects with Relapsed and/or Refractory Multiple Myeloma*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a trial of treatment of patients with autologous T cells that are transduced to express a CAR that recognizes a molecule expressed on the surface of multiple myeloma cells, namely BCMA. It is a first in humans. PBMC will be obtained from patients and shipped to the sponsor, where they will be lentivirally transduced with the CAR molecule. The lentivirus is VSV envelope pseudotyped, third generation, self-inactivating, and replication incompetent. The cells will be infused into patients at UW.
- Lentivirus insertional mutagenesis and cytokine release syndrome safety issues are present for patients. The subcommittee also commented that the cell product should not contain residual transduction-competent lentivirus capable of entering the cells of personnel who might be exposed to the cell product.
- A second molecular for the target is a convenient way to track transduction efficiency. There have been positive responses to other CAR products targeting BCMA from other companies.
- The labs are inspected under a core facility. No additional lab inspection is required for this BUA approval.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Green. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Green.

e. Shadman, Mazyar, new, *A Global Randomized Multicenter Phase 3 Trial To Compare The Efficacy And Safety Of Jcar017 To Standard Of Care In Adult Subjects With High-Risk, Transplant-Eligible Relapsed Or Refractory Aggressive B-Cell Non-Hodgkin Lymphomas (Transform)*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- The objective of this study is to compare the efficacy in subjects treated with JCAR017 versus subjects treated according to standard of care defined as event-free survival. The Phase 1/2 portion of this Phase III study has been completed. It is not a first in humans.
- RCL and insertional mutagenesis is a concern, although neither has been detected with JCAR017 to date. If a RCL is detected the patient will be followed until negative. If CAR-T cells compromise is greater than 1% of blood cells at any point after 12

months then integration analyses will be done to determine if the pattern is consistent with a predominant insertion site.
- The consent form was not reviewed due to the proposed changes to the *NIH Guidelines.*
- The labs are inspected under a core facility. No additional lab inspection is required for BUA approval.
- All of the required trainings have been completed.
- The draft BUA letter was shown.
- A member made a motion to approve the draft BUA letter for Dr. Shadman. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Shadman.

10. FOR YOUR INFORMATION:

- **Operations Manual and Charter Revisions**: Minor changes to both documents were presented by a biosafety officer and reviewed with the Committee. The Committee voted unanimously to approve all changes made to the IBC Operations Manual and Charter.
- **NIH Incident Reports**: Two incident reports were presented. One was a follow up to an incident involving an abrasion caused by a macaque swipe who had received recombinant viruses. The NIH OSP stated that the University's response was appropriate, and that no further action was required. Another incident involved an individual who was bitten on the fingertip by a squirrel monkey that had be injected with adeno-associated virus. The Committee is waiting on an assessment from NIH OSP.
- **National Biosafety Month**: A biosafety officer presented on the history of National Biosafety Month, and gave University of Washington biosafety updates from this past year. The focus for 2018 is promoting a culture of safety.
- **Proposed Changes to NIH Guidelines:** The IBC submitted comments regarding the proposed changes to NIH Guidelines. The comment supports these changes, but asks for more technical guidance for IBC review of human gene transfer in lieu of RAC review.

11. ISSUES FROM THE FLOOR & PUBLIC COMMENTS:

There were no issues from the floor, and no public comments.

12. MEETING ADJOURNED AT APPROXIMATELY *10:50* A.M.