INSTITUTIONAL BIOSAFETY COMMITTEE

UNIVERSITY of WASHINGTON

Meeting Minutes

Date: Wednesday, September 19, 2018
Time: 10:00 AM – 12:00 PM

Location: Health Sciences Building, Room T-478

Members Present:

1. Thea Brabb, Comparative Medicine *(Animal Containment Expert)*
2. H.D. "Toby" Bradshaw, Biology *(Plant Expert)*
3. Lesley Colby, Comparative Medicine *(Animal Containment Expert)*
4. Richard Grant, Washington National Primate Research Center
5. Garry Hamilton (*Community Member*)
6. Kevin Hybiske, Allergy and Infectious Diseases
7. David Koelle, Allergy and Infectious Diseases
8. Stephen Libby, Laboratory Medicine (*IBC Chair*)
9. Matthew R. Parsek, Microbiology
10. Tina Rogers *(Community Member)*
11. Eric Stefansson, Environmental Health & Safety (*Biosafety Officer, Animal Containment Expert*)
12. 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 10:00 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 August 15, 2018 meeting.
   - A member made a motion to approve the August 15, 2018 minutes. Another member seconded the motion.
   - The committee voted unanimously to approve the August 15, 2018 meeting minutes.

4. **OLD BUSINESS:**
   - At the August meeting, Dr. Baker's BUA was approved pending updated training. Training has since been updated.
   - At the August meeting, Dr. Beliveau's BUA was approved pending a lab inspection upon the Investigator's arrival.
   - At the August meeting, the committee voted unanimously to table Dr. Cheung's review.
   - At the August meeting, Dr. Lee's BUA was approved pending the addition of an influenza occupational health comment on the BUA letter. This has been completed.
   - At the August meeting, Dr. Papayannopoulou's BUA was approved pending the change of biosafety level for the lentiviral vector. The BUA letter has since been sent out.

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. Freeman renewed a BUA for *Use of FACS for engineering E. coli for optimal botryococcene production.* This BUA approves the use of E. coli, non-pathogenic strains in vitro.
      - Dr. Zhang added the use of human source material in mice to their BUA.
      - Dr. Dicheck added the use of the Pathology Flow Cytometry Core Facility for previously approved agents to their BUA for *Gene Transfer in Cardiovascular Disease.*
      - Dr. Murry renewed a BUA for *UW Medicine Heart Regeneration Program (HRP).* This BUA approves work for human blood, tissue, body fluids, and cell lines in vitro.
      - Dr. Doty renewed a BUA for *Transgenic plants for remediation,* using transgenic poplar plants.
      - Dr. Baird renewed a BUA for *Tissue Diagnostic Development.* This approves in vitro use of human blood, tissue, body fluids, and cell lines.
      - Dr. Prasad renewed a BUA for *Ontogeny of drug metabolizing enzymes.* This approves in vitro use of human blood, tissue, body fluids, and cell lines.
      - Dr. Cao became the new PI for *Predicting Therapy Response,* previously ran by Dr. Jeffrey Schwartz. This project uses human cells transduced with gammaretroviral vectors, replication deficient and amphotropic (tested negative for RCV), in mice and in vitro. It also uses human blood, tissue, body fluids, and cell lines in vitro.

- Dr. Mustelin received a new BUA for *Molecular mechanism of Rheumatoid Arthritis and Lupus.* This BUA approves use of recombinant or synthetic non-viral DNA/RNA enhanced gene delivery methods in vitro, as well as human blood, tissue, body fluids, and cell lines.
- Dr. Eichler added the use of the Immunology Cell Analysis Facility for previously approved human cells in vitro.
- Dr. Maier renewed a BUA for *Sample Processing for Clinical Research Studies.* This BUA approves in vitro use of human blood, tissue, body fluids, and cell lines.
- Dr. Ladiges added the use of the Pathology Flow Cytometry Core Facility for previously approved agents.
- Dr. Stella received a new BUA for *ST in PD-GBM*, using human blood, tissue, body fluids, and cell lines in vitro and in mice.
- Dr. Buckner added the use of wild type strains of bacteria in vitro to *Buckner antiparasitic and antibacterial drug discovery*.
- Dr. Pepper added the use of Pseudomonas aeruginosa in vitro to *The Differentiation and Protective Function of Memory T and B cells*.
- Dr. Telfer received a new BUA for *Robotic system to study injuries and surgical treatments of the knee, the ankle, and the foot.* This BUA approves for in vitro use of human blood, tissue, body fluids, and cell lines.
- Dr. Paik became the new PI for *GNAC facility*, previously ran by Dr. Hajjar. This project uses human feces and mycobacterium bovis, BCG strain in mice.
- Dr. Gale added a new lab at SLU 3.2, as well as an additional room for live imaging of Salmonella.
- The following Investigators were approved to move to the ARCF: Dr. Kiem, Dr. Hu, Dr. Adams Waldorf, Dr. Woodrow, Dr. Berger, Dr. Fuller, Dr. Stamatatos, and Dr. Murphy.
- The following Investigators were approved to move to SLU 3.2: Dr. Lagunoff, Dr. Sweet, Dr. Gale, Dr. Mullins, Dr. Mougous, Dr. Smith, Dr. Woodward, Dr. Reniere, and Dr. Hyde.
- 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. Bothwell, Mark, change, *Neurotrophin Receptor Interactions*
   - The assigned IBC Primary Reviewer presented the Primary Review.
   - This change adds lentiviral vectors for in vitro use in human iPS cells.
   - 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. Bothwell.
   - <u>The Committee voted unanimously to approve the draft BUA for Dr. Bothwell.</u>

b. Cheung, Kevin, new, *Mechanisms Regulating Collective Cell Invasion and Multiclonal Metastasis*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This study will model steps in tumor invasion and metastasis using an experimental platform leveraging normal and tumor organoids. Genetically modified organoids will be injected into immunocompromised mice at FHCRC and then transported to UW for a series of PET/CT images.
- This project returned from last month's committee meeting because the application was unclear. Questions from the reviewers and biosafety officer have been answered. There are no DCM concerns from the reviewer and biosafety officer.
- 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. Cheung.
- The Committee voted unanimously to approve the draft BUA for Dr. Cheung.

c. Davis, Jennifer, renewal, *The cellular and molecular mechanism of cardiac wound healing and fibrotic remodeling*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This project attempts to identify the cells required for fibrotic response to injury in the heart, skeletal muscle, and skin.
- The greatest hazards are working with third generation lentiviral vectors with various genes during injection into mice and using adenoviral vectors to transduce human and rodent cell lines.
- 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. Davis.
- The Committee voted unanimously to approve the draft BUA for Dr. Davis.

d. Greenberg, Philip, renewal, *Mechanisms of Murine Tumor Eradication*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This project uses murine models to identify the most effective use of T cell based immunotherapy to treat various types of cancers.
- The lab was inspected and no deficiencies were identified.
- All of the required trainings have been completed.
- The draft BUA letter was shown. One item, murine AAV, is to be removed.
- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Greenberg.
- The Committee voted unanimously to approve the draft BUA for Dr. Greenberg pending the removal of murine AAV from the BUA letter.

e. Greninger, Alexander, new, *Discovery and Characterization of Virus-Host Interactions*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The goal of this project is to use unbiased screens to discover how virus proteins use host proteins for viral replication.

- The greatest biohazardous risk to laboratory personnel s the use of lentiviral vectors.
- The committee discussed the possible uses of the recombinant viruses at BSL2. The biosafety officer will ask the lab to list their use on the BUA application to ensure that there is no purposeful gain-of-function.
- The lab has not yet been set up. The biosafety officer will inspect the lab once 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. Greninger pending lab inspection and clarification from PI.
- The Committee voted unanimously to approve the draft BUA for Dr. Greninger pending a successful lab inspection.

f. Miao, Carol, new, *Non-viral Gene Transfer to Canine Liver*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The research goal is to develop non-viral gene therapy to allow patients affected with Hemophilia A to produce their own functional factor VIII clotting protein. Canines used in this project will undergo surgery, imaging, and recovery at the University of Washington. No lab spaces will be used at UW.
- 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. Miao.
- The Committee voted unanimously to approve the draft BUA for Dr. Miao.

g. Najafian, Behzad, renewal, *Non-invasive biomarkers and models of kidney disease*

- The assigned IBC Primary Reviewer presented the Primary Review.
- The project goal is to understand molecular mechanism of kidney disease initiation and progression, and to develop biomarkers for kidney disease.
- Biohazards include use of a gammaretroviral vector with an oncogenic insert, as well as fixatives for microscopy.
- The lab inspection is pending.
- 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. Najafian pending a successful lab inspection.
- The Committee voted unanimously to approve the draft BUA for Dr. Najafian pending a successful lab inspection.

h. Oberst, Andrew, renewal, *Programmed Cell Death and Immunity*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This renewal strives to understand the mechanisms that control the cellular suicide programs called “programmed cell death,” and the immunological consequences of different types of programmed cell death in vivo.
- Lentiviral vectors, influenza virus, gammaretroviral vectors, Zika virus, and West Nile virus are used on the project both in vitro and in mice. A question was asked about whether adenoviral vectors are used. Adenoviral vectors are not used, only AAV.

The PI will remove a lingering reference to adenoviral vectors on the BUA application.
- 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. Oberst pending the removal of adenoviral vectors stated on the current BUA application.
- The Committee voted unanimously to approve the draft BUA for Dr. Oberst pending BUA revision.

i. Paredez, Alexander, renewal, *Study of the Cytoskeleton and Membrane trafficking in Giardia lamblia*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This project renewal strives to understand signaling and regulation of the cytoskeleton in the basal eukaryote Giardia lamblia using fluorescent reporter genes and manipulation of endogenous gene expression with morpholinos.
- The greatest biohazard is experiments to encyst the parasite.
- 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. Paredez.
- The Committee voted unanimously to approve the draft BUA for Dr. Paredez.

j. Polyak, Stephen, renewal, *Virus-Host Interactions in Cell Culture*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This project studies how viruses interact with host cells. This renewal is to focus on hepatitis C and Zika, and to perform studies under BSL2 or BSL2 with 3 practices. This does not involve any animal work.
- Poliovirus type 2 research is subject to special regulations because wild poliovirus type 2 has been declared eradicated. The Polyak lab is only using poliovirus type 1, which is not of concern. The biosafety officer has received clarification on Newcastle Disease from the source.
- There is a medical management plan in place for polio vaccine requirements.
- 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. Polyak.
The Committee voted unanimously to approve the draft BUA for Dr. Polyak.

k. Poolos, Nicholas, new, *Epilepsy and Dendritic Excitability*
- The assigned IBC Primary Reviewer presented the Primary Review.
- This project studies the effect of ion channel dysfunction (HCN1) and epilepsy. AAV encoding the HCN1 gene are administered intracranially to rats and mice to study the effects of specific mutations in this gene. Resected human brain tissue is also studied for possible associations between HCN1 and epilepsy.
- The lab was inspected and no deficiencies were identified.
- The PI needs to complete required trainings
- The draft BUA letter was shown.

- The IBC Primary Reviewer made a motion to approve the draft BUA for Dr. Poolos pending completion of training and clarification of species use.
- The Committee voted unanimously to approve the draft BUA for Dr. Poolos pending training completion.

l. Smith, Jason, change, *Antiviral Mechanisms of Defensins*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This change adds human, canine, feline, and murine parvoviruses, as well as recombinant virus-like particles based on the capsids of these viruses for use in cell culture experiments.
- Occupational Health has been consulted for groups at risk from parvovirus. A letter of recommendations of information regarding biohazardous agents and medical counseling will be made available to all lab personnel. Women of child bearing potential are especially at risk.
- The lab was recently inspected, so a new 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. Smith.
- The Committee voted unanimously to approve the draft BUA for Dr. Smith.

m. Tang, Chongren, new, *Cholesterol Transporters, Inflammation, Atherosclerosis, and Insulin Resistance*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This project uses lentiviral vectors to transduce GFP fusion constructs into mouse or human cells to study signal transduction.
- A final lab inspection is needed.
- 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. Tang pending final lab inspection and corrections on BUA application.
- The Committee voted unanimously to approve the draft BUA for Dr. Tang pending a successful lab inspection.

n. Wong, Rachel, change, *Development of the retina (mouse)*

- The assigned IBC Primary Reviewer presented the Primary Review.
- This change requests use of adeno-associated viral vectors in vivo via intraocular injection to study the development of retinal neurons in mice.
- The lab was recently inspected, so a new 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. Wong.
- The Committee voted unanimously to approve the draft BUA for Dr. Wong.

8. SUBCOMMITTEE REPORTS:

o. Collier, Ann, new, *HIV-1-Gag Conserved-Element DNA Vaccine (p24CE) as Therapeutic Vaccination in HIV-Infected Persons with Viral Suppression on Antiretroviral Therapy*

- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This study is to evaluate the safety, immunogenicity, and preliminary efficacy of a novel vaccine encoding conserved parts of the HIV-1 core protein (p24Gag) as a therapeutic vaccine in persons with HIV infection who have been treated with antiretroviral therapy. The vaccine will be reconstituted at the Harborview Medical Center (HMC) pharmacy and then given by injection in a clinic at HMC.
- The lab was inspected and no deficiencies were identified.
- 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. Collier. Another member seconded the motion.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Collier.</u>

p. Disis, Mary, new, *Phase I study evaluating benefit of PRGN-3005 (autologous MUC16-specific CAR T cells) delivered by intravenous infusion (IV) in advanced stage recurrent platinum resistant ovarian cancer patients*

- Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a T cell adoptive therapy trial in patients with advanced chemo-resistant ovarian cancer, and will evaluate the first-in-man use of PRGN-3005 cells in patients. [redacted]
- Accidental parenteral exposure of staff or family to the cell product or patient blood could lead to transduction of cells by residual plasmids in the infusion product. The concern is reduced because the cell product is washed prior to infusion. Sharps control is most important for occupational workers.
- There is no concern of SB-11 transposes in regards to the human genome, because it is designed not to integrate. Patients are also not at risk for secondary cancers from this study.
- The lab was inspected and no deficiencies were identified.
- 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. Disis. Another member seconded the motion.
- <u>The Committee voted unanimously to approve the draft BUA for Dr. Disis.</u>

q. Disis, Mary, new, *Phase I study evaluating benefit of PRGN-3005 (autologous MUC16-specific CAR T cells) delivered by intraperitoneal infusion (IP) in advanced stage recurrent platinum resistant ovarian cancer patients*

- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This is a T cell adoptive therapy trial in patients with advanced chemo-resistant ovarian cancer, and will evaluate the first-in-man use of PRGN-3005 cells in patients. The PRGN-3005 *Sleeping Beauty* therapy is a non-viral system of modified T cells that allows integration of the MUC16 CAR, membrane bound IL-15, and HER1t kill switch transgenes

in autologous T cells collected from the patient by electroporation, given by intraperitoneal infusion (IP).

- Accidental parenteral exposure of staff or family to the cell product or patient blood could lead to transduction of cells by residual plasmids in the infusion product. The concern is reduced because the cell product is washed prior to infusion. Sharps control is most important for occupational workers.
- There is no concern of SB-11 transposes in regards to the human genome, because it is designed not to integrate. Patients are also not at risk for secondary cancers from this study.
- The lab was inspected and no deficiencies were identified.
- 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. Disis. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Disis.

r. Paulson, Kelly, new, *ATTAC-MCC: Phase I/II study of Autologous CD8+ and CD4+ Transgenic T cells expressing high affinity MCPyV-specific TCRs combined with Avelumab and Class I MHC -upregulation in patients with metastatic MCC refractory to PD-1 axis blockade*

- Two members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.
- This trial tests the safety of a form of recombinant T cell therapy to treat Merkel Cell Carcinoma.
- The lab was inspected and no deficiencies were identified.
- 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. Paulson. Another member seconded the motion.
- The Committee voted unanimously to approve the draft BUA for Dr. Paulson.

10. FOR YOUR INFORMATION:

- It was stated that a new ad hoc reviewer will be assisting the UW IBC beginning in October 2018.
- Proposed NIH Guidelines changes include streamlining oversight and removing duplicate reporting, revising the scope of the IBC, and limiting RAC review. Principal Investigators at UW have been asked to share thoughts and feedback to the IBC by October 10, 2018.
- An NIH reportable incident occurred on August 17th. An employee received a potential cut or scratch from a non-human primate (NHP) while loading enrichment devices. The NHP had been administered recombinant SHIV. The employee washed the hands and sought medical attention and follow-up care. In future, the employee can use a device placed between the cage and the person while refiling the devices.
- October is National Biosafety Month.
- Jude Van Buren, Director of UW Environmental Health & Safety, is retiring after serving in this position since 2009.

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

12. MEETING ADJOURNED AT APPROXIMATELY 12:00 P.M.

Previous Minutes	
s. Disis, Mary, new, *Phase I study evaluating benefit of PRGN-3005 (autologous MUC16-specific CAR T cells) delivered by intravenous infusion (IV) in advanced stage recurrent platinum resistant ovarian cancer patients* • **Three members of the IBC served as the Subcommittee Reviewers. One of the Subcommittee Reviewers presented the Subcommittee Report.** • **This is a T cell adoptive therapy trial in patients with advanced chemo-resistant ovarian cancer, and will evaluate the first-in-man use of PRGN-3005 cells in patients. The PRGN-3005 *Sleeping Beauty* therapy is a non-viral system of modified T cells that allows integration of the MUC16 CAR, membrane bound IL-15, and HER1t kill switch transgenes in autologous T cells collected from the patient by electroporation, given by intravenous infusion (IV).** • **Accidental parenteral exposure of staff or family to the cell product or patient blood could lead to transduction of cells by residual plasmids in the infusion product. The concern is reduced because the cell product is washed prior to infusion. Sharps control is most important for occupational workers.** • **There is no concern of SB-11 transposes in regards to the human genome, because it is designed not to integrate. Patients are also not at risk for secondary cancers from this study.**	

• **The lab was inspected and no deficiencies were identified.** • **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. Disis. Another member seconded the motion.** • **<u>The Committee voted unanimously to approve the draft BUA for Dr. Disis.</u>**	