Boston University
Institutional Biosafety Committee (IBC)
August 20, 2024 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 12:55 PM

Members Present:	R. Ingalls, R. Davey, E. Muhlberger, I. Afasizheva, W. Lu, V. Gouon-Evans, X. Brown, T. Winters, N. Dey, C. Thurman, J. Keeney, R. Timmerman, V. Britton, S. Ghosh
Guests Present:	A. Ellis, A. Ahmad, J. Wood, P. Richmond, C. Fernald
Staff Present:	C. McGoff, L. Campbell

I. Review of July 16, 2024 IBC Meeting Minutes (R. Ingalls)
No concerns were voiced.
Motion: Approved
For: 13; Against: 0; Abstain: 1; Absent: 0

II. Chair's Report: Nothing to report.

III. New Business:
A. IBC Office Updates: Members were encouraged to attend the upcoming IBC Public meeting on September 17, 2024.
B. Review of Research Occupational Health Program (ROHP) and Environmental Health and Safety (EHS) Report: No incidents to report from ROHP.

IV. Protocol Review
1. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2645	[redacted]	Evaluation of medical countermeasures in rodents	4	4	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rob Davey Additional Reviewer: M. Mazur
Applicable NIH Guidelines: Sections III-D-1-c, III-D-4-a, III-D-4-b	

Meeting Comments: PI's recently approved BSL4/ABSL4 IBC protocol studies countermeasures in small animal models infected with high hazard BSL4 viral pathogens. The actual animal work of this protocol is detailed separately in Animal Research Service (ARS) Center Director's IBC protocol [redacted] that it is carried out by ARS staff. This protocol nevertheless, does provide a broad overview of the types of studies being carried out. The proposed amendment will add recombinant DNA work through the use of adenoviral vectors and VSV expressing various GP of targeted viruses being studied. The lab members are experienced in handling a variety of viral pathogens including adenoviral and VSV vectors. The rDNA section lists the mouse strains that will be involved in these studies. The viral vectors proposed include replication deficient adenovirus CHAdOx1, replication deficient rAd26 and rAd5, and a replication deficient VSV virus. The PI states these constructs are replication deficient although it is unclear if the VSV vector meets those standards since the G protein is being replaced by another viral protein as part of this work, that may reinstate replication competence. It remains unclear how these recombinant viral vectors will be used sequentially with the infection model. There is no mention of the use of these recombinant viruses in the description of laboratory procedures and manipulations. The following will be communicated to the PI:

- Although the overall objective of the protocol is to evaluate countermeasures in rodent models, there is no clear statement in this amendment to suggest that the work is designed to test vaccines. Please provide appropriate statement to clarify the purpose of the amendment.
- Provide a brief statement of the flow of work with these recombinant vectors (for example: animal immunization in ABSL2 followed by challenge with RG4 pathogens in ABSL4; or as appropriate).

- Please provide brief scientific background of how adenovirus CHAdOx1, rAd26 and rAd5 are replication defective and why they are chosen for this project.
- It is unclear how the VSV vector meets the standard of being replication incompetent since the G protein that is being replaced by another viral protein as part of this work, may reinstate replication competence. The rDNA section H question #16 says they are replication incompetent. Please clarify.
- The referenced ABSL2 IBC protocol [redacted] only has mention of VSV vector, not the adenoviral vectors. Please clarify what is their source and any rDNA modifications are being done on them in this protocol.
- If the use of adenovirus CHAdOx1, rAd26 and rAd5 are going to be used for animal immunization in protocol [redacted], that protocol needs to amended.

Motion: Conditional Approval (Admin Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz –Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2642	[redacted]	Propagation and Characterization of Risk Group 4 viruses	4	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Robin Ingalls

Applicable NIH Guidelines:

Meeting Comments: The objective of this protocol is to receive, store and limited propagation of BSL4 viruses. The protocol covers transport into the NEIDL, work, analysis of virus amounts, storage and inactivation. This includes a number of filoviruses; arenaviruses; bunyaviruses; and paramyxoviruses. There is no animal work proposed for this protocol. All processes have been reviewed previously and approved. This amendment will add the use of some SARS-CoV2 strains that have been propagated in the BSL4 suite and therefore can't be moved down to BSL3, which is the acceptable biosafety level for SARS-CoV2 propagation. The liquid and solid waste decontamination between this virus and the others included will not differ. Overall, appropriate precautions, in the BSL4 lab, appear to be used. The amendment also removed Dr. [redacted] and [redacted] as research mentors.

Motion: Approve	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2659	[redacted]	Regulatory mechanisms of mitochondrial DNA packaging and gene expression	2	N/A	BUMC

Primary Reviewer: Valerie Gouon-Evans	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, Section III-E-1

Meeting Comments: This is a new BSL2 project from a new investigator in Boston University. The goal of this project is to understand how mitochondrial DNA (mtDNA) gene expression activity is regulated to meet cellular energetic needs and how errors in this process contribute to cancer, neurodegeneration, and age-related decline. They will specifically investigate the mechanisms that lead to altered mtDNA expression in response to distinct stimuli and explore the biochemical pathways underlying genome activation and silencing. These studies will be conducted in human culture cells and with reconstituted systems using genomics, molecular biology, and biochemistry. They will perform subcellular fractionation to isolate mitochondria. They will create recombinant lentiviruses for stable expression of proteins in human cells using 3rd generation inducible or constitutive lentiviral expression vectors and will use various chemicals and stressors to inhibit aspects of mitochondrial activity and biology. They will also use plasmids to produce recombinant proteins in *E. coli*. All centrifugations of viruses will be performed in sealed centrifuge rotors. Lab work will be performed using lab coats, gloves, and protective eye wear when working with viruses. All consumables coming into contact with lentiviruses will be disinfected using 10% bleach for at least 10 minutes (for surface cleaning) and 30 minutes for liquid waste. This is a well written and complete protocol.

BUA Site Assessment: The lab is new and is in the process of settling in. All safety trainings are current. New biosafety cabinets has been ordered. PI is currently using an existing biosafety cabinet, which is still certified for use.					
Motion: Approve	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2523	[redacted]	Study of Selective Neuronal Vulnerability in Alzheimer's Disease	2	1	BUMC

Primary Reviewer: Weining Lu | Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1; Appendix B-I, C-I, C-II.

Meeting Comments: The goal of this project is to molecularly dissect the pathological mechanisms neuronal degeneration in Alzheimer's disease (AD). They will develop induced pluripotent stem cells from AD patients where they will modulate expression of specific neuronal transcription factors via lentiviral transduction or conditional knock-out cell line model. Additionally they will also use Alzheimer's mouse models to decipher the pathological cascade that leads to neurodegeneration in AD. Experimental procedures include using culture of human induced pluripotent stem cells and fibroblasts, overexpression genes of neurogenic factors and other transcription factors using lentivirus produced in the lab or mediated by the piggybac transposon system. The project will also use unfixed macaque or human brain tissues to perform transcriptomic and proteomic profiling studies and cell sorting at the flow cytometry core. Alzheimer's disease knock-in or transgenic mouse models will also be studied, including stereotaxic injection of adeno-associated. The protocol is clearly written. The following will be communicated to the PI:

- Where/When and Related experience questions need to be addressed for [redacted] and [redacted].
- [redacted] and [redacted] need to complete rDNA/IBC Policy training.
- The CORE FACILITY UTILIZATION FORM, for the question "Please indicate whether any of these biological materials were isolated from human sources or were exposed/derived from other potentially infectious biohazardous material," only "iPSC and fibroblasts from human sources" are listed. Please also add "human or macaque unfixed brain tissues/cells", which will also be sorted in the Flow Cytometry Core Facility.
- Please describe what PPE will be used during the lab procedure of homogenization of macaque or human unfixed brain tissues using a motorized homogenizer.
- IBC recommends few specific names of the genes that you plan to get synthesized from the company Twist.
- Please clarify why "Back fastening gowns" are checked for this ABSL1 protocol?
- Please provide information for BSC Make, Model, and Serial Number.
- The protocol states that "Human cells and human and macaque brain samples are transported on dry ice to Boston University, in full accordance with IATA/ICAO requirements." Where will human and macaque brain samples be transported from on dry ice to Boston University?
- IACUC approval through 10/4/2024, triennial is open currently.

BUA Site Assessment: Not completed at the time of the meeting.

Motion: Conditional Approval (Admin Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

V. List of Protocols reviewed by DMR (not discussed in the meeting

A list of protocols that were reviewed by DMR was displayed in the meeting