Boston University
Institutional Biosafety Committee (IBC)
July 18, 2023 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 1:45 PM

Members Present:	R. Ingalls, B. Slack, E. Muhlberger, R. Davey, V. Gouon-Evans, X. Brown, W. Lu, T. Winters, R. Morales, C. Thurman (joined 1:17 PM), R. Timmerman (joined 1:36 PM), N. Dey, S. Ghosh
Guests Present:	A. Ahmad, T. Killeen, M. Fitzgerald, J. Presedo
Staff Present:	C. McGoff, L. Campbell

I. Review of June 20, 2023 IBC Meeting Minutes

No concerns were voiced.

Motion: Approve

For: 11; Against: 0; Abstain: 0; Absent: 2

II. Chair Report:

Members were reminded that if protocols reviewed by DMR contain any lingering concerns, further discussion could be allowed during IBC meetings.

III. New Business:

A. IBC Office Updates: Nothing to report.

B. Incident Report:

- Members were provided with summaries from ROHP and EHS ahead of the meeting regarding two incidents that occurred since the June IBC meeting.
- S. Ghosh informed members that the June 27, 2023 incident, cited at the previous IBC meeting, was reported to NIH, as required; the NIH response contained no concerns in the handling and follow up of the incident.

C. Review of Research Occupational Health Program (ROHP) Report: Nothing to report.

D. Environmental Health and Safety (EHS) Report: Nothing to report.

IV. Protocol Review

1. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2613	[redacted]	Regulation and evolution of phenotypic plasticity	1	N/A	CRC
Primary Reviewer: Barbara Slack		Secondary Reviewer: Pinghua Liu			
Applicable NIH Guidelines: Section III-D-2-a, Section III-D-4-a					

Meeting Comments: The goal of this protocol is to understand how environmental factors affect organismal development. Their research particularly focuses on insulin/insulin-like signaling pathway and MAPK pathway, which mediate nutrition responsiveness in other systems. The PI's group use horned beetles and nematodes as their model. They use RNA interference and CRISPR-Cas technology to modulate signaling in the model animals. They introduce dsRNA into hemolymph of beetle and inject CRISPR-Cas into nematodes targeting gonad. No viral vectors are used. The genes they target are those that are involved in beetle or nematode response to nutrition and growth. Guide RNA will be designed computer software that will eliminate selection of off-target sequence. Some of their experiments may include cloning of beetle or nematode gene fragments and propagation of the plasmids in E. coli. Additionally, they will also use yeast two-hybrid assay for protein-protein interactions, which involves cloning and expressing protein in common yeast strains. Disinfectants used include 70% ethanol and RNAse away, which is known decontaminant for RNA and DNA. The following will be communicated to the PI:

- Section III.3- Please make sure to complete the ROHP clearance for the PI.

- Section VII.3- Please state the source of beetles and nematodes. Provide brief description of beetle and nematode handling for the proposed work.
- Section VIII.1- please check 'culture stirrers/shakers' and 'Plating/colony counting', since plasmids will be propagated in bacteria
- Section VIII.3/4- lab coats and goggles or safety glasses should be used as PPE when working with rDNA.
- Section VIII.6- States that "Needles are re-usable and are carefully resheathed." This is not appropriate. Needles should be discarded in sharps container after use. If case a single needle is used to inject multiple beetles, a needle block may be use, but needle must not be resheathed under any circumstance.
- Section VIII.7- please specify that bleach at a final concentration of 10% will be used to disinfect liquid waste.
- Section H.17- Indicates use of transgenic animals. Does this refer to nematodes injected with rDNA?

BUA Site Assessment: This was not completed by the IBC meeting day.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

2. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1788	[redacted]	Use of Flow Cytometers in the core facility	2+	N/A	BUMC

Primary Reviewer: Elke Muhlberger | Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol represents the activity of Boston University Flow Cytometry Core facility (FCCF). The goal of this FCCF is to support the cell analysis and sorting needs of researchers at BU and researchers from outside institutions. The core has 6 pieces of equipment: 1 FACSCalibur, 1 FACSCanto, 1 Aurora, 1 LSRII, 1 MoFlo, and 1 FACSAria. The BU FCCF uses both fixed and non-fixed cells on the applicable pieces of equipment. All are closed systems in terms of fluidics and therefore don't produce aerosols except for two particular machines. Appropriate disinfectant are added to the waste tank prior to use. The cell sorters are operated by dedicated personnel are predominantly used with live cells of all types ranging from BSL1 to BSL2. The facility requires the user fill up a Core Facilty Use form which details the nature of the work as well as safety training of the researcher who will be using the equipment.Risk will be assessed (through the IBC FCCF Core Supplemental Form) before sorts can be initiated and agent training will be provided if necessary. The protocol provides detail description of work that are generally performed in the facility and all safety measures they undertake for their work. The PI requested transferring the protocol to the current Director of the FCCF. Committee was informed that IBC office will transfer the protocol to the new director who will then be able to respond to the meeting comments and update the protocol as necessary. The following will be communicated to the PI:

- Please add to the procedure section that liquid waste collected in the waste containers and mixed with an appropriate disinfectant will be incubated for the appropriate inactivation time before poured down the sink.
- Remove the use of red bags from the liquid waste section.
- Please list the disinfectants that are currently used in the core (if different from bleach).
- Add incubation time for waste treated with bleach or other disinfectants.
- The 70% ethanol is not an approved disinfectant. It might be used for sensitive equipment, though. This should be made clear.
- Update BSC certification dates.
- The recombinant DNA section is checked but no information has been provided. Either uncheck “recombinant DNA” or provide rDNA info.

BUA Site Assessment: This was not completed by the IBC meeting day.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

3. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1336	[redacted]	Effects of gene knockdown (Sigma-1 receptor, CRF and CRF-1 receptor, DeltaFosB, DeltaJunD, etc.) on signal transduction systems	2	2	BUMC

Primary Reviewer: Valerie Gouon-Evans	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Section III-E-1, Appendix B-2

Meeting Comments: The goal of this protocol is to investigate the molecular mechanism of alcohol and food addiction. They propose to silence, and over express genes thought to be critical for addiction in conjunction with addiction triggers such as alcohol or food intake and anxiety, to identify those that could be modified as potential therapy for addiction. Those includes genes related to neurotransmitter systems and two transcription factors which contribute to drug-induced changes in gene expression. They mainly perform in vivo experiments on rats and mice. For their in vivo studies: they use recombinant adeno-associated (AAV) viruses that express genes of interest or shRNAs. AAVs are obtained either from the UPenn viral vector core, the UNC viral vector core, Addgene, the University of Barcelona, or from collaborators. Recombinant AAVs are injected into specific brain area using Hamilton microseringe mounted on a kopf stereotaxic arm and are performed in animal facility under a fume extractor. Because it is a minimally invasive surgery and AAVs are BSL1, the procedure falls under ABSL1 regulation. Brain will be collected to measure protein and transcript levels. Homogenizing, tissue grinding and vertexing brain tissues are all performed in biological safety cabinet because of potential of generation of aerosols. Axonal transport inhibitor colchicine (which is a CCL3 chemical) is also used in some experiments. Committee discussed whether a BSL2 and ABSL2 containment is necessary for the use of colchicine and EHS recommended that because it is a chemical hazard, it should not affect biosafety containment level of the protocol and the protocol activity with colchicine may be performed at BSL1/ABSL1 containment. The following will be communicated to the PI:

- Section VIII.1. Check animal handling/cage changing.
- Section VIII.5. Provide current biological safety cabinet certification date (last certification was in 2020).
- Section IX. Because colchicine is a chemical hazard (even though it is CCL3), it may be used in BSL1/ABSL1 containment. Please change your highest biosafety and animal biosafety level in the Materials Used in Research section appropriately.
- Section IX. IACUC protocols [redacted] and [redacted] do not exist anymore. Please provide IACUC approval numbers for the remaining protocol in the new naming format.
- Section H: Provide all active IACUC approval numbers in the rDNA animal experiments section also.

BUA Site Assessment: This was not completed by the IBC meeting day.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

4. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1409	[redacted]	Replication strategies and host response mechanisms of RNA viruses with a focus on filoviruses	2	N/A	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewers: Weining Lu

Applicable NIH Guidelines: III-D2, III-D3, III-E1, III-F, App. B, App. G

Meeting Comments: This BSL2 protocol investigate how gene transcription of negative strand RNA viruses associated with serious human diseases are regulated and how individual viral components interact with cellular proteins and impair immune responses of the host against these viruses. Viruses studied in this protocol involve mostly risk group 4 viruses and the RG3 virus SARS-CoV-2, although no live RG3/RG4 virus work is being done in this protocol. However, the protocol does include cell culture infection with several RG2 negative strand RNA viruses or their recombinant varieties. Rather, this protocol employs a variety of complex recombinant nucleic acid manipulation techniques to

achieve their goal. These approaches include minigenome assays, infection with virus like particles, virus replicons and a transcription-replication competent virus-like particle system. Each of these systems is described in great detail including respective safety measures in use. The protocol uses a large number of human cancer cells, NHP cell lines, bat cell lines as well as primary bat cells. Vaccinia virus (MVA-T7), pseudotyped VSV, and 3rd generation lentivirus systems are also used. Each of the downstream experiments carried out with these systems, such as RNA/DNA isolation, RNA analysis, cytokine expression, analysis of innate immune response are also described in great detail. The protocol also includes testing survival of bacteria in an evaporation chamber so that the system can be further tested for survival of RG3/RG4 agents in BSL3 or BSL4 laboratories. In this 3-year renewal, no new procedure has been added. Only a few human cell lines and primary cells (organoids) have been added, a new source of inactivated biological materials have been added and the personnel list has been updated. All the amendments submitted for this protocol since its last 3-year renewal have now been integrated into the main procedural description. This is a well described protocol. The following will be communicated to the PI:

- Since LCMV is a reproductive hazard for pregnant or wanting to be pregnant women, the committee recommends that the protocol should include a statement indicating that this information will be provided to all members of the lab.

BUA Site Assessment: Biosafety cabinets are all duly certified. Safety training and ROHP clearances are current for all members.

Motion: Conditional Approval (Administrative Review)	For: 10	Recuse: 1	Against: 0	Abstain: 0	Absent: 2

5. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1395	[redacted]	Mitochondria-nuclear communication in the maintenance of metabolic homeostasis	2	2	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Section III-D4-a, Section III-E-3, Section: III D2, Section: III D3

Meeting Comments: The goal of this protocol is to study the relationship between lipid metabolism and inflammation and their connection to the development of Type II diabetes. In their earlier studies this group identified a protein called GPS2 in the transcriptional complex that regulates lipid metabolism in the obese fat tissue. They are extending now extending their studies to characterize this GPS2 and other accessory proteins with a long term goal to develop therapies for type II diabetes. They are using mouse and human cells lines to express or knockout GPS2, and related proteins. Transgenic animals are made and used for the work involving the same genes. The main risk components are handling of mouse and human tissue samples that includes adipose (fat) samples. Further, laboratory processes like tissue homogenization, centrifugation and vortexing each create aerosols, need to be contained. Recombinant DNA work is done involving E. coli for production of plasmid DNA which are standard mammalian expression plasmids. A commercially purchased 3rd generation lentivirus vector, which is also self-inactivating and is thus safer to use, is used for production of desired proteins in cultured cells. Work is performed at BSL2 using a BSC and PPE that includes safety glasses, face shield, double gloves and lab coat which are appropriate for the work. Needles are used for cell disruption and making protein extracts. These are single use and disposed of in a sharps container. A 10% fresh bleach with 30 minutes exposure time, is used for decontamination of liquid wastes. Tamoxifen is used for in vitro cell culture to suppress estrogen receptor signaling. It was noted that xenograft tumors will be induced in mice using different human cancer cell lines. The following will be communicated to the PI:

- Committee recommends use of methods other than needles to disrupt cells for making protein extracts to avoid possible needle prick injury. Cell lysis buffer and cell scaper followed by vortexing may be used as an alternate procedure.
- VIII. 4. Use of Respirator and back-fastening gowns as mentioned in section VIII.4 may no longer be necessary in the ABSL-2 animal facility. Please consult with EHS and animal center checked, on this matter.

- Section A. Generation of xenograft tumors in mice using human cell lines as stated in Hazardous Biological Agent list (Section A.4) should be classified as ABSL2 work. Please revise the ABSL level.

BUA Site Assessment: This was not completed by the IBC meeting day.

Motion: Conditional Approval (Administrative Review)	For: 11	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

6. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2450	[redacted]	Lsd1 in oral cancer; Regulation of osteoarthritis by Loxl2 and other proteins	2	2	BUMC

Primary Reviewer: Xin Brown	Secondary Reviewer: Colleen Thurman

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a, III-E-1

Meeting Comments: The objectives of this project are 1) to determine the role of Lysine specific demethylase 1 (LSD1) in oral cancer growth and metastasis and 2) to determine the role of Lysyl oxidase like-2 protein (LOXL2) in osteoarthritis cartilage and bone regeneration. For the first objective, 4- nitroquinoline-1-oxide (4NQO) will be used to induce oral squamous cell carcinoma in mouse with reduced LSD1 activity (either conditional knockout mice are used, or LSD1 inhibitors are used), the tissues will be processed for protein, RNA and histological analysis. For the second objective, the expression of LOXL2 will be manipulated in mouse using expression plasmids, Lentivirus or Adenovirus, mouse tissues will then be collected for histology and other analysis. Some in vitro work using those constructs on commercially purchased human chondrocytes will also be done. In this protocol, viral vectors used are replication incompetent, appropriate PPEs are used when handling toxic chemicals (4NQO, Tamoxifen), treatment of biohazardous material is also appropriate. Protocol also provides clear description of all the animal work and all safety measures applied to those work. The following will be communicated to the PI:

- Grant administered through CRC while the location of the lab is in BUMC? Is this correct?
- Three PIs are listed under “descriptive role” column, besides Dr. Bais. are the others co-PIs?
- “State how many years experience, when and where” column needs to be completed and make sure the experience matches the name. Currently the PI of the project Dr. Bais is described as having 6 months of experience in the PI’s lab, which obviously is a mistake.
- Under ROHP clearance, some members’ IBC # is NA, if certain lab members do not participate in this project, they do not need to be listed.
- In the protocol it is also mentioned nanoparticle encapsulated LSD1 inhibitor will be applied to mice. What is the nature of the nanoparticles? How and where are the nanoparticles generated? How will they be used and disposed of?
- Animal handling and cage changing must be checked. Extensive animal handling is described in the protocol.
- BSC make cannot be a room number. Please provide company name for the BSC.
- Materials used in research, several items should be unchecked:
  - This project does not use synthetically derived DNA.
  - This project does not use inactivated biological samples.
- Provide IACUC approval numbers in the new format and provide their approval dates.
- For the Question 3 in Section H, “Will the experiments involve rDNA molecules capable of expressing a pathogenic polynucleotide or polypeptide?” Clarify why the answer is yes. Are LSD1 and LOXL2 pathogenic?

BUA Site Assessment: This was not completed by the IBC meeting day.

Motion: Conditional Approval (Administrative Review)	For: 12	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

7. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

1046	[redacted]	Molecular Pathogenesis of Kidney and Urinary Development and Dis ease, SLIT2/ROBO2 and ZEB2 signaling pathway, and novel therapeutics development	2	1	BUMC
Primary Reviewer: Robin Ingalls		Secondary Reviewer: Steve Niemi			
Applicable NIH Guidelines: 2019 NIH rDNA Guidelines: Section III D2, Section III D4, App G					
Meeting Comments: The goal of this protocol is to examine the underlying disease mechanism of congenital anomalies of the kidney and urinary tract (CAKUT) and chronic kidney disease (CKD) and kidney failure observed in children and young adults. This group previously identified three genes ROBO2, SLIT2 and ZEB2 that are involved in the pathogenesis of CAKUT and CKD. In this project they have created conditional knockout mice for those genes and are in the process of further characterization of those animals to get better understanding of the mechanism of molecular signaling associated with ROBO2, SLIT2 and ZEB2. The protocol basically involves histological analysis of mouse kidney tissues and also involves rDNA work where human and mouse proteins are expressed in human cells. The mouse work also involves use of tamoxifen and bromo deoxyuridine (BrdU). However, PI has provided detail description of their use and biosafety practices associated with their use. There are no significant changes in the protocol since its last renewal. The personnel list is updated, safety trainings are all current, although ROHP clearance for members are in the process of being updated. The committee recommended approval of the protocol upon completion of the BUA site inspection. BUA Site Assessment: This was not completed by the IBC meeting day.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

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

List of protocols (below) that were reviewed by DMR was displayed in the meeting.

[redacted]

8. Bhz –New Application

BUA	(PI)	Title	BSL	ABSL	Campus
1234	[redacted]	Diabetes Clinical Research Group	2	N/A	BUMC
Primary Reviewer: Tom Winters		Secondary Reviewer: Rob Davey			
Applicable NIH Guidelines: N/A					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

9. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
581	[redacted]	Movement Disorder Studies & Stroke Prevention Studies	2	N/A	BUMC
Primary Reviewer: Tom Winters		Secondary Reviewer: Bob Timmerman			
Applicable NIH Guidelines: N/A					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

10. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
935	[redacted]	Lens-Amyloid Biomarker for Early Detection of Preclinical Alzheimer's Disease Clinical validation of a laser eye scanner for AD	2+	2	BUMC

		Effects of Blast and Impact Neurotrauma on Alzheimer's Disease Pathogenesis Mechanisms of Repetitive Neurotrauma and Chronic Traumatic Encephalopathy (CTE) Gadolinium Distribution in Rat Brain After Systemic Administration of Gadolinium-Based Contrast Agents Assessed by High-Resolution Metallomic Imaging Mass Spectrometry (MIMS) RETROSPECTIVE HUMAN BRAIN STUDY: Regional Gadolinium Distribution and Concentration in Postmortem Human Brains from Subjects Exposed to GBCAs Evaluated by MIMS Brain Mapping			
Primary Reviewer: Barbara Slack			Secondary Reviewer: Steve Niemi		
Applicable NIH Guidelines: N/A					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

11. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2462	[redacted]	Transcriptome analysis during mitosis	2	N/A	BUMC
Primary Reviewer: Weining Lu		Secondary Reviewer: Valerie Gouon-Evans			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, Section III-E-1					

12. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2234	[redacted]	Mechanisms of cortical oscillations	1	1	CRC
Primary Reviewer: Pinghua Liu		Secondary Reviewer: Ron Morales Additional Reviewer: Steve Niemi			
Applicable NIH Guidelines: Section III-E-1, Section III-D-4, Appendix B-1					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

13. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2425	[redacted]	NSF Nanosystems Engineering Research Center for Directed Multiscale Assembly of Cellular Metamaterials with Nanoscale Precision: CELL-MET	2	N/A	CRC
Primary Reviewer: Xin Brown		Secondary Reviewer: Sajal Ghosh			
Applicable NIH Guidelines: N/A					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

14. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

1375	[redacted]	Apolipoprotein A-I and HDL; Structure, Formation and Function	2	N/A	BUMC
Primary Reviewer: Robin Ingalls		Secondary Reviewer: Ron Morales			
Applicable NIH Guidelines: Section III-D-2, Appendix B, Appendix G http://oba.od.nih.gov/rdna/nih_guidelines_oba.html					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

15. rDNA/Bhz – Three-Year Renewal

BUA	**(PI)**	**Title**	**BSL**	**ABSL**	**Campus**
2471	[redacted]	Microscopic Foundation of Human Neuroimaging: Physiological Mechanisms of Neurovascular/-Metabolic Coupling and Neuromodulation in Health and Disease	2	2	CRC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Colleen Thurman			
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-a; Appendix G-II-A, G-II-B ,M-II-A, and M-II-B.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 0