Boston University
Institutional Biosafety Committee (IBC)
December 13, 2022 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:03 PM End time: 2:34 PM

Members Present:	R. Ingalls (left 1:15), B. Slack, I. Afasizheva, V. Gouon-Evans, T. Winters, E. Loechler, R. Morales, S. Niemi, J. Keeney, R. Timmerman, V. Britton, J. Barton (joined 1:12), S. Ghosh, E. Muhlberger, X. Brown, R. Davey
Guests Present:	A. Ahmad, A. Broos-Caldwell, J. Wood, N. Dey, T. Killeen, M. Fitzgerald
Staff Present:	L. Campbell, C. McGoff

I. Review of November 15, 2022 IBC Meeting Minutes

No concerns were voiced.
Motion: Approve
For: 15; Against: 0; Abstain: 0; Absent: 1

II. New Business:

A. Revisions to IBC Review Categories

Members were provided with a copy of proposed changes to the current IBC review category process prior to the meeting for comments. Members discussed the requirements of annual renewals in the first year for all BSL3 and BSL4 protocols or shift to a three -year review. Suggested edits will be made and the revised policy will go out to members by email for a vote so this new process can be implemented.

B. SQAP Report:

The IBC Program Manager informed members that the reviewer's checklist should be implemented in early 2023.

C. Review of Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Incident Report:

No reportable incidents.

III. Protocol Review

1. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2342		Identification of inhibitors of high containment virus infection	4	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Guillermo Madico
Applicable NIH Guidelines: Section III-D-1-c	

Meeting Comments: The goal of this protocol is to test small molecule inhibitors against all BSL4 viruses that NEIDL investigators work as well as Coronaviruses SARS-CoV-1, MERS-CoV and SARS-CoV-2. This has been reviewed many a times by this committee and there are no changes in this annual renewal. Because the protocol involves isolation of escape mutants, the DURC boxes are checked, but the DURC review committee has already determined it to be non-DURC protocol because those are naturally occurring viruses.

The committee voted that no Annual Renewal will be required for this protocol next year; this protocol will be reviewed at its three year renewal.

PI recused himself from voting.

Motion: Approve	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 1

2. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus

2345		Identification of host factors controlling virus infection	4	N/A	BUMC
Primary Reviewer: Elke Muhlberger			Secondary Reviewer: Guillermo Madico		
Applicable NIH Guidelines: III-D-1-a, III-D-2-a, III-D-3, III-E-1, III-F-8; Appendix C-I					
Meeting Comments: The goal of this protocol is to study the role of various cellular proteins in supporting virus infection. The lab generally uses CRISPR or other methods to overexpress or knock down individual cellular proteins and then test how virus infection proceeds in the presence or absence of specific protein. Mutational analysis of SARS-CoV-2 proteins will be generated and detail plan of handing of any escape mutant with gain of function has been clearly described. DURC subcommittee previously has already reviewed this protocol and determined that it is not a DURC protocol. No changes except updating the biosafety cabinet has been made in this annual renewal. The committee voted that no Annual Renewal will be required for this protocol next year; this protocol will be reviewed at its three year renewal. *PI recused himself from voting.*					
Motion: Approve	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 1

3. Bhz – New Application

BUA	**(PI)**	**Title**	**BSL**	**ABSL**	**Campus**
2558		Prematurity Risk assessment combined with clinical Interventions for improving neonatal outcomes	2	N/A	BUMC
Primary Reviewer: Tom Winters			Secondary Reviewer: Valeda Britton		
Applicable NIH Guidelines: N/A					
Meeting Comments: This is a prospective randomized controlled trial study where the safety and efficacy of preterm birth prevention strategies versus standard care approach are investigated. The goal is to advocate better plan for reduction in neonatal morbidity and mortality and reduction of neonatal hospital stay. They will randomize 6500 pregnant women 1:1 to each group: the preventive arm versus the control arm. Blood will be collected during pregnancy in the OB-GYN clinic of Yawkey at BMC. Samples will be transported to the Max Finland lab for processing, freezing, storage, and shipping to a sponsor. Biosafety risks involve handling of blood samples but bloodborne pathogen standard is invoked as they are drawing blood and processing. Personal protective equipment appears appropriate. Sharps will be used. Liquid and solid waste are handled appropriately. Disinfection is done by treatment with bleach at a final concentration of 10%. Transport training has been provided according to the protocol. The IRB is stated but the number is not included in the registration. The following will be communicated to the PI: • BioRAFT trainings need to be completed for (LST, BSL1/2, BBP, Chem Safety) and (BSL1/2 and Chem Safety) • ROHP clearance needs to be secured for Pfau. • Laboratory locations (Room and) need to be added. • Check “Other Potentially Infected Materials” checkbox. • Complete Section B indicating type of clinical samples being collected, their source and IRB approval number and expiration date. BUA Site Assessment: The lab locations (and are not mentioned in the protocol. Biosafety Cabinet is not required for the project. No sharps used in the lab. No other biosafety concerns noted.					
Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

4. Bhz – New Application

BUA	**(PI)**	**Title**	**BSL**	**ABSL**	**Campus**

2580		Systems immunology approach to reveal human immunity to viruses and vaccines	2	N/A	BUMC
Primary Reviewer: Barbara Slack			Secondary Reviewer: Bob Timmerman		
Applicable NIH Guidelines: N/A					

Meeting Comments: The goal of this protocol is to use systems immunology approach that combines experimental and computational methods, to interrogate viral protective immunity and identify essential pathways involved in producing the immune response to viruses. Hazardous materials include human cell lines; human primary nasal epithelial cells, blood, plasma serum, tonsils; seasonal flu virus strains; live attenuated influenza vaccine from Merck, and Ad5-SARS-CoV2 vaccine from Astrazeneca. Blood and tissue samples are obtained from individuals infected with seasonal flu or SARS-CoV-2, or vaccinated with flu or SARS-CoV-2 vaccines. Peripheral blood mononuclear cells (PBMCs) and tonsil mononuclear cells (TMCs) are isolated, stimulated with lysate from cells infected with seasonal flu, SARS-CoV-2, or treated with a peptide library. Cells will be stained, fixed, and analyzed by cytometry. PCR amplification will be done for bulk TCR sequencing in Microarray and Sequencing facility. Tonsil obtained from volunteers undergoing tonsillectomy will be used for organoid cultures. Specific populations of T, B and antigen-presenting cells using FACS sorter will be depleted and infected with influenza or SARS-CoV-2, or treated with peptides followed by analysis of cell differentiation and antibody secretion. Cells for FACS sorting will be fixed if from injected patients; unfixed if from healthy patients. Serum samples will be analyzed in Proteomics Facility (at the CRC). Lab coats, goggles, double gloves will be worn while working with human cells and viruses or any other hazardous materials. All hazardous work will be done in BSC. The following will be communicated to the PI:

- Section VII.3- What is the source of the human tonsils? Where are they being collected and by whom? How are they coming to the lab?
- Section VIII.11- Please provide more detail about how samples be transported for analysis at the CRC Proteomics facility (as checked in section V), including: the nature of the samples (just serum?), whether they will be transported in a private vehicle by lab personnel, and please describe the secondary containment that will be used.
- Section IX-Table B- human cells from infected individuals listed in Section A should be moved to Section B. Are cells from vaccinated individuals from the same source (i.e. Johns Hopkins or U. Oxford)? Cells from individuals infected with SARS-CoV2, and cells from vaccinated individuals, should also be listed here, and the source specified.
- Section IX- Table B. A number of sources are listed in this table for human clinical samples. Please specify which material is provided by which source (for example, are the tonsils provided by the National Research Disease Interchange?) Please verify that all samples are all de-identified, and therefore IRB exempt (since no IRB number is provided). If any of the samples are received through IRB approved clinical studies, IRB approval number and expiration date needs to be mentioned.

BUA Site Assessment: PI is a new faculty in Boston University. No concerns were noted. Some parts of her lab are still being set up.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

5. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
1166		Antibody-based Contraceptive MPTs: Advancing the Human Contraceptive Antibody (HCA) Through Clinical Trials	2	N/A	BUMC
Primary Reviewer: Robin Ingalls			Secondary Reviewer: Xin Brown		
Applicable NIH Guidelines: N/A					

Meeting Comments: The goal of the project is to evaluate the potential of using human contraception antibody (HCA) as a birth control method and a method to prevent sexually transmitted diseases. the HCA from various sources

(either expressed from mouse hybridoma or secreted by transfected animal vaginal tissues) will be added to donated sperm samples in various model systems, and the effect of the antibody on the sperms will be studied under a microscope. In some experiments complements isolated from cervical mucus from consented women or from rhesus macaques will also be added to the sperm samples from in presence of HCA antibody for functional assays such as hemolysis, sperm immobilization or complement fixation. In some experiments HCA mRNA from outside collaborators will be transfected in human cell lines or Epivaginal tissue models for production of HCA for testing antibody functionality. Biohazards in this protocol include many different types of human and animal bodily fluids and tissue samples that are sometimes potentially infectious. All laboratory work will be done in BLS2 containment with BSL3 practices. The proposed disinfection method is adding D-125 to the unused samples, let stand for 24 hours then poured down the drain. The following will be communicated to the PI:

- ROHP clearance update required for and .
- Please clarify where blood is being drawn in the healthy donors.
- If no recruitment will be done any longer for the Complement and Cervical Mucus Study, update the laboratory procedure section accordingly.
- Clarify whether the semen samples are collected at GCRU or by donors privately and brought to the PI lab.
- Under PPE, face shield should be checked because it is mentioned in the laboratory procedure section of the protocol.
- State at what final concentration of D-125 will be used for disinfection and for how long. Clarify if chlorine bleach is also used for disinfection of liquid wastes (because D-125 is usually used to disinfect surfaces).
- Please remove mouse hybridoma cell lines from the biohazard table as those are not biohazardous.
- Provide expiration date for IRB protocol in Section B and clarify which samples are coming through this IRB approval.

BUA Site Assessment: PI's rDNA/IBC training needs to be updated. It was noted that for complement and cervical mucus study, recruitment of participants is currently closed and it will not happen in the future. Sharps are used; therefore "yes" should be selected in the protocol. D-125 disinfectant is used at 1:64 dilution.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

6. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1171		An In Vitro Model of Cell-Associated HIV-1 Transmission	2+	NA	BUMC

Primary Reviewer: Elke Muhlberger | Secondary Reviewer: Robin Ingalls

Applicable NIH Guidelines: N/A

Meeting Comments: In this protocol uses human cervical vaginal epithelial cell system to study cell-associated HIV transmission. They use quantitative assays to study attachment of HIV to the infected cells and then penetration through these epithelial layers and transmission of HIV to the cells within or below the epithelial layer. The main goal of this protocol is to study vaginal microbicide candidates to see whether or not they can stop HIV infection of this specific organoid that they use here. Their work includes propagation of different HIV strains in PBMCs from healthy donors to generate stock culture and then to use them to infect lymphoid and macrophage cell lines. Infected cell lines subsequently will be used to infect Epivaginal tissue model. They use the TZM-beta lactamase assay to quantify HIV titers and to assess antibody-mediated HIV neutralization. A primary natural killer T-cell derive line CD16+KHYG is also used in this protocol for measuring cellular cytotoxicity. The protocol is straightforward. Most of the procedures are well described, although little more elaboration may be useful for some others. The following will be communicated to the PI:

- Will blood be drawn from normal 'healthy' donors? It is stated that it will be drawn from "normal" donors. Please clarify that IRB approval is not necessary for "normal donors".

- Phlebotomy is not permitted in normal office spaces as any spill can be cleaned properly in carpeted office spaces. Please clarify and also describe how the blood will be transported from PI's office to the lab.
- A brief description of TZM-bl assay is recommended.
- Liquid waste – final concentration of bleach should be 10% and contact time should be 30 minutes. Please change accordingly. Please add final concentration of D-125 disinfectant used for inactivation.
- The TZM-bl assay is based on the use of Env-pseudotyped viruses which is rDNA. The recombinant DNA section needs to be checked.
- Remove Gag-EGFP KP97-Bal virus-like particle from Section A since this is not a hazardous material.
- Move all primary human cells to the section B (Human monocyte-derived macrophages and Leukopak).
- Delete all cell lines from Section B (TZM-bl, CEM, HEK293T, Mouse hybridoma). This section is only for primary human or non-human primate cells, tissues or body fluids.
- Complete the rDNA section for using recombinant TZM-bl cell line. Also add Gag-EGFP KP97-Bal virus-like particle genome.
- Use Section III-D-1-a as the applicable NIH Guidelines.

BUA Site Assessment: HIV training to the lab personnel is provided by the CFAR and additional training is provided by the PI. Bleach contact time should be 30 min instead of 20 min.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

7. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1173		Vaginal/Cervical tissue models: endocrine effects and susceptibility to infection	2+	NA	BUMC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Valerie Gouon-Evans

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this protocol is to study the immunological features of the vaginal tissues, how infection occurs and how to prevent infections. They use cervical tissue model and cell culture system to study how these tissues and cells respond to infections by agents that cause sexually transmitted diseases such HIV, Herpes simplex and trichomonas vaginalis. They will infect these models with the microbial agents and will analyze various parameters of infection such cell associated and cell free spread of the agents, cytokine release pattern, test the efficacy of antimicrobial agents. Hormonal or other influences on infection (such as with human contraceptive antibody) will be investigated. Biohazards in the protocol include discarded surgical vaginal and cervical tissues from the clinic, vaginal and cervical cell lines, human cervical organotypic culture (EpiVaginal – obtained from Massachusetts based company MatTek Corporation), blood and semen samples from donors via approved IRB studies, and microbial agents HIV-1, HSV-2 and *Trichomonas vaginalis*. In all they use electron microscopy, immunohistochemistry, ELISA, RT-RCR or related methods to test fidelity between the *in vitro* and *in vivo* tissues. All personnel will use universal precautions when working with any of these agents. All work will be done in BSL2 lab with special practices of BSL3 by highly trained individuals. Further, all cells will be inactivated or fixed in methanol or TRIzol (as appropriate) before using in any assay. BSO noted that the parasite infection study on vaginal tissue is no longer continued. The following will be communicated to the PI:

- Check the rDNA box in Materials Used in Research and complete Section H (recombinant DNA Eukaryotic experiments section for the use of recombinantly engineered HIV strains (various VSV-G pseudotyped single-cycle infectious viruses, including the one that expresses mCherry).
- If discarded surgical or vaginal tissues are no longer received from BUMC Pathology, please update the protocol accordingly.
- If Trichomonas study is no longer continued, update the protocol accordingly.
- If sharps are used in the lab, mark "Yes" in the VIII.6 and clarify what they are how they are disposed of.

- If chlorine bleach is not used for disinfection in the lab, please update your waste disposal and disinfection statements.

BUA Site Assessment: The discarded surgical tissues are not procured from BUMC anymore. Blood is drawn in the lab. The Trichomonas work is also not being done anymore. Sharps are used; therefore "yes" should be selected. The mention of chlorine bleach should be removed.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

8. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
983		The redox biology of vascular and metabolic diseases	2	2	BUMC

Primary Reviewer: Valerie Gouon-Evans	Secondary Reviewer: Steve Niemi

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

Meeting Comments: This study investigates the role of oxidants and lipids in cardiovascular and liver diseases. They will specifically determine the role of reactive nitrogen and oxygen species in metabolic cardiovascular (MCD) and non- alcoholic fatty liver disease (NAFLD). They will test whether overexpression of oxidant resistant activators prevent MCD and NAFLD caused by diabetes and obesity. They will use glutaredoxin transgenic and knockout mice and overexpress in vivo wild-type and mutant oxidant resistant activator proteins via injection of viral vectors. They will also investigate how those manipulations affect ischemic limb in diabetes, burden of atherosclerotic lesion and arterial stiffness. Hazardous materials used in the protocol are human cell lines, recombinant viral vectors and perchloric acid. Techniques used in the protocol include culture of various mouse and human cell lines, plasmid transfection, and molecular cloning in commercially available replication-incompetent adenoviral, adeno-associated viral, and lentiviral vectors, all being done in biosafety cabinet. In vivo transfections with viral vectors will be done via Matrigel subcutaneous plugs implanted into tail vein, femoral artery, and hindlimb muscle of mice. An N95 mask and double gloves are used routinely for viral injections. They will also create chimeric mice which will have genetically different bone marrow-derived cells (use of irradiation to ablate the bone marrow by Irradiator. The following will be communicated to the PI:

- If Room is no longer being used, please remove it from the list.
- Please include a statement of purpose of use of Tamoxifen in your animal research work.
- VII.3.9.G. Please correct to "-80C" instead of "we will prepare small aliquots of viral stock, stored at 80 C until ready for use".
- VII.3.13. (also in VII.3.8.I) Please correct to liquid waste will be treated with "a final dilution of" 10% beach for 30 min instead of "with 10% beach" for 30 minutes in section VII. 3.13.
- VIII.1. Check Animal Handling and Cage changing.
- VIII.7. include "final" concentration of 10% bleach and allowed to stand 30 minutes VIII. 11. Please precise: "Biohazardous materials will be transported in shatter-proof, leak-proof and spill-proof, double-bagged containers".
- G. Radiation and X-ray: Question 3: "Will you perform X-ray or other imaging of specimens?" and the instructions, 'Specify which modality to be used and the location of the device", the answers given are "To determine tibia length of mice" and "Scheduled through LASC/core facility". The laboratory procedure does not describe use of X-ray anywhere. Please clarify your response.
- G. Radiation and X-ray: Question 4: Will you use the Irradiator? Should be YES.

BUA Site Assessment: Room should be removed. BSCs certified till 03/2023. Only AAV work is being done and no lentiviral and adenoviral work is currently performed in the lab. The 10% fresh bleach contact time should be changed to 30 minutes. Mice irradiation work is also not going on right now. Animal handling/cage changing should be selected. Cryotome SOP and cut resistant gloves were not available at the time of assessment.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

9. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2408		Rapid Detection of Pathogens by Microfluidics-Based Nucleic Acid Amplification Tests	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: Section III-D-2-a: The 147 base pair fragment we will be working with comprises ~0.6% of the Ebola virus genome (147 bp/18219 bp). The 150 base pair fragment we will be working with on Zika virus comprises 1.4% of the genome (150bp/10272 bp).

Meeting Comments: The goal of this study is to develop point-of-care system to detect pathogens using loop-mediated isothermal amplification (LAMP) of RNA and DNA. Enzymes and reagents are inkjet-printed onto a chip. Chips are soaked in virus or virus fragment-containing samples, then processed and imaged by fluorescence microscopy. They are using several virus or virus genome fragments as their test samples. These include a) 150bp DNA fragment from Zika virus and certified inactivated Zika virus from commercial sources which they extract RNA from or convert to RNA and then amplify for in vitro diagnostics; b) 150bp ebolavirus L protein and clone into T7 promoter containing vector for RNA transcription; c) previously purified Chlamydia trachomatis genomic DNA; and d) influenza A and rhinovirus stock from ATCC (only for nucleic acid extraction, not for propagation). All work is done in BSC, PPE include N95 mask, lab coat, nitrile gloves, safety glasses. They purify genome or dilute live virus in pooled human saliva (commercially purchased); add samples to LAMP or qRT-PCR reactions. They consider as if viruses are active until treated with 10% bleach. All chips and tubes are disposed of in biohazard containers. Medical Director confirmed that since only certified inactivated Zika virus or fragments are being used, precautions regarding personnel with potential to be pregnant is not necessary. The following will be communicated to the PI:

- Section III-Training info for is not complete. He is listed as lab safety coordinator, not handling rDNA or infectious agents). He may be removed from the personnel list.
- Section III-Update ROHP status for .
- Section VII.3- HEK293 cells listed in Section A, but lab procedures section for ZIKA virus states that no eukaryotic cells will be used in this project. Maybe it was meant to say that ZIKA RNA will not be put in eukaryotic cells. Please restate the sentence.
- Section VIII.3- Use of PPE PAPR is not necessary for this protocol. Please uncheck.
- Section H-rDNA. Lab Procedures indicates that the 150 bp fragment from Ebola virus (and Zika virus?) will be cloned and propagated in *E. coli*, so the response to question 1 should be “Yes” and Prokaryotic Experiments section in the table should be filled out.
- Section H-15. Question: Are viral vectors used in this study defective? “Yes” is checked, but engineered viral vectors are not being used for transduction of cells, so 'N/A' should be checked instead.

BUA Site Assessment: needs to be removed from the personnel list as he doesn’t work with Biologicals or rDNA. The lab is only working with influenza virus and no longer works with Zika virus; no Zika virus stock is available in the lab. PAPR use needs to be deselected. Only *C. trachomatis* DNA is used by the lab and not the live bacteria.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

10. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1825		Defining novel pathways that arrest genetically unstable tetraploid cells	2	N/A	BUMC

Primary Reviewer: Xin Brown	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-E-1; Appendix B-II-D

Meeting Comments: This is a three-year renewal. The goal of the project is to find out how inappropriate activation of common oncogenes affects the fidelity of chromosome segregation during mitosis in human cancer cells, and the mechanism that enables cancer cells to withstand such genomic instability. Biohazards in the protocol include several human cancer cell lines as well as cell lines that stably express fluorophores that label various cellular macromolecules. The lab will use siRNA, CRISPR technology and replication defective retroviral and lentiviral vectors obtained from commercial sources to manipulate gene expression and study its effect on mitosis using high resolution microscopy, FACS analysis, western blots, RT-PCR and micro-array analysis. Because methods used to manipulate human cancer cell gene expression can have potential off target effects, all member of the protocol are made aware of the safety issues. All safety precautions are in place. The following will be communicated to the PI:

- Please list the PI on the Personnel list and answer all associated questions.
- EHS indicated that there are additional individuals working in the project. Please include them in the personnel list.
- Provide title of each listed personnel.
- Sterge and Vedula must secure ROHP clearance before starting laboratory work.
- Laboratory spaces in K-building rooms and need to be added.
- Uncheck imaging core if it is no longer used.
- Update the Biosafety Cabinet certification date.
- Please add disinfectant Vasphene (indicating concentration and exposure time) as it is being used in your lab.

BUA Site Assessment: PI's name is missing from personnel list. Additional personnel need to be added to the protocol. Trainings are missing/expired for some lab members. Some lab spaces like and needs to be added. The lab doesn't use the imaging core anymore. SgRNA and Cas9 variants are expressed in different plasmids. Designated BSC is used for LV and Crispr/Cas 9 work. Vasphene is used as a disinfectant and should be added to the protocol. Sharps The lab doesn't use disposable glass pipets. BSC certifications expired in Nov 2022, but the vendor has been contacted for recertification. is used for lentiviral work. This info will be communicated to PI and addressed with EHS staff.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

11. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1000		Molecular basis of cancer metastasis and the elucidation of genetic and epigenetic markers for diagnosis and therapy of cancer and psychiatric disorders	2	2	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: April 2019; Sections III-D-1-a, III-D-2-a, III-E-1, III-D-4-a; Appendix B-II-D

Meeting Comments: The aim of this project is to develop models of cancer progression to help with the discovery of biomarkers for diagnosis and prediction of therapy effectiveness. Using breast, colon and pancreatic cancers cell lines, including cancer stem cells and tissues as models they investigate various cellular signaling pathways that affect cancer metastasis, and response to chemotherapeutic drugs. They also use variety of nanoparticles (commercial inorganic type Qdots as well as lipid-gold particles and PLA types made by colleagues at BU) for directly targeting cancer cells or for inducing immune cells to invoke cell-mediated immunity. The work also involves taking frozen or preserved tissues containing tumors from patients and studying gene expression in them. In addition to an extensive list of related human stable cell lines from ATCC, induced pluripotent Stem Cells (iPSCs) from patients will also be used to make organoids. Additionally, they will study the role of genetics and epigenetics in the pathogenesis of major psychiatric disorders such as schizophrenia (SCZ) and bipolar disorder (BD). Tumor samples and postmortem

brain tissue samples used in the study are obtained from nationally recognized tissuebanks such as NDRI, CHTN, SMRI, Harvard Brian Tissue Resources, etc. It is stated that these materials are verified as free from infectious agents and provided without identifiers to the scientists. The committee discussed that it is important to know what specific infectious agents have been verified in these samples. In the absence of such information, rigid personnel safety measures should be practiced. Mouse retrovirus vectors (such as p-Babe) and 3rd generation lentivirus vectors (such as pLKO) as well as CRISPR/Cas9 technology are used to manipulate expression of various proteins to analyze their role in signaling pathways. Small amount of cholera toxin will be used for growing primary mammary cells. The protocol provides great detail of all the laboratory procedures that are used and the safety practices. All are appropriately described. The following will be communicated to the PI:

- Please clarify how nanoparticles wastes are disposed of. They should be collected separately and be disposed of as per EHS's recommendation (https://www.bu.edu/ehs/ehs-topics/environmental/chemical-waste/chemical-waste-management-guide/#nanoparticles-chemical-waste).
- For postmortem brain tissues, it is stated that "these samples are collected by these repositories using their own guidelines free of infectious agents and provided without identifiers". Please state which specific agents they are actually tested to be free of (such as HIV, HCV, and any others, as well as Prion). Please state that if the specific information is not available or the samples may contain those agents, Universal precautions will be followed. In such cases brain tissue samples must be disinfected by treating them with 1N NaOH or 40% bleach for at least one hour before disposal.
- It is indicated that the lab hold cholera toxin amounts below the human LD50. Citing such an amount seems an odd limit to list. It would be better to remove this comment and just state that the lad hold a maximum of 1 mg quantities (as has been done) at any one time.

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

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

12. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
610		Saliva and Asthma	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Tom Winters

Applicable NIH Guidelines: N/A

Meeting Comments: The goal of this protocol is to determine the cause of asthma exacerbations by evaluating the cytokine fingerprint and protein quantity in saliva to enhance the identity of causes of exacerbations of asthma. The common known exacerbations of asthma include bacterial infections, viral infections, allergic exposures, and irritant induced asthma. A point of care test is stated goal to help identify early asthma in asthma patients. In the past they have collected blood, saliva, nasal lavage samples but they are stored and are being analyzed. No active collection of samples are being pursued at this time. Therefore, the biosafety risks in the protocol is minimal. Liquid and solid waste are appropriately handled. Disinfection is appropriate using bleach 10 %. There are no transport needs of this group as the samples are in storage. The following will be communicated to the PI:

- PI must complete the rDNA/IBC Policy training in BioRAFT.
- Remove Culture stirrer/shaker option from the procedures.
- The contact time for liquid disinfection by bleach (final concentration of 10%) needs to be changed to 30 minutes.

BUA Site Assessment: PI needs to complete chem safety and rDNA/IBC training. No bacterial or viral stocks are being stored. The culture stirrer/shaker option needs to be removed from the procedures. PPE is adequate. 10% bleach contact time should be 30 minutes instead of 5 minutes as mentioned. This info will be communicated to PI and addressed with EHS staff.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

13. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2173		Molecular Biology of Melanoma	2	1	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a; Appendix B-II-D

Meeting Comments: The goal of this study is to investigate protein-protein interaction within various transcription factor complexes involving initiation, progression, and metastasis of melanoma. Recombinant DNA technology will be used to create expression vectors containing genes of transcription factors and their mutants for overexpression or RNAi repression. Human and mouse cell lines used in the study will be purchased from the ATCC or received from NIH/NCI collection banks. To study melanocytes (cells in the skin and eyes that produce the pigment melanin). PI has already developed transgenic mice model for human melanoma using Cre/lox inducible gene expression system. Skin of control/ transgenic group of mice will be used as a source of the melanocytes. Cells will be grown in the culture containing collagen that mimics skin. Tamoxifen will be used for activation of the oncogene and suppression of the targeted gene. Committee discussed that more Information about safe handling of tamoxifen should be provided as it is a potential carcinogen and could be harmful for unborn babies. According to BU requirements (https://www.bu.edu/researchsupport/forms-policies/tamoxifen-treatment-in-animals/) animals treated with Tamoxifen should be handled in ABSL-2. The following will be communicated to the PI:

- Following safety training updates required:
  - BBP for and ;
  - Chem Safety for and ;
  - rDNA/IBC Policy training for
- Section VII.1. Layman's Terms – please define "melanocyte" for lay readers.
- Section VII.3. Since tamoxifen is a potential carcinogen and could be harmful for unborn babies, please state briefly how stock solutions of tamoxifen will be prepared and stored safely.
- State what precautions the laboratory personnel will be following while using tamoxifen in animal housing facility (CCL3 practices?).
- For the Animal PPE, check head cover and N95 musk.
- Update biosafety cabinet certification date.
- Highest animal biosafety level for this protocol should be marked as ABSL-2.

BUA Site Assessment: Personnel trainings are expired/missing. Headcover needs to be added for animal work. BSCs are certified until 02/2023 but not updated in the protocol. This info will be communicated to PI and addressed with EHS staff.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

14. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1260		DEFINING CELL POLARITY AND HIPPO PATHWAY SIGNALING IN DEVELOPMENT AND DISEASE	2	2	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewers: Steve Niemi

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

Meeting Comments: The goal of this project is to study cellular signaling linked to epithelial cell architecture and cellular polarity during development. These evolutionarily conserved signaling pathways play a crucial role in both development and disease. They will assess the roles for different genes via their expression from transiently transfected plasmids, or through the down-regulation of gene function with the use of RNAi (either synthetic siRNA, or plasmid-based shRNA expression). Expression of growth factor proteins will be done using replication incompetent retrovirus/lentiviral vectors or adenoviral vectors. Lentivirus vectors appear to be of 3rd generation system. Each protein controls growth of cells and gene transcription but the wild type proteins are not directly oncogenes. They will use mammalian expression plasmids as well as retrovirus vectors to induce expression of protein in stable cell lines. NIH-registered human stem cell line will also be for the study of stem cell renewal and differentiation used. These are done at BSL2 which is appropriate. Xenograft work with mice and human cell lines will also be done in transgenic mice including in some that are made conditional with the expression of cre-recombinase using tamoxifen. In studies to analyze immune response to lung injury, vaccine strain of influenza virus will be used. These experiments will be carried out at BSL2/ABSL2 containment which is appropriate, and the vaccine strain provides reduced risk. PPE appears appropriate for work being done. Work is performed in BSC with current certification date. Disinfectant is 10% bleach with 30 minutes contact time for liquid waste but Indicates that pipettes contaminated with recombinant lentivirus vectors will be treated for more than 45 minutes before disposal. Needles are used once and then disposed of appropriately in sharps containers. Transport of biohazardous materials will be in screw-capped tubes placed in shatterproof secondary container. Radioisotopes are used with proper permit. The following will be communicated to the PI:

- Since -80°C freezer and liquid nitrogen dewar are kept in and , respectively, please add them them on the Room list.
- Layman's Terms – please simplify the following words and terms for lay readers: polarity proteins, polarity regulated signals, dysregulated.
- The lentivirus vectors used in the protocol pLVX-puro and Lentiguide-puro are 3rd generation vectors. Please state in the laboratory procedure section that this protocol uses 3rd generation lentivirus vectors.
- It is stated that "For lentivirus experiments, all pipets, tools and cells that come in contact with viral particles will be treated with freshly prepared 10% bleach for a minimum of 45 minutes prior to their disposal as biohazardous waste. The bleach will subsequently be poured down the drain." The committee recommends making this the same as liquid waste (30 minutes) to make consistent and reduce potential confusion over protocols.
- If Wescodyne is not used in the lab, remove its use from the list of disinfectant. Add Virkon S to the list as that one is being used.
- It is stated in the hazardous agent list that Adenovirus used is "Wt". This appears to be a typo as only adenoviral vectors are used in the protocol which are replication incompetent. Please correct or clarify.

BUA Site Assessment: is a common space where -80 freezer is kept and has liquid N2 dewar where biological materials are stored. The influenza virus work (with PR8 strain) has not yet started in the lab. Virkon S disinfectant is used by the lab for lentiviral work and it should be added to the protocol. Sharps in the lab are not exposed to the lentiviral work. Wescodyne is not used in the lab. This info will be communicated to PI and addressed with EHS staff.

Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

15. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2099		BME Core Facility	2	N/A	CRC
Primary Reviewer: Pinghua Liu		Secondary Reviewer: Ron Morales			
Applicable NIH Guidelines: Section III-D-2-a					

Meeting Comments: The protocol covers the activities for the Biomedical Engineering Core Facility. The facility houses instruments for imaging (microscopes and slide scanner), chemical analysis (spectrometer, FTIR, rtPCR) mechanical testing (nano-indentor, AFM, Instron, Rheometer), surface characterization (QCM, DLS, contact angle goniometer, tensiometer) and physical manipulation (sonicator, cryostat, microtome). The core facility also includes a shared mammalian tissue culture space and storage space. This protocol will allow researchers to bring recombinant DNA, bacteria, mammalian cells, animal and human tissue samples into the facility to be analyzed or stored. Undergraduate students will perform standard molecular biology and mammalian cell culture procedures. For the teaching component, the course numbers and relevant experiments are outlined. For the research component, the protocol indicates that they will maintain a record of the IBC protocols of the PIs that use the facility. The following will be communicated to the PI:

- The PI needs to complete her annual Bloodborne Pathogen Training. Her last training was taken on 2019.
- Please make sure that the personnel list is current.
- Please check "OTHERS" and indicate cryogenic gloves on Section VIII, #3.

BUA Site Assessment: It is a core facility protocol. One personnel left the lab. PI's BBP training is expired. Sharps are not used for biological materials. For cryotome cut resistant gloves are available but an SOP needs to be adopted for the equipment for its safe use. Two biosafety cabinets available in the facility are certified till 06/2023.

PI recused herself from voting.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 1