Boston University
Institutional Biosafety Committee (IBC)
October 18, 2022 Meeting Minutes
Location: Zoom and/or by phone
Start time: 12:00 PM End time: 3:00 PM

Members Present:	R. Ingalls (left 1:37 PM), B. Slack, E. Muhlberger, R. Davey, I. Afasizheva, P. Liu, W. Lu (left 1:02 PM, rejoined 1:58 PM), V. Gouon-Evans, T. Winters, R. Morales, S. Niemi, J. Keeney, R. Timmerman, J. Barton, V. Britton, S. Ghosh
Guests Present:	N. Dey, P. Richmond, M. Fitzgerald, J. Wood, R. Zacks
Staff Present:	L. Campbell, C. McGoff

I. Review of October 18, 2022 IBC Meeting Minutes

No concerns were voiced.
Motion: Approve
For: 14; Against: 0; Abstain: 2; Absent: 0

II. New Business:

A. SQAP Report:

- IBC Noncompliance Policy
  Members were informed that a new policy was drafted to address the IBC protocol noncompliance. The drafted policy was sent with agenda materials for any input by members; members were asked to send any input on the policy to IBC Program staff.
- Upcoming Biosafety Manual review/revisions
  Members were informed that the revisions to the Biosafety Manual will be available for review at the next IBC meeting.

B. Review of Research Occupational Health Program (ROHP) & Environmental Health and Safety (EHS) Incident Report: There were no incidents to report to the committee.

III. Protocol Review

1. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2578		Micronutrients, biomarkers of gut health and infant growth in Zambia	2	N/A	CRC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: N/A	

Meeting Comments: The overall goal of this protocol is to study the relationship between biomarkers of gut health and child growth/nutritional status in Zambian infants enrolled in a trial in 2021 evaluating home growth charts and/or nutrient supplements on child growth. The PI will analyze blood specimens for markers of inflammations and micronutrients, and rectal swabs for microbiome. PI is the only personnel listed and she has appropriate experience to work with human samples. Assays on blood will be run in the Analytical Instrument Core (AIC), and microbiome studies will be done by an outside collaborator. The biohazards are: Human blood samples, Human rectal swabs (stool). Potential for polio if the human subjects were infected with the WT circulating strain. CDC has been notified and required documents submitted on the CDC portal. Appropriate training done by PI, including shipping which is relevant to this protocol. AIC will store the samples and conduct assays on the serum samples. In the Laboratory Manipulations checklist pipetting infectious liquids is checked: human blood, including potential for wild polio type 2 given the epidemiology of the region where samples were collected. PI has appropriately contacted CDC. The committee discussed that if the AIC core is helping the PI as a pay-per-service basis, they do not need to be listed as personnel in the protocol as the core has their own IBC approval. The following will be communicated to the PI:

- Please clarify if the AIC core PI is a co-investigator for this protocol or you are going to be using the core as a pay-per-service facility. If AIC core PI is indeed a co-investigator, her name must be included in the personnel list.
- Will the blood sample be centrifuged in the AIC? If so, please check the centrifugation and ultracentrifugation box in the PPE Section.
- Please note that a BUA site inspection must be completed for this protocol to receive approval. Please arrange such inspection with EHS (Dr. Nilay Dey; nilaydey@bu.edu).

BUA Site Assessment: Not completed yet.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

2. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2564		Immune cell engineering for cancer applications	2	N/A	CRC

Primary Reviewer: Inna Afasizheva | Secondary Reviewer: Ron Morales

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

Meeting Comments: The goal of this protocol is to fine tune the currently available chimeric antigen receptor therapy (CAR-T) for cancer treatment. The protocol essentially involves in vitro manipulation of patient's own T-cells to produce receptor for tumor-specific antigen. These engineered T-cells are then introduced back in the patient where they will identify specific tumor cells and will invoke cytotoxic killing of the tumor cells. However, current versions of receptor are not always tuned properly and thus causing the engineered cells to sometime respond too strongly, too weakly, or not specific enough toward cancer cells. Consistent with such finding, some recent clinical trials noted that patient's non-cancerous cells expressing low level of tumor antigens are also killed by these engineered T-cells causing significant adverse effects in the patients. PI's lab is interested in designing novel signaling circuits that will allow them to precisely tune the threshold of activation. Protocol describes cell engineering, basic molecular biology methods and immunological tools. Plasmids will be created based on E. coli expression system. Genetically manipulated Jurkat T-cells and replication deficient retroviral and lentiviral vector systems will be received form BU collaborator. Primary T-cells will be isolated from leukopak purchased from various blood bank around Boston area. The following will be communicated to the PI:

- Pearlman Morales and Dr. need to complete the annual Lab Safety Training module.
- Please make sure to update ROHP clearances for all listed members.
- Please provide description of the lentivirus and retrovirus manipulations work. Indicate the name and source of the cloning vectors and packaging extracts. State if the genes that you will be expressing in these viral vectors are oncogenes. Indicate which generation vectors will be used for lentiviral vectors (Use of 3rd generation vectors are encouraged.
- Two human breast cancer cell lines and one ovarian cancer cell line are listed in Section A hazardous biological agent list. But the purpose of their use is not described in the laboratory procedure section. Please clarify.
- Please indicate which "Boston area blood banks" are referred in your IBC protocol.
- Please identify Dr. appropriately in Section A.1. of the protocol (such as BU College of Engineering faculty).
- No animal research is proposed in the protocol. Please remove animal facility use reference from PPE question #11.

BUA Site Assessment: Not completed yet.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

3. Bhz –New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2570		Chronic kidney disease of non-traditional origin (CKDnt): BU study freezer storage	2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting Comments: This proposal supports storage for specimens from two NIH studies in the Department of Environmental Health at BU School of Public Health. They are investigating the causes of chronic kidney disease of non-traditional origin (CKDnt) in Central America, a disease that has high mortality rates in the region among young men and whose causes are unknown. The goals of our projects are to evaluate environmental and individual-level risk factors for CKDnt. The first study is of an occupational cohort across Nicaragua and El Salvador. The study group are more than 500 male workers that were evaluated for metal exposure, heat exposure, and chemical exposures that may cause chronic kidney disease. The second study is a cohort for a longitudinal study for exposure to chemicals, metals and heat-related illness as possible cause of chronic kidney disease. Biohazard materials are blood, urine, feces, saliva and respiratory samples will be stored in a -80 centigrade freezer at BU School of Public Health biology lab. Personal protective equipment appears appropriate and freezer gloves are included in protection of the researchers. There is no liquid waste, solid waste is discarded into biohazard bags. They use Sporocidin wipes as a disinfectant. Transport of samples from the field to BU lab is done by World Courier Room in an insulated box with screw top tubes of samples shipped on dry ice by a world courier. IRBs appear up to date and current. It was clarified that since they do not thaw or aliquot the samples, surgical masks is not required in their work. The following will be communicated to the PI:

- Please add room to the protocol as that room is used for sample sorting and repackaging for shipment.

BUA Site Assessment: Room needs to be added; this location is where samples are sorted for repackaging and shipping. It was noted that lab do not do any work with the samples, and only stores and ships to other facilities for analysis.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2574		- An internet-based study of time-to-pregnancy in North America (PRESTO - parent grant) - Prospective Study of Endocrine Disrupting Chemicals and Time to Pregnancy (EPRESTO)	2	N/A	BUMC

Primary Reviewer: Tom Winters	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A

Meeting Comments: The objective of this project is to investigate endocrine disrupting chemicals and their role in reproductive problems and adverse birth outcomes through evaluation of internet-based survey and human samples (urine, blood. and vaginal fluid). These samples are either collected by trained phlebotomist in the GCRU clinic or through mail-based sample collection procedure (for urine samples and dry blood spot samples). All samples are sent to outside laboratories for analysis. Biosafety risks involved in the protocol include use of human blood samples, urine samples and vaginal samples. The PI's lab aliquots phlebotomist collected human blood samples in biosafety cabinet and store them in -80C freezer. Mailed-in blood spots are stored in sealed bag with desiccant. Disposable gloves, goggles and surgical mask will be worn while processing samples. Liquid wastes will be treated with 10% bleach and disposed of in the sink after 30 min incubation. Urine samples are poured into 10% bleach, as well as cups will be submerged. Dry ice used in packages are disposed of in well ventilated area under fume hood. Surface disinfection will be done with 70% ethanol or 10% bleach. Urine samples are transported in cups within plastic cups,

in white cryobox, in large plastic biohazard bag. Blood spots are in sealed plastic bag inside larger plastic box. Blood samples are in cryovials inside cryobox. The following will be communicated to the PI:

- PI Dr. must complete rDNA/IBC policy training in BioRAFT.
- does not have any training record. She must take all biosafety trainings.
- Must provide a response to the "Experience" and "State how many years experience, when and where" questions for all listed personnel.
- Add room to the protocol as that room is used for sample sorting and repackaging for shipment.
- Check pipetting infectious liquid (as they are blood samples that may contain blood borne pathogens).
- Add lab coat for blood sample processing.

BUA Site Assessment: Complete. Room needs to be added; this room is used for sorting and repackaging of samples. Training update needed for the PI and Annette.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

5. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2575		Cellular and tissue physiology with genetic perturbations and in situ profiling	2+	N/A	CRC

Primary Reviewer: Sajal Ghosh | Secondary Reviewer: Bob Timmerman

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

Meeting Comments: The goal of this application from the newly developing Computing and Data Science department is to identify network of cellular signaling pathways intracellularly and intercellularly. They propose to identify such network through computational analysis and then validating those circuits by highly efficient *in situ* fluorescent imaging and other advanced molecular techniques. Their broad objective is to profile spatial organization of gene expression at a single cell level. The work include extensive data compilation and work plan development, but the validation part require laboratory work with cell lines including lots of gene manipulation work. They will manipulate gene expression in different human cell lines obtained commercially or through collaborators. They will construct vectors to make CRISPR guide RNAs, and will engineer commercially purchased lentivirus vectors to expression proteins of choice.in the lab with commercially purchased vector and packing plasmids. The donor sequences in their cloning work will contain regulatory regions and coding regions of nonpathogenic fungi, bacteria and viruses, human, and animal DNA sequences. It appears that fluorescent imaging, western blotting or similar experiments will be carried out as read-out for their experiments. The protocol includes extensive detail of expected biohazard handling risks and complete mitigation plan including personnel training (including Hep-B vaccination plan for those who work with human cells), PPE use, liquid waste disposal following the use of bleach at final 10% concentration for 30 minutes and solid waste in red-biohazard bag and sharps in separate sharps container. They also provided a detail description of safe use of laboratory chemicals including spill management and removal of chemical wastes. Overall, very nicely written protocol. The following will be communicated to the PI:

- Section IV: CILSE is marked as BSL2+. Not clear what is being done that require BSL2+ containment?
- Section VIII.5. BSC is checked but no detail provided.
- Section A. *E. coli* DH5alpha does not need to added to the list, as it is not a biohazardous agent.
- Section H. Recombinant DNA: Name the donor genes in prokaryotic experiments and name the lentiviral vector/vectors in the Vector packaging box.
- Section H. Update the applicable NIH guidelines question response to include "Sections III-D-1-a, III-D-2-a and III-E-1."

BUA Site Assessment: This is a new lab and in the process of setting up work space, laboratory research SOPs and others.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

6. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2399		Molecular Epidemiology of Preterm Birth H-23525 BMC Children's Health Study H-23237	2	N/A	BUMC

Primary Reviewer: Weining Lu	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: N/A	

Meeting Comments: The study aims to investigate the role of environmental factors, genetic factors, and gene-environment interactions in determining preterm birth among a multi-ethnic U.S. population enrolled at BMC, including Black, Hispanic, White, and others. Clinical samples are collected from women who deliver a preterm or low birth weight baby and also from controls cases with term and non-low birth weight births who are women of similar age, race and have delivered around the same date. This study started in 2004 and followed the health, growth, and development of the women and children who participated in the study if their children came to BMC or one of the neighborhood health centers for medical care. The laboratory procedures include the collection of cord blood and piece of the placenta by labor and delivery unit nurses at BUMC. NICU nurses will also collect newborn stool meconium for microbiota study. All sharps will be disposed of in the maternal room's sharp container, and gloves will be in the biohazard bag. In addition, maternal oral swab samples will be collected by a Research Assistant. The study will also collect urine and blood samples from children enrolled yearly. Biospecimens (e.g., oral swabs, urine, blood, placenta, and meconium) will be transported to PI's lab immediately in a biohazard bag. Potentially infectious materials (such as evacuated blood collection tube) will be placed in a well-constructed container with a secure lid for transportation. The laboratory procedures at BMC is mainly temporarily store biospecimens and centrifugation of blood until subsequent shipment to the study collaborators and overall PI's repository site at Johns Hopkins for further molecular and epidemiology analysis. The biospecimens will be obtained from an ongoing clinical project with two approved IRB protocols at BMC. Due to Covid-19, this project was on hold for the past 2.5 years but will resume once approved in the clinical setting of human subject research and recruitment at BMC. No significant changes to this IBC protocol have been made in the past three years except for a new lab space. The following will be communicated to the PI:

- Please give the full name of some abbreviations when they first appeared in the protocol. E.g., PTB in Part VII, Section 2 microbiota analysis on page 11.
- In Part VII, Section 3, Describe laboratory procedures; there are Item 4 (Oral swab samples) and Item 7 (Cord blood samples and placenta). But there are no labels for Items 1-3 and 5-6. Please clarify.
- Also, in Part VII, Section 3, Item 4, please specify "Maternal" oral swab samples (as no children's oral swab samples will be collected from the study).

BUA Site Assessment: Not complete yet.

Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

7. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2577		Development of novel therapeutic approaches for ocular diseases	2	2	BUMC

Primary Reviewer: Rob Davey	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-II-D, G-II-B	

Meeting Comments: The goal of this protocol is to understand the mechanism of ocular cell maintenance, regeneration of ocular tissue and develop new therapeutic approaches to treat ocular diseases, such as cataract, glaucoma, dry eye, limbal stem cell deficiency, etc. To do this, They use animal models of limbal stem cell deficiency,

corneal wound healing and genetically modified mice, along with human and mouse eye tissues and primary cultured mouse and human cells and cell lines including induced pluripotent stem cells. Biohazards in the protocol include human eye cornea and other material as well as cells from the mouth and human cell lines. The human samples have been screened and are free of common bacterial and human bloodborne viruses that include HIV, HBV and HCV. Cells will be modified to express genes related to cytoskeleton and some growth factors. The growth factors are not proto-oncogenes. Genes will be delivered using 3rd generation lentivirus vectors, which limits risk. They have 6 years of experience working with such systems. To decontaminate samples they will use 0.5% hypochlorite solution (10% bleach) for 30 minutes. Sharps will be disposed on in sharps containers. The PPE checked for their lab and animal work seems appropriate. Preparation of cholera toxin and Tamoxifen and their handling safe storage are well described. The following will be communicated to the PI:

- Note that initiation of all animal work depends on submission and approval of IACUC protocol.
- VIII.3. Lentivirus and iPSC use in live animals is planned, but IACUC protocol not yet submitted. Please briefly describe use of these materials in the mouse model in section VII for completeness.
- VII. 3. Tamoxifen, for application to the ocular surface of the mouse will this be with a pipette or a syringe?
- VIII.3. Also indicate how unused portions of the stock solutions of cholera toxin and tamoxifen will be treated to render them inactive before their disposal in biohazard bags.
- VIII. 4. For ABSL2 work in a BSC you'd only need lab coat, disposable double gloves. If the work will occur on benchtop, that PPE requirement may increase.
- VIII.11. Appropriate use of secondary containers is indicated for transporting tissue samples and other materials but should indicate that the container is shatterproof.

BUA Site Assessment: Not complete yet.

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

8. Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2583		Nanomaterials to Program the Immune System	2	2	CRC

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

Applicable NIH Guidelines: N/A

Meeting Comments: This is a new project from a new Faculty on the CRC. The lab focuses on engineering nanotechnology to control immune cell function to develop new therapeutics and improve vaccines against cancer and infectious diseases. To do so, the lab synthesizes DNA and porous materials (with metal-organic frameworks) that they will combine together to induce expression of gene in immune cells in vitro and also to inject in mice *in vivo*. The nanostructures will be synthesized in a chemical fume hood and purified/characterized using the departmental core facility. Primary immune cells from mice or from humans (from commercial sources or immortal immune cell lines will be treated with the nanostructures in a biosafety cabinet and immunological outputs will be analyzed via microscopy, flow cytometry, or protein or gene-based assays (e.g., ELISA). They will then use the best performing structures to do *in vivo* analyses to determine therapeutic benefits, such as tumor regression, antibody production, etc. Disposal of biohazard wastes and transport of biohazardous materials across buildings are well described. They will generate synthetically derived nucleic acids but those will be exempt experiments under NIH guidelines. The committee recommended use of N-95 respirator for nanoparticle work outside the fume hood or biosafety cabinet. The following will be communicated to the PI:

Section III. The PI should include herself and indicate her experience/trainings/ROHP.

- Section III. 1. State experience level (in the 'State how many years experience, when and where') even if inexperienced and state who will be training on necessary lab procedures.
- Section III. 3. needs ROHP clearance.

- Section IV. Animal BSL should be changed to ABSL2.
- Section VIII.3. Synthesis of nanomaterials should require N95 respirator if not done in the fume hood.
- Section VIII.4. PPE in animal facility requires N95, double gloves and back fastening gowns.
- Section VIII.5. the biological safety cabinet needs the certification date.

Note that EHS Industrial Hygiene specialist will need to evaluate engineering control in your lab for the location where you will prepare nanoparticle. Please contact Research Safety Director Ron Morales (rmorales@bu.edu) in this regard.

BUA Site Assessment: Lab is not set up at this moment. They will use two fume hoods. Biosafety cabinets are not calibrated yet. The nanoparticles they will use are in the range of 15 to 300 nm. Because of the size of the fume hood, will need to keep DNA synthesizer outside the fume hood; N-95 respirator is recommended. Industrial hygiene specialist from EHS will check on whether N95 must be used if nanoparticles are used outside the hood.

Motion: Conditional Approval (Primary, Secondary Reviewer and R. Morales Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

9. rDNA/Bhz – New Application

BUA	(PI)	Title	BSL	ABSL	Campus
2390		Multimodal characterization of prefrontal and premotor circuits underlying perceptual decision making in the rhesus monkey	2	2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Steve Niemi

Applicable NIH Guidelines: III-D-1, III-D-4, III-E-1, Appendix B-V, Appendix G-II-B, Appendix Q-1

Meeting Comments: The goad of this protocol is to study how The prefrontal cortex (PFC) communicates with many sensory, memory, emotional, and motor brain structures. The lab uses non-human primates (NHP - rhesus monkeys) as model for their study. They perform surgical procedures to inject light sensitive opsin proteins that can be stimulated by an optic fiber in-vivo to conduct these experiments. The Opsins are injected with recombinant AAV viruses. The PI has prior experience with CNS recording in NHP at Princeton, Stanford, Max Planck in Tubingen. The proposed experiments will be done in collaboration with another BU faculty (listed as personnel on this protocol) who also is highly experienced. Biohazard risks in the protocol include the use of rhesus monkeys and handling tissues from them. AAV particles obtained from viral cores are injected into the brain of anesthetized NHP. Deeply anesthetize, Transcardial perfusion with ice-cold buffer is also done on deeply anesthetized animals. Optogenetic stimulation and live recording 6-12 weeks after AAV injection. Some fresh tissues are snap frozen, used for biochemical assays under BSL2 precautions. Some tissues are harvested for in vitro recording, then perfuse with paraformaldehyde for IHC. Then slices fixed with paraformaldehyde. Small amounts of tetrodotoxin (TTX) used by Luebke- below select agent levels. ABSL2 precautions are followed for live tissue handling, recording. Surgical instruments are disinfected, washed, autoclaved (10% fresh bleach and/or Quatricide). Hazardous materials- diaminobenzidine, osmium tetroxide, paraformaldehyde, are stored, handled and collected appropriately. Solid tissue waste collected in doubled red bags and incinerated. No BSC use listed. The following will be communicated to the PI:

- Section III.1- PI needs to be added to list of personnel, along with description of experience, Lab training dates, ROHP clearance, etc. Note that PI will be training five of the other personnel listed. The only person on the project with experience (besides PI) is Dr. .
- Section III.3- ROPH clearance for Wang should be updated
- Section IV.- W746 should be listed as ABSL2 if live NHP will be handled in the room.
- Section VII.3 and VIII.2- is homogenization of fresh brain tissue performed in a BSC or fume hood? (No BSC is listed). How are personnel protected from aerosols? Gasket homogenizers?
- Section VIII.7A- liquid waste- please specify that bleach at a final concentration of 10% will be used.

• Section IX. High Hazard Chemicals is checked, but none are listed in Table F. Please list any chemicals that apply in Table F (e.g. osmium tetroxide). Radiation and X-ray is checked. Please uncheck if these will not be used (Section G indicates that such use is not contemplated.) BUA Site Assessment: Most of the rooms listed in the protocol are under Dr. Dr. and Dr. Most of the live animal work is done in PI's lab but tissue collection from anaesthetized animals are done in the laboratory of other listed collaborators.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

10. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
989		Innate Immune Responses to Neisseria and Chlamydia, and Their Role in Pathogen Induced Inflammation	2+	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewers: Tom Winters

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

Meeting Comments: The objective of this project is to study the cellular pathways of human innate immunity to common bacterial sexually transmitted infections (chlamydia trachomatis and Neisseria gonorrhea) through in vitro investigation of human immune cells. The biohazardous materials used in the protocol include **u**se of mutant strains of N. gonorrhoeae resistant to tetracycline, ampicillin and chloramphenicol. Clinical strains are also used which were tested for multidrug resistance, but none demonstrate high level ceftriaxone resistance. *Chlamydia trachomatis* and *C. pneumoniae* strains are also used. Human leukocyte cells are purchased from NY Biologics and tested for HIV, Hep B & C, syphilis and West Nile virus. They do not actively do any rDNA work but possess *E.coli* and *N. gonorrhea* bacteria and cells that stably express recombinant DNA. All bacterial manipulations are done in the biosafety cabinets and grown in CO_2 incubator. They use laboratory coat, gloves (double gloves for *C. pneumoniae*) and safety glasses at a laboratory bench. Liquid wastes are treated with 10% bleach added, 30 min incubation, then down the sink. Solid waste are disposed of in red bag lined biohazard box. As disinfectant, 70% ethanol or 10% bleach and Roccal-D are used. It was noted that no animal work is being done at this time. The following will be communicated to the PI:

- Check surgical mask (for the work with infectious bacteria)
- Add Roccal-D (with working dilution level) to the list of disinfectants. Note that production of Roccal-D has been discontinued. Alternates such as Dupont 904 may be considered.
- Please remove reference to animal work in the Hazardous biological agents, table 4 since there is no plan of use of animals.

BUA Site Assessment: PI is the only one listed in the protocol. No work is currently being done. The -80°C freezer and the ultracentrifuge need biohazard sticker. Biosafety cabinet is duly certified. Exposure control plan is in place.

Motion: Conditional Approval (Administrative Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

11. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2407		Assessing the Use of Firefighter Turnout Gear to Create Heat Acclimation-Induced Increases in Performance and Cardiovascular Health	2	N/A	CRC

Primary Reviewer: Pinghua Liu	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: N/A

Meeting Comments: The purpose of this research study is to determine whether using a typical firefighter turnout gear could be a useful technique to reduce cardiovascular risk, by providing a heat stress type of training. In the proposed study, the PI will recruit study participants and collect basic health information just as is done during a

typical doctor office visit, including cardiovascular function, estimating energy expenditure (e.g., breathing into an exercise mask to collect air), arterial stiffness etc. The participants will then wear the typical firefighter turnout gear and conduct exercise in a hot chamber. The internal temperature will be closely monitored, and the same type of parameters will be measured. In the last phase, PI will determine whether there are beneficial effects compared to the starting point. The only part that needs to be taken care of are those spirometry equipment, mouthpieces etc. They will be cleaned by detergent solution, bleach solution and rinsing with sterile water. Overall, no appreciable biohazard risks were identified in this protocol.

BUA Site Assessment: Not completed yet.

Motion: Approve	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

12. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1848		Repeat-containing RNA Binding Proteins of Trypanosomes	2	N/A	BUMC

Primary Reviewer: Elke Muhlberger | Secondary Reviewer: Valerie Gouon-Evans

Applicable NIH Guidelines: Sections III-D-1-a; Appendix B-III-C - Risk Group 2 (RG2) - Parasitic Agents

Meeting Comments: PI is interested in understanding RNA metabolism in unicellular parasite *Trypanosoma brucei* which is known to cause sleeping sickness. These organisms have unique mechanism of RNA editing in mitochondria for the generation of messenger RNAs that involve specific uridylation and adenylation of the RNA. The group is interested in analyzing specific proteins involved in RNA adenylation and uridylation. The work includes expression of recombinant proteins in *E. coli* and *T. brucei* and construction of *T. brucei* cell lines for protein expression and RNA interference studies. The lab uses two insect forms of *T. brucei* (TRUE927 and Lister 427) that cannot cause human or animal infection. They collect materials for PCR analysis, mass spectroscopy, cryomicroscopy and crystalization of proteins. Handling of biohazardous materials are well written. PI stated that presence of high density lipoprotein (HDL) protects humans from infection with this parasite. Committee wanted clarification on what minimum serum HDL level in a researcher would make them eligible to work with *T. brucei?* The following will be communicated to the PI:

- The rDNA/IBC Policy training needs to be updated for all members including the PI.
- Chemical Safety training needs to be updated for
- Update biosafety cabinet certification date.
- It is stated in the laboratory procedure section that presence of high density lipoprotein (HDL) protects human from parasites and HDL -resistance strains of the parasite are not maintained in the lab. Please clarify the minimum level of blood HDL necessary to protect humans from parasite infection. In other words, should individuals with low levels of blood HDL be restricted to work with *T. brucei* TRUE927 and Lister 427 strains?

BUA Site Assessment: Biosafety Cabinet is duly certified. rDNA/IBC Policy training expired for all members. Some equipment need biohazard sticker.

PI recused herself from approval decision voting.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 14	Recuse: 1	Against: 0	Abstain: 0	Absent: 1

13. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1820		NIH R01 EB00262 Local regulation of angiogenesis by microenvironmental cues	2	2	CRC

		NIH R01 EB008396 Engineering Multicellular Tissue Structure, Function, and Vascularization NIH UH2 EB017103 Integrated Heart-Liver-Vascular Systems for Drug Testing in Human Health and Disease NIH R01 Mechanoelectrical interactions between cardiac myofibroblasts and myocytes NIH R01 Notch signaling and adhesion regulation NSF Collaborative Research: The Effects of Extracellular Matrix Alignment of Cellular Mechanotransduction in 3D Architectures NSF Nanosystems Engineering Research Center for Directed Multiscale Assembly of Cellular Metamaterials with Nanoscale Precision: CELL-MET Engineering high density functional vascular, lymphatic, and ductal trees Engineering Branching Networks Through Synthetic Turing Morphogen Circuits			

Primary Reviewer: Rob Davey	Secondary Reviewer: Valerie Gouon-Evans

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

Meeting Comments: P I is studying cell adhesion and cytoskeleton structure and how they affect cellular functions. Primary human and rodent cell types are obtained from commercial sources and modified to express recombinant genes using plasmids and virus vectors that include adeno associated virus and retroviral vectors. The latter is a 3rd generation system that limits risk to personnel. The AAV is non-replicating. The genes being tested are all cytoskeleton related and each are non-oncogenic. Mice are also used and will be made to overexpress proteins using the virus vectors. Greatest risk is use of high titer lentivirus vectors (such 10^8 per mouse per dose). BSC is used for injection on anesthetized mice. It would be better to indicate use of a needle block, that helps to limit exposure to needles when multiple animals are being dosed. PAPR is using surgical coverings and is appropriate to reduce risk. Sharps are disposed of in sharps container and 10% fresh bleach is used for liquid waste. For transporting virus material is double bagged and. Please indicate that a liquid will be used and secured. It would be better to use a shatterproof container with a sealable lid. A 2-20 mg/ml stock solution of Tamoxifen is used for animal injection. Overall, the experiments are appropriately described to mitigate risk. The following will be communicated to the PI:

- Following training updates required –
  - LST: , ,
  - BSL1/2: , , , , ,
  - BBP: , , , , , ,
  - rDNA/IBC Policy: , , , , , , .
- ROHP update needed for ALL except: , , , , , and
- IV.1. CILSE is marked as ABSL3, please change it to ABSL2. There is no ABSL3 in CILSE.
- VII.3. The committee recommends use of a needle block, that helps to limit exposure to needles when multiple animals are being dosed.
- VIII.5. Please update recent BSC certification date (should be within less than one year; it is currently stated as 7/19/2017)
- VIII.11. It is stated that virus-containing tubes will be placed into a polystyrene box. This secondary container must be leakproof and shatterproof. Please confirm.
- Please note that BUA Site Inspection must be completed for the approval of this protocol. Please contact BSO Dr. Nilay Dey to have this done.

BUA Site Assessment: Not completed yet.

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
681		Microchip to detect HIV viral RNA in whole-blood samples using branched-DNA hybridization	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Sajal Ghosh
Applicable NIH Guidelines: Sections III-D-2-a, Appendix C-II, Appendix B-II-D	

Meeting Comments: This lab is developing low-cost chip assays for measuring HIV1 concentration in clinical samples using microfluidics technology. The lab has significant expertise in developing such platform and are constantly trying to improve them. This low-cost device that is easy to operate in field setting, will be helpful in determining viral load during test of an antiretroviral therapy regime. The protocol essentially trying to set up the entire branched-DNA hybridization technique on a chip using the microfluidics technology. They use commercially purchased human plasma samples spiked with HIV RNA segments as test samples. They are not doing any rDNA work but use plasmid (or Phage) DNA that contain HIV sequences for PCR amplification and RNA preparation by in vitro transcription. The biohazard part is the use of culture supernatant from lymphoblastoid cell line HIV-8E5LAV, which produce non-infectious HIV strain LAV. They also use other reference human serum sample as realistic test material for their assay development. All procedures are described in detail and waste disinfection of samples and used chip disks are clearly stated. IRB approval is not needed for commercially purchased serum samples. The following will be communicated to the PI:

- Section I- box for amendments should be left blank
- Section III.1- Please specify who will train Lab Tech .
- Section III.3- some ROHP clearance dates need to be updated.
- Section VII.3- The descriptions of virion or blood-contaminated plastic pipette tip disposal in rooms B08, 709, and 720 is confusing. It is stated that tips will be "soaked with 10% bleach overnight"... then "drained of ethanol and placed inside a ... sharps container, where we will leave the lid open such that all remaining liquid ethanol evaporates prior to disposal". Bleach would be the decontaminant of choice, but possibly the last part of the sentence was not properly removed from the previous submission. Please remove this part or clarify.
- Section VII.3- Chips used for assaying DNA isolated using gold nanoparticles linked to streptavidin will be discarded in biohazardous waste boxes or sharps containers (for plastic chips), according to the protocol. A separate waste stream is needed for chips and other waste containing gold nanoparticles.
- Section VIII.5- please update BSC certification date.
- Section VIII.7A- Please make sure the statement for plastic tip disposal is consistent throughout.
- Section H. rDNA- It does not appear that any rDNA is being expressed in any eukaryotic hosts. If so, the eukaryotic experiments section does not need to be filled out.

BUA Site Assessment: Not completed yet.

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

15. Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2152		A Rapid and Sensitive Antibiotic Susceptibility Test for Urinary Tract Infections	2	N/A	CRC

Primary Reviewer: Sajal Ghosh	Secondary Reviewer: Pinghua Liu
Applicable NIH Guidelines: N/A	

Meeting Comments: The original protocol is to develop a quick antibiotic sensitivity testing method for diseases like urinary tract infection (UTI). Development of such a rapid testing device would benefit testing at a point of care

setting. Conventional antibiotic sensitivity testing requires 24-48 hour and forces doctors to prescribe generic antibiotics which often does not work. Their method involves microfluidic analysis of urine sample spiked with bacterial culture placed on the chip in presence or absence of test antibiotics. This is a very simple straightforward project where biohazards are urine samples and cultured bacteria. Urine samples are purchase commercially where the supplier provide certificate of non-infectious nature of the samples. Detail methods of culturing *E. coli, Streptococcus epidermidis, K. pneumoniae and Bacillus subtilis* are described quite well. Liquid wastes are treated with 10% bleach (final) for 30 min before sink disposal and solid waste including chips with bacteria and urine are first treated with bleach, liquid decanted and then disposed in red biohazard boxes. PI states that the project is inactive at present but wants to maintain the IBC and hopes to restart when pending grant applications get funded. The following will be communicated to the PI:

- PI needs to update safety trainings (BSL1/2, BBP, Chem safety and rDNA/IBC Policy).
- needs to update BSL1/2 and BBP training.
- Please add the room where biohazardous materials are stored.
- In the experimental section, various risk group 2 bacteria will be used. The PI did not mention any protection procedure or de-contamination procedure for them. Please provide brief statement on them.
- Bacterial names are different in the lab procedure and in the Section A. This needs to be reconciled.
- For the urine samples, It is stated that the supplier certifies that they are 'viral negative', but do they provided information about other pathogen such as bacteria?
- Check vortexing, centrifugation, culture stirrers/shakers.
- In the CRC pipet tips are considered as sharps – please dispose them in the sharp container
- Please indicate if the access to the bacterial storage freezer has access restriction.

BUA Site Assessment: Addition of other room where pathogens are stored is needed. Training needs to be updated for both the PI and the graduate student. Lab needs to check all the applicable aerosol generating devices. They have been previously trained by Dr. Kurosawa

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

16. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2142		Epithelial Stem Cells in Homeostasis and Diseases	2	2	BUMC

Primary Reviewer: Weining Lu	Secondary Reviewer: Steve Niemi

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

Meeting Comments: This is a 3-year renewal application from a School of Dental Medicine PI on a basic science project to study the role of stem cells in cancers and autoimmune diseases. The original PI of the protocol has left BU few months ago and the protocol now has been transferred to the current PI. For this 3-year re-submission, only the personnel section and lab space have been changed from previous PI's lab to the current PI's lab in the 4th floor of the Evans building. There are four specific aims in this project focusing on the p63 signaling pathway of P63, where they will analyze the roles of the functional domains of p63 in control of the proliferation, differentiation, and self-renewal of epithelial stem cells. Multiple mouse models, including specific p63 exon knockout animals, or animals with tissue-specific expression coupled with ectopic expression of p63 will be tested to identify required factors for cancer development. The project will also use number of human cell lines to perform functional analysis of the signaling pathway, including cell culture and expressing p63 mutant proteins using retroviruses and lentiviruses. Laboratory procedures in the projects include using mice to isolate epithelial stem cells (EpiSCs) and assess their proliferation, differentiation, self-renewal, and apoptosis in vitro. All cell culture and tissue collection procedures will be performed under a biosafety cabinet, and immunohistochemical staining will be performed under a fume hood. Personal protective equipment, including gloves, coats, and safety glasses (or goggles), will be used at all times. All lentivirus and retrovirus used in this protocol are non-replicating. Virus liquid waste will be treated with 10% bleach (final) overnight and autoclaved. Some potential hazardous chemicals and high-hazard chemicals (DMBA, cycloheximide)

will be used in cell culture *in vitro* experiments and mouse model in vivo experiments. Appropriate PPE, engineering control, and steps or procedures to limit the potential hazards are described. Committee learned from the BUA site assessment and from BSO's meeting with the PI, that most of the work described in the protocol are no longer being done or will be done. The IBC protocol is being maintained to allow completion of the remaining work of the graduate student of the original PI. Committee recommended a thorough revision of the submission to indicate what exact research work is ongoing remove all of the rest originally proposed experiments that will no longer be performed. The following will be communicated to the PI:

- It is unclear why immunohistochemical staining needs to be performed under a fume hood.
- The protocol indicated that virus liquid waste would be treated with 10% bleach (final) overnight and autoclaved. It is unclear why an autoclave is needed for virus liquid after 10% bleach treatment.
- In Section VII. RESEARCH PROJECT DESCRIPTION: four human cell lines are described. However, six human cell lines are listed in Section IX, Section A. Hazardous Biological Agents. Please reconcile.
- BrdU is cytotoxic and can cause heritable genetic damage, harm to the fetus, reproduction disorders, and may alter genetic material, so a replacement with EdU is recommended.
- Section F. High Hazard Chemicals listed two chemicals: DMBA and Tamoxifen. Because Cycloheximide used in Experiment 2 is also classified as a highly hazardous substance in the US, it should be listed in Section F.
- Please check the box for "Animal handling, cage changing"

BUA Site Assessment: Most of the procedures are already completed. The protocol is being renewed only to allow some remaining tissue sectioning and imaging work needed for the completion of thesis work for the graduate student. Once those are completed, the protocol will very likely be closed. Biohazard stickers need to be put on multiple equipment.

Motion: Conditional Approval (Primary and Secondary Reviewer Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent:1

17. rDNA/Bhz – Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2255		Proteomic analysis of protein interaction networks in models of human health and disease	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1	

Meeting Comments: The goal of this study is to understand protein-protein interaction in different cells and tissues in normal or diseased conditions. The working hypothesis is that composition of such interactions are critical determinant of the biological processes they are involved in. The lab focuses on mapping protein networks in cultured cancer cells and biochemically fractionated neuronal (synapse) samples, generated and processed in collaboration with several research groups. Their objective is to identify novel macromolecular associations and mechanistic relationships using proximity labeling chemistry and mass spectrometry proteomics. Workflow includes molecular cloning to produce expression constructs in bacteria, viral vectors and eukaryotic cell, culturing human mammary epithelial cell line and lysis/sonication of post-mortem frozen human organs and tissue. Protocol includes two approved amendments for work with human specimens and inactivated SARS-CoV2 infected cells and tissue lysates. They also use cholera toxin for growth of normal breast epithelial cell line, but at a concentration well below LD50 level. The committee noted that stringent inactivation protocol and handling safeguard will be practiced for handing human brain samples (such as a 40% bleach treatment for minimum of 30 minutes, or 1hr autoclave at 121 C) are used for disinfection. The following will be communicated to the PI:

- ROHP clearance is not updated for nine members of the lab.
- Since Dr. is no longer the PI of this protocol, reference to his personal experience and laboratory set up plan in Laboratory procedure section must be removed. A new introduction may be provided.

• Please include protocol for manipulations with lentivirus and AAV. Both systems are included rDNA section. • Update biosafety cabinet certification date. • Hazardous biological agent MDA-MB-468 is obtained from unknown source indicated as BU researcher. Please provide name. Also clarify who is and indicate that is BU faculty. • Provide names of vectors and donors in the prokaryotic experiments part in the rDNA section. BUA Site Assessment: Not completed yet.					
Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent:1