Boston University
Institutional Biosafety Committee (IBC)
March 17, 2020 Meeting Minutes
Location: Zoom Meeting
Start time: 12:00pm End time: 3:50pm

Members Present: I. Afasizheva, R. Ingalls (left 2:30 PM), B. Slack, E. Muhlberger, R. Davey, C. Abraham, R. Morales, T. Winters, R. Varada (left 2:40 PM), S. Kurnick, J. Keeney, R. Timmerman, V. Britton, J. Barton, R. Georgiadis (left 1:42 PM), X. Brown
Guests Present: T. Killeen, N. Yun, S. Benjamin, K. Tuohey, F. Ennever, M. Auerbach, J. Davis, A. Ahmad, R. Filler
Staff Present: J. Hutchinson, S. Ghosh, C. McGoff

I. Review of January 28th & February 25th, 2020 Meeting Minutes

No comments or questions were voiced.
Motion: Approve
For: 16; Against: 0; Abstain: 0; Absent: 0

II. New Business

Research Occupational Health Program (ROHP) & Environmental Health & Safety (EHS) Report: Members were informed that incident reports will be provided at next month's meeting and that there was an incident that occurred on March 3, 2020 that is being reported to NIH OSP/BPHC; an assistant professor sustained a small laceration to his finger when mincing tissue from a clean transgenic mouse.

III. Protocol Review

1. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2375		Evaluation of treatments for high containment viruses using rodents	4	4	BUMC

Primary Reviewer: Elke Muhlberger Additional Reviewer: Nadya Yun	Secondary Reviewer: Susanna Kurnick
Applicable NIH Guidelines: N/A	

Meeting comments: The PI would like to add coronaviruses: SARS-CoV-2, MERS-CoV, and SARS-CoV for use at BSL-4/ABSL-4. It was noted that in contrast to the BSL4 viruses, these viruses cause respiratory disease. Members discussed whether this has any impact on precautions when handling infected animals; it was stated that: there would not be any additional precautions as all animal handling will occur in a BSC and positive pressure suits will be used, cages are never opened outside of the BSC, necropsies are performed on a downdraft table, and all caging is individually ventilated. It was observed that SARS-CoV is a Select Agent and needs to be added to the CDC registration and agent specific training must be completed.

- There is a review and approval process in place for the validation of SA inactivation procedures. The inactivation documents will be reviewed by the RO or ARO. Upon approval, the documents will be reviewed by the IBC chair. Please change accordingly.
- Briefly describe the mouse work performed with the coronaviruses, specifically the differences compared to the described work with the BSL4 viruses. For example, will there be differences in the route of infection, e.g. intranasally? Is it planned to use mouse-adapted strains or hACE2 knock-in mice?
- SARS-CoV-2, SARS-CoV, and MERS-CoV are positive sense RNA viruses whose genomes can be used to generate infectious virus by transfecting cells. Describe precautions for handling inactivated samples containing RNA at BSL2 (e.g. restricted access, complete disruption of RNA).
- SARS-CoV RNA is classified as a select agent. Describe procedures for how this RNA will be handled when removed from the BSL4 lab.
- Add S. Kurnick as the responsible veterinarian (rather than K. Hardcastle) under personnel information. N. Macgregor should be removed as she is no longer with ASC.
- VII- specifically states "hemorrhagic fever viruses"- please amend to include coronaviruses.
- VII #3- The mice used to test SARS-CoV interventions are not technically "knockouts" as stated in the protocol, they are transgenic for the human ACE2 receptor; please amend accordingly.

• VII #3- Clarify in procedures that no needle will be attached to syringes for the intranasal inoculation required for coronaviruses. • P 16. Briefly describe or reference the disease development of MERS and SARS in humans and animal models.					
Motion: Conditional Approval (Administrative Review)	For: 15	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

2. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2361		Testing medical countermeasures against high consequence pathogens in rodents	4	4	BUMC

Primary Reviewer: Rob Davey Additional Reviewer: Nadya Yun	Secondary Reviewer: Rao Varada
Applicable NIH Guidelines: N/A	
Meeting comments: The PI would like to add SARS-CoV-2 and a transgenic mouse line needed for studying SARS-CoV-2. Work will be performed in the BSL4 for access to equipment, trained personnel and containment environment. Medical countermeasures in a mouse model of infection will be evaluated. The PI is experienced working at BSL4 and documentation of training of staff is well detailed. S. Kurnick has been added as the veterinarian for ABSL4 work. The BSL-4 BSO indicated that the PI has already addressed her comments. • Viruses will be obtained from biomolecule production core or BEI resources; Dr. Corley's virus repository should be added. • Non-DURC project boxes at bottom of page 12 need to be checked. • Unless inactivation methods will be validated for SARS-CoV-2, it should be indicated that those procedures that have been validated for inactivation of Ebola viruses, also inactivate SARS-CoV-2 (see: Darnell et al., 2004 121:85-91 J. Virol. Meth. and Kumar et al. 2015 223:13-18, J. Virol. Meth). Also indicate that TRIzol treatment results in nonviable genomic material, with no virus recoverable upon intentional transfection into cells. A statement should be made to indicate that Microchem Plus has activity against coronaviruses (the reference would be Zhang (as cited but for another reason) and the manufacturer's documentation). • Update the BSC certification dates (several are listed with 2018 dates). • VII-verify that the language describing the viruses is correct throughout and consistent with the addition of SARS-CoV-2 (this virus is not RG4). • Verify that intranasal inoculation is covered by the listed SOPs for guinea pigs. If not, these SOPs will need to be created or specific procedures listed in this protocol. • IX- Clarify if SARS-CoV-2 will be the only coronavirus used or if others will be used as controls.	

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

3. Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2352		Propagation and characterization of viruses	4	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Nadya Yun
Applicable NIH Guidelines: N/A	
Meeting comments: The PI is doing in vitro work including propagation of virus. This amendment is to add SARS-CoV-2 (which is a BSL-3 virus) for use in BSL-4 space, using BSL-4 practices. The BSL-4 BSO indicated that the virus can be safely used at BSL-4 and that EHS has no concerns about the virus being used at a higher biosafety level. She also noted that the PI has addressed all of her comments.	

Motion: Approve	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

4. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2286		Biomolecule Production Core - Propagating BSL4 pathogens	4	N/A	BUMC

Primary Reviewer: Rob Davey	Secondary Reviewer: Nadya Yun
Applicable NIH Guidelines: N/A	
Meeting comments: The PI is adding SARS-CoV-2 and MERS-CoV and has updated procedures to ensure consistency with SOPs. Viruses will be obtained from the BSL-3 suite or directly from the repository supervised by Dr. Corley. Once in the BSL-4, virus does not leave the BSL-4. Work will be performed in BSL-4 containment. The PI is experienced and training of staff is detailed. This is a non-DURC project. Inactivation follows methods validated for BSL-4 pathogens and reported to work against SARS-CoV. Since SARS-CoV and SARS-CoV-2 are related, it is expected with high confidence that the latter will be similarly inactivated. Sharps in the form of glass coverslips are used, these were previously approved for use with Ebola virus. The same safety precautions will be used. The BSL-4 BSO indicated that the PI has addressed all of her comments.	

Motion: Approve	For: 15	Recuse: 1	Against: 0	Abstain: 0	Absent: 0

5. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2356		Testing medical countermeasures against high consequence pathogens in non-human primates	4	4	BUMC

Primary Reviewer: Elke Muhlberger Additional Reviewer: Nadya Yun	Secondary Reviewer: Rao Varada
Applicable NIH Guidelines: N/A	

Meeting comments: NHPs will be used to study SARS-CoV-2.

- Complete the requested DURC questions.
- Briefly describe the planned work with SARS-CoV-2, specifically any differences compared to the BSL4 virus infection models. For example, is there a need to adjust the precautions because this virus causes a respiratory disease and might spread more easily within the BSL4 facility compared to the BSL4 viruses? Will there be differences in the route of infection, e.g. intranasally?
- Add that only inactivation methods will be used that have been approved for BSL-4 viruses.
- Add that BSL-4 inventory control procedures will also be used for SARS-CoV-2 samples.
- SARS-CoV-2 is a positive sense RNA virus whose genome can be used to generate infectious virus by transfecting cells. Describe precautions for handling inactivated samples containing RNA at BSL2 (e.g. restricted access, complete disruption of RNA).
- The virus should be listed as BSL-3 (not BSL-4).
- VIII-check off animal handling/cage changing.
- There is insufficient detail regarding procedure specifics for SARS-CoV-2. Intranasal inoculation would be the likely route of infection. This procedure needs to either be listed in this protocol or the relevant NEIDL SOP cited. The current substance administration SOP that is cited in this protocol does not cover intranasal inoculation.
- Include additional details on disease development in NHPs.

Members were asked if they want to see the protocol next year for annual review, it was noted that the full committee will continue to review all amendments that necessitate full committee review and 3-year renewals.

Motion: Not to review the protocol annually.

For: 16; Against: 0; Abstain: 0

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

6. Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1823		Storage, Propagation and Distribution of Fracisella tularensis; Storage, Propagation and Distribution of Yersinia pestis; Receipt and Storage of the 2019 novel Coronavirus and other coronaviruses	3	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Shannon Benjamin
Applicable NIH Guidelines: N/A	

Meeting comments: The PI is adding clinical samples from patients with SARS-CoV-2. There were no concerns voiced.					
Motion: Approve	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

7. rDNA/Bhz – Annual Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2284		Arbovirus pathogenesis and cellular interactions	3	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Shannon Benjamin				
Applicable NIH Guidelines: Sections III-D-1-b and III-D-2-a					
Meeting comments: No changes were submitted by the PI. • Clarify if A. Gold needs to be added to the protocol. If so, please add.					
Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

8. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2442		Investigating the role of viral proteases in disease pathogenesis	3	N/A	BUMC

Primary Reviewer: Elke Muhlberger	Secondary Reviewer: Shannon Benjamin				
Applicable NIH Guidelines: N/A					
Meeting comments: The protocol includes cell culture work with SARS-CoV-2. It was stated that procedures are well described. The reviewers noted that many of their comments (i.e., related to use of Cavicide, aligning waste handling with SOPs, etc.) have already been addressed by the PI. It was noted that BSL-3 training for the PI and all listed personnel is in progress and that referenced inactivation SOPs have been reviewed by EHS and are being revised. • VII.3: Sample removal: describe decontamination procedures for the tubes and inner surfaces of the transport containers; if there is an applicable BSL-3 SOP, this should be noted. • X, Section A. Hazardous Biological Agents: add iPSC-derived human cell cultures to list. • All personnel need to complete BSL-3 training (before engaging in protocol related activities). Site Assessment: No findings; all BSC certifications are current and BSL-3 training is ongoing. **Motion: Not to review the protocol annually.** For: 16; Against: 0; Abstain: 0					
Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

9. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2443		Investigating host-pathogen interactions regulating the pathogenesis and immunogenicity of BSL-3 viral agents.	3	N/A	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Shannon Benjamin				
Applicable NIH Guidelines: N/A					
Meeting comments: The PI is studying SARS-CoV-2 at BSL-3. No animal or rDNA work is proposed. The protocol proposes to examine interaction of SARS-CoV2 virus with host cells, and the effects of neutralizing Ab's against viral proteins and looking at gene transcription, infecting human and NHP cells. PPE includes use of a PAPR. The BSL-3 BSO indicated that she had many of the same comments for this protocol as 2442, and that the PI has addressed all of her comments. It was noted there should be consistency across protocols to ensure that precautions for handling inactivated samples containing RNA have been described in the protocol; the BSL-3 BSO indicated that it had been recommended to the PI and Dr. Saeed that this language be added and this was done by both PIs. It was remarked that the applicable transport SOP is in DRAFT and that BSL-3 training needs to be completed. • All personnel need to complete BSL-3 training (before engaging in protocol related activities). Site Assessment: No findings; all BSC certifications are current and BSL-3 training is ongoing. **Motion: Not to review the protocol annually.**					

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

10. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
1528		Microchip to Detect Influenza Infection and Type in Nasopharyngeal Swabs Integrated Microfluidic Platform for Detection and Diagnosis of Avian Influenza Portable Low Power Nucleic Acid Extraction Module	2	N/A	CRC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: III-D-2-a, Appendix C-II, Appendix B-II	

Meeting comments: This is a protocol to develop methods to identify virus in swab samples. They are collecting nasopharyngeal swab samples from de-identified patients collected by a collaborator at Boston Children's Hospital. These samples will be sent to the PI (in dry ice) via a courier service and will be opened in the lab by lab personnel wearing proper PPE. Samples will be aliquoted and stored or subjected to RNA extraction using a guanidine thiocyanate buffer and tested for the presence of flu virus, RSV and SARS-CoV-2. They also will use plasmids that code for SARS-CoV-2 genes for the validation of their detection methods. Members discussed that the proposed work does not require BSL-3 containment however, enhanced PPE should be used to keep individuals from touching their face; the proposed work should be done at BSL-2 with special practices of BSL-3.

- Lab procedures section 4a and 4c. Re: RNA extraction with guanidine thiocyanate. "The waste [/chemical supernatants] is [/are] poured into 10% bleach…". Should be amended to indicate that the final bleach concentration will be adjusted so that it is 10%, then allowed to sit for 20-30 min before disposal.
- Section VIII.7- liquid waste: "blood and virion-contaminated waste will be added to container filled with 10% ethanol." Should be either 70% ethanol or bleach at a final concentration of 10%.
- Clarify the lab's sick monitoring protocol, in the event that personnel become exposed and sick.
- Clarify if a kit is used for inactivation.
- Include a sentence in the protocol to indicate that the proposed work will be done at BSL-2 with special practices of BSL-3 (this should also be designated as the highest BSL). EHS can advise re: what practices/PPE should be used and provide training if needed.
- Agent Specific Training is needed; ROHP is the point of contact.

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

11. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2113		Zika virus growth and characterization	2	N/A	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Ron Morales
Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, and III-D-3-a; Appendix B-II-D, and G-II-B-3	

Meeting comments: SARS-CoV-2-infected cells are lysed and subjected to nucleic acid extraction prior to suspension in TE buffer and used at BSL-2.

- Indicate what is used for extraction prior to suspension in TE buffer.
- Revise the title to include proposed work.

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

12. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2397		Host and viral determinants regulating Flaviviridae pathogenesis and immunogenicity.	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Ron Morales				
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-3-a, III-E-1; Appendix-B-II-D, Appendix G-II-B					
Meeting comments: The amendment is to add RV particles pseudotyped with coronavirus spike protein (CoV-S). This protein is a potential target for vaccine and therapeutic development. SARS-CoV, MERS-CoV, and SARS-CoV-2 spike proteins will be expressed as described in the approved protocol for other viral proteins.					
Motion: Approve	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

13. rDNA/Bhz – Amendment

BUA	(PI)	Title	BSL	ABSL	Campus
2355		Material transfer to NEIDL/BUMC New Title: Characterization of cellular proteins cleaved during virus infection	2	N/A	BUMC

Primary Reviewer: Ron Morales	Secondary Reviewer: Tom Winters				
Applicable NIH Guidelines: Section III-D-1-a, III-D-2-a, III-D-3-a, III-E-1					
Meeting comments: The laboratory has been approved to identify and study host proteins targeted for cleavage upon virus infection. The lab has identified several known and novel cellular proteins targeted for cleavage in virus infected cells. One amongst the targeted proteins has previously been shown to have a role in innate immunity against some RNA and DNA viruses. To this end, the lab would like to add BSL-2 human coronavirus (HCoV-NL63). The virus will be used to infect human cells to examine viral kinetics. All viral infections will be performed in a BSC utilizing appropriate PPE. It was noted that 3rd generation lentiviral vectors will be used. • Although it was indicated that viral infections would all be performed in the BSC, N95 respirators should be available and used in the event that there is a need to clean up and disinfect spills outside of the BSC; this should be stated in the protocol. • At the time that the original protocol was reviewed and approved, it was indicated that researcher H. Conway was not experienced with infectious agents and would be trained by the PI; provide the current status of this personnel's training.					
Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

14. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1459		Uremic vascular disease and cancer biology	2	2	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rao Varada				
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-D-4-b, III-E-1; Appendix B-II, G-II-B					
Meeting Comments: The protocol includes two (2) studies focused on vasculogenesis and endothelial cells: 1) studying vascular disease in renal failure; and 2) studying vasculogenesis in cancer. These studies include adding dialysis patient serum to cells in vitro to test vascular response. Lipid transfection or retroviral transduction is used to transfer DNA to cancer cell lines to "modulate signaling". The study also includes a zebrafish model and nude mouse model for colon cancer to look at intestinal cell proliferation and tumors. EHS staff indicated no concerns regarding HHC use. • Clarify where phlebotomy is being done - if it is being done in BMC, indicate if Dr. Sulis has been contacted as requested in the application. • Move the description of manipulations from the biohazards table to the project description (laboratory procedures section). • Update the BSC certification date. • Update the IRB approvals to reflect the addition of urine samples. • Provide the current IACUC approval information. • Liquid waste must be disinfected by adding fresh bleach solution to a final concentration of 10%. Site Assessment: Has a ECP; BSC is certified; and ROHP clearance is needed for a few individuals.					
Motion: Conditional Approval (Administrative Review)	For: 16	Recuse: 0	Against: 0	Abstain: 0	Absent: 0

15. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
785		Molecular and Pharmacological studies of neurodegenerative diseases	2	1+	BUMC

Primary Reviewer: Robin Ingalls	Secondary Reviewer: Rao Varada

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

Meeting Comments: The laboratory is investigating the pathophysiology of neurodegenerative disorders like Alzheimer's disease, Parkinson's disease and Amyotrophic Lateral Sclerosis. These diseases are characterized by clumps of Tau, TDP-43, Synuclein and LRRK2 in the brain. The goal is to develop approaches for reducing Tau, TDP-43, Synuclein and LRRK2 clumps generated in the lab. Lentiviruses or adenoassociated viruses (AAV) that express cDNA or RNAi that modulate expression for TDP-43, tau, synuclein, LRRK2, parkin, PINK1, TIA-1 and other genes linked to neurodegenerative diseases will be used. Fibroblasts, iPSC or microglial cells are transduced with these constructs to identify the cellular changes they induce. Some of these constructs are also used in transgenic animal models to study in vivo effects. Frozen human brain tissue and fixed human brain tissue will be used for gene expression analysis and immunohistochemistry. Cell line expressing tau protein clumps will be subjected to CRISPR-mediated knockdown of cellular proteins to identify the role of cellular protein(s) in protein clumping. It was noted that tau proteins do not cause human disease.

- Clarify if fresh brain donations are from presumed healthy persons or persons with Alzheimer's. The biohazard table states using frozen or fixed brain from brain banks at BU, other academic sites.
- Indicate what precautions are being used for handling fresh human brain.
- A statement should be added to the protocol to clarify if tau proteins can cause human disease.
- Indicate what decontamination procedures are being followed for fresh human brain as well as the engineered Tau, TDP-43, Synuclein and LRRK2.

Site Assessment: Needs to be done, no one was available in the lab to participate.

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

16. rDNA – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
801		Structure and assembly of apoB lipoproteins	1	N/A	CRC

Primary Reviewer: Ed Loechler	Secondary Reviewer: Jim Keeney

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

Meeting Comments: The PI is using non-human cell lines to determine how cellular mechanisms form low density lipoproteins. The goal of the investigation is to produce a protein (baculovirus) from merged commercially available bacteria and inject cell lines in an effort to shed light on how these LDLs are produced. The sources of the lines are identified. It was noted that the PIs training is current and that a BSC does not need to be used, no infectious materials are being used.
Site Assessment: No findings.

Motion: Approve	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

17. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
796		Genetic and biochemical analysis of genes from Arabidopsis thaliana involved in root development and indole-3-acetic acid biosynthesis Cellular and Subcellular Resolution of the Tryptophan-Related Pathways	1-P	N/A	CRC

Primary Reviewer: Ed Loechler Additional Reviewer: Elena Kramer (ad-hoc)	Secondary Reviewer: Ron Morales

Applicable NIH Guidelines: Sections III-D-5 and III-E-2.

Meeting Comments: The goal of this project is to understand how plants regulate their metabolism and growth in response to the environment. Studies focus on genes that synthesize the plant growth regulator, indole-3- acetic acid (IAA) and related defense compounds (e.g., indolic glucosinolates--IGs). The model systems is the plant Arabidopsis thaliana, though bacteria and bakers yeast are also used as heterologous expression systems. The BSO noted no environmental concerns/risks to the environment. • Section VIII, 6. - indicate how sharps (including razor blades and syringe needles) are disposed of. Site Assessment: No findings.

Motion: Conditionally Approve (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

18. Bhz - Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1164		Osteoarthritis Findings Before and After Bariatric Surgery (OABS)	2	N/A	BUMC

Primary Reviewer: Ron Morales	Secondary Reviewer: Valeda Britton

Applicable NIH Guidelines: N/A
Meeting Comments: The lab studies how weight loss may impact knee structure and improve knee pain. The lab is looking at the effects of bariatric surgery and how patients (that have undergone this form of treatment for osteoarthritis) who lose several pounds over a short period of time show improvement in their knee pain. The lab will obtain MRI scans, ultrasounds, and blood and urine tests of individuals before and after bariatric surgery and compare these tests to individuals who are obese who do not have the surgery and do not lose a lot of weight. Blood samples will be drawn from patients in the Phlebotomy room of the Nutrition and Weight Management Center located at the Preston Family Building by clinical phlebotomists and transferred to the laboratory at Evans using appropriate leak-proof containers. Samples are centrifuged, aliquoted and stored in the -80 freezer. Urine samples are collected in the bathrooms located at the Nutrition and Weight Management Center on the 1st floor of the Preston building. Urine samples are transported via a closed, leak proof, shatter proof container to the Laboratory in Evans 535 where they are aliquoted and stored in a -80 centigrade freezer for future use. Lab personnel will wear lab coats, disposable gloves, and safety glasses. • The PIs ROHP clearance needs to be updated and he needs to complete the BBP training. • Ensure that current related IRB information is included. • Check the centrifugation box in Section VIII. • Discarding of leftover urine samples: should discard all leftover samples in a container and add bleach to a final concentration of 10% and let stand for 30 minutes, discard down the sink with a final rinse by opening the faucet for final disposal. • If sample collection is no longer occurring, remove from the protocol. Site Assessment: It was noted that no sample collection is occurring at this time; and there is no ECP.

Motion: Conditionally Approve (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

19. Bhz - Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
658		Center for Biomedical Mass Spectrometry; Methods for determination of glycoprotein glycosylation similarities among disease states (R01GM133963); Legacy Support During Closure of the Mass Spectrometry Resource for Biology and Medicine (R24GM134210); High-Throughput De Novo Glycan Sequencing (R01GM132675)	2	N/A	BUMC

Primary Reviewer: Inna Afasizheva	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: N/A
Meeting Comments: This protocol aims to determine changes in the protein, glycoprotein, proteoglycan or lipid composition in biological specimens during disease development. The PI uses a variety of human tissue and blood

samples. Human cell lines will be received from tissue banks and collaborators. Procedures are well written and provide information about sample preparation for MS and MS imaging. Extracted proteins, glycoproteins, carbohydrates and lipids will be analyzed by mass spectroscopy (MS) and MS imaging.

- Manipulations of potentially infectious materials (including human blood and tissues) require BSL-2 practices, use of a BSC is not indicated consistently throughout, this should be reconciled.
- Provide references for the method of inactivation of infectious materials with 0.5% Triton X-100.
- Provide procedures and references for using detergent for inactivation of Influenza A virus.
- Clarify that bleach will be added to a final concentration of 10%.
- Mark N/A as the highest animal biosafety level.
- Specify the sources of human tissue.
- Ensure that training is current for all listed personnel (Laboratory Safety Training and/or BSL-1/2 appears to be expired for some).
- Ensure that all personnel listed have current ROHP clearance (appears to be out of date for some).
- Check the last box of the Agreement Policy.

Site Assessment: Lab is updating the ECP; engineering controls are in place; and ROHP clearance not current for some.

Motion: Conditionally Approve (Primary Reviewer Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

20. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1125		The Role of Interferon Regulatory Factor 5 in the Pathogenesis of SLE	2	1	BUMC

Primary Reviewer: Inna Afasizheva | Secondary Reviewer: Rao Varada

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

Meeting Comments: This study focuses on the role of over-expression of the IRF5 transcription factor responsible for interferon regulation in mammalian immune cells. It has been shown that increased levels of IRF5 expression are linked to developing of SLE (Lupus disorder). The PI uses mice and mouse and human cell lines overexpressing or lacking IRF5 and mice and cell lines expressing different human isoforms of the IRF5. An adenoviral replication-deficient system is used to introduce IRF5 or deletion mutants to perpetual macrophage, and dendritic cell lines derived from mice and human or primary cells is used. A lentiviral system is used to generate IRF5 and introduce to mice overexpression constructs. It was noted that that there will be no injection of constructs into animals and that the use of ethanol as a disinfectant can remain in the protocol.

- A. Pellerin and R. Bonegio need to complete the rDNA/IBC Policy training.
- Shoe covers and head covers should be checked (VIII.4).
- Bleach should be used to a final concentration of 10% for 30 minutes.

Site Assessment: ECP is in place; the BSC is certified; and ROHP clearance needs to be updated for some personnel.

Motion: Conditionally Approve (Administrative Review)	For: 15	Recuse: 0	Against: 0	Abstain: 0	Absent: 1

21. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
603		Characterization of drug delivery from biomaterials and bioconjugates	2	2	CRC

Primary Reviewer: Rob Davey | Secondary Reviewer: Rao Varada

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

Meeting comments: Drug delivery methods using nano-particulate material will be studied. The PI has over ten (10) years of experience with mammalian culture work. Human cell lines are cultivated (therefore BSL-2) and then treated with different types of material. Uptake and viability will be monitored. Materials used for treatment are composites of biologically compatible polymers and drugs. Drugs include paclitaxel, eupenifeldin, or verticillin A incorporated within the nanoparticles, SN-38 (an irinotecan derivative) incorporated within the films and meshes, and mertansine, a microtubule inhibitor, conjugated to the antibody. Recombinant work will involve treatment of cells with shRNA or CRISPR guide RNA encoding lentiviruses to block expression of cell proteins. Targets are YAP1 (cancer growth), AXIN2

(knockout can induce cell growth), CTNNB1 (metastasis), LATS2 (tumor suppressor), and human alpha synuclein and synapsin (vesicle trafficking). While each could be found dysregulated in cancers, each alone is unlikely to induce a cancer state and so each has low associated risk if personnel are exposed. Bleach will be used to a final concentration of 10 % and sharps are disposed of in a sharps container. Adeno-associated virus, which is of a low risk (not replication competent) will be used. It was noted that nanoparticles are administered to animals via the tail vein and that animal work is covered by an IACUC approved protocol. Members discussed that more information is needed on the animal work to complete a risk assessment.

- For Mattes and Kirsch indicate if these individuals have specific training in recombinant techniques or with infectious agents. If not, indicate if training/mentoring will be provided.
- Provide a more detailed description of recombinant work.
- Indicate use of adeno-associated virus in the laboratory procedures section.
- Lentivirus use is indicated but generation is unclear, use of a 3rd generation system is preferable.
- Additional details of the animal work are needed.

Site Assessment: A ECP is in place; the BSC is certified; and ROHP clearance for some personnel needs to be updated.

Motion: Conditionally Approve (Secondary Reviewer Review)	For: 14	Recuse: 0	Against: 0	Abstain: 0	Absent: 2

22. rDNA/Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2437		Relaxin-2 as a treatment for hypertrophic and keloid scar formation	2	1	CRC

Primary Reviewer: Rob Davey	Secondary Reviewer: Rao Varada

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

Meeting comments: Cell lines treated with pro-fibrosis/inflammatory cytokines such as TGF-beta as well as relaxin-2 (and insulin like peptide hormone) are studied in order to examine impact on treatment of scar tissue. Use of a biologically degradable hydrogel as delivery of relaxin-2 to animals will also be used. The PI is experienced in mammalian culture work and other listed personnel have appropriate related cell culture experience. Bola-bis urea (BBU) and glycosyl nucleoside fluorinated (GNF) amphiphiles are used to make hydrogels. Relaxin-2 is produced recombinantly using transfection of cells with encoding plasmids; there is little risk associated with this plasmid if personnel are exposed. Disinfectant use (bleach) is appropriate, sharps will be disposed of in sharps containers, and PPE is appropriate.

Site Assessment: ECP is in place; the BSC and fume hood are certified; and PIs ROHP clearance needs to be updated.

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

23. rDNA/Bhz - Three-Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
934		Orthopaedic Research; Role of Pro-inflammatory Cytokines in Fracture Repair; Mechanism(s) of Obesity-Related Osteoporosis in the Absence of Insulin Resistance; Role of Angiogenesis in Distraction Osteogenesis	2	1	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Susanna Kurnick

Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, III-E-1, III-E-3; Appendix B-II, G-II-B

Meeting comments: The Orthopedic Research laboratory focuses on various aspects of the molecular and genetic mechanisms that control bone healing after either surgery or trauma. Mice and cell lines will be used and the human serum proteome after fracture will be studied. Researchers will collect human femoral heads, bone chips and marrow from joint replacements with the objective of correlating the bone cell transcriptomes to the genome to establish candidate genes associated GWAS of osteoporosis. Defective lentivirus constructs to introduce shRNA or specific cDNAs into cells and then ex vivo into mouse tissues is done. It was noted that BMC's Epidemiologist had no concerns related to infection control.

- It is indicated that "Lentivirus vector stocks generated with packaging systems devoid of the HIV envelope gene will be tested for RCV by serial transfer in a competent cell line and ELISA assay for p24 antigen prior to approval for use at BSL-1 and ABSL-1". Clarify if this is a different lentivirus and what RCV is.
- Update the BSC certification date.
- Liquid waste: final concentration of bleach should be 10 %.
- It is indicated that "environmental safety will remove as chemical waste" clarify if this should read biohazard waste.
- Reconcile ABSLs and BSLs throughout; this information is inconsistent.
- VIII- if animals are treated with tamoxifen, check off animal handling/cage changing.
- Provide the current IACUC protocol number(s).
- Tamoxifen is on the BU highly hazardous chemical list - check off in section IX; Tamoxifen treated animals should be ABSL-2.

Site Assessment: The BSC is certified and personnel training is current.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

24. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1729		Role of protein ubiquitination in angiogenesis	2	2	BUMC

Primary Reviewer: Barbara Slack | Secondary Reviewer: Susanna Kurnick

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

Meeting Comments: This protocol is designed to study genes that regulate angiogenesis and tumor growth, mainly VGEF and its transmembrane type receptors and three (3) novel genes that they characterize. Primarily human cultured cell lines and tumor cell lines (where they overexpress genes via retroviral vectors or downregulate expression by siRNA expression or by CRISPR technology) are used. They extract protein and RNAs and run standard assays for migration, adhesion, proliferation and survival. It was noted that no animal work is described, and it needs to be clarified if animal work is being done.

- Check 3-year resubmittal (not annual renewal).
- Provide title and role for R. Ho and a description of experience for Ho and Rahimi.
- Edit the final sentence of Project description (Section VII.2) as a few words appear to be missing. If animal work will be done, provide a brief description of the proposed animal work (ABSL-2) in this section.
- Provide a brief description of how lentiviral and retroviral vectors will be used, and the viral packaging method used (e.g. which generation of packaging system will be used for lentiviral vectors).
- Section VIII.1-check plating/colony counting (bacterial transformations) and pipetting infectious material (viral vectors/particles).
- Section VIII.7- Liquid wastes: specify that liquid waste will sit for 30 minutes after adding bleach to a final concentration of 10% before being disposed of down the sink.
- Section A (Hazardous Biological Agents) should include retroviral and lentiviral vectors.
- Section H. rDNA table: Remove E. coli strains from Eukaryotic host list. Table should include the commercial source and type of the packaging systems to be used. The Animal Experiments section of the rDNA table lists angiogenesis, wound, and tumor assays under "host" but provides no information about vectors or donors. Please provide this information, along with an updated IACUC approval number. (Approval date listed is 9/30/2013).

Site Assessment: ECP is in place; BSC is certified; and personnel training is current.

Motion: Conditional Approval (Administrative review if no animal work)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

25. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
2162		Transcriptomic Studies of Smoking-related lung disease -2016	2	N/A	BUMC

Primary Reviewer: Carmela Abraham	Secondary Reviewer: Jim Keeney
Applicable NIH Guidelines: N/A	

Meeting comments: This protocol includes local recruitment at BUMC of subjects who are thought to have lung cancer or have been exposed to various tobacco products. Collected biospecimens will be profiled for gene expression for the effects of tobacco exposure and cancer on the airway epithelium. These gene expression profiles can be used as biomarkers for early detection of lung cancer and provide insight into how the body responds to being exposed to various tobacco products. Additionally, samples are received from collaborators to profile gene expression in airway specimens from patients that are exposed to various toxins (e.g. tobacco smoke, diesel exhaust) and/or have lung disease (e.g. COPD and lung cancer). The goal is to develop gene expression profiles that can be used as biomarkers for early detection and diagnosis of lung diseases and to provide insight into how the airway responds to various exposures. Further, the aim is to identify molecular targets for potential therapeutics.

- Indicate how blood samples are treated and if serum or plasma is prepared before aliquoting.
- Update the BSC certification date.
- Bleach should be to a final concentration of 10%.
- Provide current IRB information.
- If samples are coming from BMC, provide the requested information regarding communication with Dr. Sulis.
- Clarify whether aerosols will be produced and if so, what engineering controls (i.e., PPE) are in place.
- Clarify source (who the collaborators are) that will be providing samples.

Site Assessment: An ECP is in place; the BSC and the fume hood have been certified; and a few personnel need to update their ROHP clearance.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

26. rDNA/Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
1013		GABA-A receptor subunit regulation and epileptogenesis; Mapping the Transcriptome of Age-Related Hippocampal Trisynaptic Circuit; Dysfunction in a Rat Model for Alzheimer's Disease; Does REST make you resilient?	2	2	BUMC

Primary Reviewer: Barbara Slack	Secondary Reviewer: Susanna Kurnick
Applicable NIH Guidelines: Sections III-D-1-a, III-D-2-a, and III-D-4-b, III-E-1; Appendix G-II-B, Appendix M	

Meeting comments: This group is investigating GABA receptor expression, a rescue model of epilepsy, and the role of various neurotransmitters in developmental disorders such as autism. They use murine cell cultures and make lentivirus constructs, which they send to collaborators at UPenn for packaging using a 3rd generation system, they also receive AAV vectors from them. They inject these vectors into in vitro cell cultures and rodent brains under ABSL-2 conditions using snorkel for ventilation. In some experiments they also electroporate expression plasmids or shRNA constructs of interest in mouse embryos to investigate the role of GABA receptors in disease. It was noted that a snorkel is used to protect personnel.

- Ensure that training and ROHP clearance are current for all personnel.
  Update or remove the biosafety cabinet certification date (expired) from the laboratory procedures section.
  Section VIII.1- check culture stirrers/shakers (bacterial cultures will be used).
- Section VIII.5- update BSC certification date (says 2016).
- Section VIII.6- indicate how sharps will be disposed of.
- Section VIII.11- viruses are transported in lucite box as secondary containment. A plastic shatterproof and leakproof (i.e. with snap on lid) container would be preferable for secondary containment.
- Check the Live Animal Use box in Material Used in Research section.
- rDNA table-Animal experiments-list should include experiments involving lentiviral injection into brains of adult rodents.
- The IACUC protocol number provided in the lab procedures section is different than the one provided in rDNA table; reconcile and update with the current protocol number.
- Section VIII.1. – check off animal handling;

• Section VIII.2. – check off "other" and indicate use of a snorkel. • IX – indicate use of live animals. Site Assessment: ECP is in place; ROHP clearance is not current for some personnel but training is complete; and the BSC and fume hood are certified.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

27. Bhz – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
581		Movement Disorder Studies & Stroke Prevention Studies	2	N/A	BUMC
Primary Reviewer: Carmela Abraham		Secondary Reviewer: Valeda Britton			
Applicable NIH Guidelines: N/A					
Meeting Comments: Clinical neurological studies for Parkinson, Huntington's and Multiple System Atrophy will be conducted. Serum, plasma, CSF and urine will be collected. • Ensure that training and ROHP clearance is current for all personnel. • Clarify if room should be added to the protocol and if so, add. Site Assessment: Need to develop a ECP and update ROHP clearance for some personnel.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

28. rDNA – Three Year Renewal

BUA	(PI)	Title	BSL	ABSL	Campus
826		Use of expression plasmids for protein production and site-directed mutagenesis	1	N/A	CRC
Primary Reviewer: Elke Muhlberger		Secondary Reviewer: Ron Morales			
Applicable NIH Guidelines: Section III-F-6, Appendix B-I					
Meeting Comments: This group is interested in the study of phosphotransferase proteins and their enzymatic activities. They express these proteins or their mutants in E. coli. They then purify these proteins from bacteria and analyze their activities. • BSL-1 should be indicated as the BSL throughout. • K. Allen needs to compelte BSL-1/2 Training and Chemical Safety Training. • Demaria, Muellers, Rebelo and Allen need to update their ROHP clearance. • Section VIII, #6, p13 – disposable sharps containers must not be autoclaved (the container will melt) and must be disposed of directly into biohazardous boxes when ¾ filled. Site Assessment: The PI has been notified about the required ROHP clearance updates.					
Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

29. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2435		Microbial-Immune Interaction in Children with Obstructive Sleep Apnea	2	N/A	BUMC
Primary Reviewer: Tom Winters		Secondary Reviewer: Bob Timmerman			
Applicable NIH Guidelines: N/A					
Meeting Comments: This protocol proposes to investigate the relationship between the oral microbiome and oral inflammatory response in children with Obstructive Sleep Apnea (OSA) compared to healthy controls. Plaque is collected via oral curette; saliva is collected via spitting and sent to an outside lab for processing. Case sample collection occurs at Boston Children's and control collection at BMC. Samples collected at Boston Children's are sent to BU's GSDM orthodontics department. BSL-2 materials are stored in a BSL-2 lab, plaque is shipped to Forsyth Institute, and saliva will be frozen at BMC. Disinfectant is adequate. Discussion with BMC's hospital epidemiologist to use clinical spaces for sample collection is pending. In response to a concern about the availability of appropriate PPE needed to conduct this research (due to the SARS-CoV-2 outbreak), it was indicated that a statement will be added to					

all IBC approval letters indicating that conduct of all research is subject to all applicable BU policies and procedures, including current (and developing) University directives related to the SARS-CoV-2 outbreak. This language will be shared with the IBC for comment following the meeting.

- It appears that samples will be shipped, indicate who will be shipping samples and ensure they have completed shipping training.
- Ensure all personnel have current ROHP clearance.
- Provide requested information in the application for consultation with Dr. Sulis, BMC's Epidemiologist.

Site Assessment: Chemical safety training for one (1) personnel is due; someone needs to complete shipping training; EHS suggested the PI to purchase a leak-proof secondary container for the transport of samples from the clinic to the lab; and ROHP clearance is due for all personnel.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

30. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2433		A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase II Study to Evaluate Efficacy and Safety of VQW-765 in Patients with Social Anxiety Disorder (SAD)	2	N/A	CRC

Primary Reviewer: Tom Winters	Secondary Reviewer: Bob Timmerman

Applicable NIH Guidelines: N/A

Meeting Comments: The goal is to look at use of new drug (VQW-765) on changes in anxiety and distress during a social stress task. Blood and urine samples will be taken at follow up visits, stored and shipped. It was noted that the study is low risk.

- Detail the PIs experience.
- Ensure all personnel have completed required training (several have not completed BSL-1/2 Training) including shipping training for personnel who will be shipping samples.
- Ensure all personnel have been cleared by ROHP.
- Indicate who will be drawing blood and their qualifications to do so.

Site Assessment: No findings, shipping training is current.

Motion: Conditional Approval (Administrative Review)	For: 13	Recuse: 0	Against: 0	Abstain: 0	Absent: 3

31. Bhz – New Protocol

BUA	(PI)	Title	BSL	ABSL	Campus
2436		The Role of the Gut Microbiome in Anxiety Disorders	2	N/A	CRC

Primary Reviewer: Tom Winters	Secondary Reviewer: Jim Keeney

Applicable NIH Guidelines: N/A

Meeting Comments: This protocol investigates gut microbiota for adults being treated for anxiety disorders. Biologic samples include saliva and stool collected before and after treatment. Samples will be self-collected at home and brought to the Center for Anxiety and Related Disorders (CARD) for storage in a freezer.

- Clarify the biosafety level of the lab space where samples will be stored.
- Provide details on testing procedures (i.e., what will be sent out vs. processed on campus).
- Ensure that training is complete for all listed personnel.
- Indicate how long surfaces will be treated with 10% bleach for disinfection purposes.
- Provide additional details on the safe packaging and transport of samples including any instructions provided to participants.

Site Assessment: Training is complete including shipping training.

Motion: Conditional Approval (Primary and Secondary Member Review)	For: 11	Recuse: 0	Against: 2	Abstain: 0	Absent: 3