This meeting is open to the public.

Present:

Members: D. Stearns-Kurosawa (Chair), R. Ingalls (Vice-Chair) (Arrived 12:12 PM), R. Morales, J. Barton, P. R. Varada (Left 1:30 PM), E. Sawyer, I. Afasizheva, E. Loechler (By phone; Left 1:30 PM), T. Winters, C. Sulis, R. Georgiadis (By phone), V. Britton, J. Keeney, R. Timmerman, J. Gonsalves.

Guests: P. Urich, M. Auerbach, A. Lowe, N. Dey, D. Banh.

Staff: S. Ghosh, C. Williams, J. Hutchinson.

Absent:

Members: K. Tuohey, B. Slack, E. Muhlberger.

I. Review of October Meeting Minutes

Motion: Approve
For: 13
Against: 0
Abstain: 1

II. New Business

A. Introductions:

Jenny Hutchinson was introduced as the new Assistant Director for Research Integrity. She is responsible for management and oversight of the Safety Committee Program, which includes the IBC, Laboratory Safety Committee, Radiation Safety Committee, and the Scientific Diving and Small Boat Safety Committee.

B. IBC Training Session:

Overview of BSL-4 Biosafety Manual (A. Lowe)

Andre Lowe, Associate Director of Research Safety, National Emerging Infectious Disease Laboratories presented on the changes made to the BSL-4 Biosafety Manual as part of the 2017 update.

C. Policy Review:

Review of BSL-4 Biosafety Manual (M. Auerbach)

The BSL-4 BSM was distributed to the IBC for review and comment. Feedback received was reviewed by A. Lowe and incorporated.

Motion: Approve the 2017 BSL-4 BSM
For: 15
Against: 0
Abstain: 0

D. Chair’s Report (D. Stearns-Kurosawa):
None.

E. Safety Committees Report:
Approved Applications/Amendments (S. Ghosh)

Since the October IBC meeting, 3 new applications, 7 three-year renewals, 15 amendments and
18 annual renewals have been approved.

At the October meeting Dr. Dow's protocol was conditionally approved. Modifications required
to secure approval were identified and given the nature of the recombinant DNA work involving
plants, ad hoc review by a plant recombinant DNA research expert was requested. Dr. Elena
Kramer, Chair, Department of Organismic and Evolutionary Biology at Harvard University
reviewed the protocol and indicated that the protocol sufficiently addresses risks associated with
the proposed work, no changes were recommended. Her comments were shared with the
reviewers. The PI has satisfactorily addressed all comments and the protocol was approved.

F. Biosafety Report:

1. Research Occupational Health Program (ROHP) Incident Report

On November 8, 2017 an animal care worker was bit by an ABSL1 rat on her left ring finger
through one pair of gloves as she was closing the top of a wire cage. She immediately washed
then applied alcohol to the site, and was further evaluated by ROHP. The staff was given an
updated Tdap vaccination and provided a prophylactic antibiotic. She was seen again by ROHP
and is doing well and has no sign or symptom of infection. Clarification was requested and
provided by the lab that although the lab is engaged in working with adeno-associated viral
(AAV) vectors, this animal had not been exposed to AAV.

2. Environmental Health & Safety (EHS) Update

EHSs investigation into the 11/8/17 incident identified the root cause to be lack of personal
protective equipment. To prevent recurrence, the individual has been advised to wear heavy-
duty ‘gauntlet’ gloves when handling rats and conducting rat cage-changes.

III. Protocol Review:

A. New Applications

1. rDNA/Biohazard (Bhz)
   Principal Investigator (PI):
   Biological Use Authorization (BUA) Tracking ID #: 2277
   Title: Gene circuitry for human diseases
   Primary Reviewer: Edward Loechler
   Secondary Reviewer: Bob Timmerman
   Biosafety Level: BSL2
   Animal Biosafety Level: N/A
   Campus: CRC
   Applicable NIH Guidelines: Section III-D-2, III-D-3, III-E-1
   Protocol Expires: New application
   Layman’s Description: We are interested in finding gene regularity systems involves in disease
   states like Type 2 diabetes and how they are different than healthy individuals. Which genetic
   factors involves in disease states is the main question of our project. Outcome of these projects
   may lead to find gene circuitry specific drug development etc.

Meeting Comments:
The PI is interested in finding alterations in gene-regulation in various diseases, including comparison to healthy individuals. A systematic genome-wide characterization of gene expression changes at single cell resolution is planned using primary human cells obtained from those disease states. New technologies such as the massively parallel single cell RNA-seq approach will be used to elucidate modifications in gene expression in a cell. In particular, gene perturbation screens will be undertaken using Perturb-seq (a CRISPR based single cell RNA-seq technique) to understand the physiological state of a cell. The ultimate goal is to find new molecular markers and novel therapeutic targets for disease states. The committee noted that some sections were incomplete and unclear and thus, in need of revision. It was also noted that the source of human tissues and blood samples needs clarification, as does the need for IRB review and approval. The committee recommended that the IBC Office work directly with the PI to address the below changes/clarifications.

**Changes/Clarifications Required:**
- **Overview and Grant Funding Information:** Please upload your (Dr. Cheng) CV.
- **Personnel Information:** Please add yourself (the PI) in the personnel list and answer all associated questions.
- **Research Project Description:** Please check the text thoroughly for typos, incomplete and difficult to understand sentences.
- Q3- Please describe clearly what are the actual sources of various patient or volunteer samples. Please provide a more descriptive rationale why IRB approval is not required for any of these human samples.
- How are these human samples being brought to the laboratory and what safety measures are in place for their handling?
- Human brain samples require further safe handling practices for possible prion contamination. Please elaborate how those issues are dealt with.
- Provide more description of what is meant by phenotypes of cells will be determined by CRISPR technology (scientifically).
- Please provide a brief statement that you will be doing recombinant DNA work, transformation and plasmid preparations.
- Please correct the two sentences in the “Lentivirus” sub-section: ‘...These are 3rd generation system with highest...because all vectors are in separate plasmids.... Also, viral proteins that are viral replication are present in vectors’.
- **PPE and SE:** Q3- Add some form of eye protection in the list.
- Q5- Biosafety Cabinet is required for your work. Please complete this section. Your BSC was last certified on 7/31/2017.
- **Hazardous Biological Agent (Section A):** Please add lentiviruses in this list. If Adult Human Brain Tissue and Peripheral Blood Mononuclear cells are all primary human materials, they should go in Section B only.
- **Other Potentially Infectious Material (Section B):** List here all primary human materials to be used in the study. Provide appropriate IRB information.
- **Recombinant DNA (Section H):** The prokaryotic experiments section also needs to be completed as you very likely will be growing plasmids for your transfection work.
- **Lab Safety Training (LST):** Lab safety training for the PI and John Cleary are not current.
- **BUA Site Assessment:** Approved. A BSC is available and was last certified on 7/31/17.
- **Recommendation:** Conditional Approval (Administrative Review)
- **For:** 15
- **Against:** 0
- **Abstain:** 0

2. **rDNA/Bhz**
   - **PI:**
   - **BUA Tracking ID:** 2243
   - **Title:** Gene circuitry for HIV
   - **Primary Reviewer:** Robin Ingalls
   - **Secondary Reviewer:** Jim Keeney
   - **Biosafety Level:** BSL2
Animal Biosafety Level: N/A
Campus: CRC
Applicable NIH Guidelines: Section III-D-2, III-D-3

Protocol Expires: New Application

Layman’s Description: It is known that substance addiction patients can be more easily infected by HIV virus than normal people. In this study, we want to examine genetic factors involved in HIV infection in substance addiction patients. We want to know which genes are different between substance addiction patients and other individuals during infection of HIV.

Meeting Comments:
The focus of this study is to investigate if higher susceptibility of opioid-addicted individuals to HIV infection is linked to altered gene expression in this group of individuals. The lab will infect PBMCs from opioid-addicted individuals and normal healthy individuals and compare expression of genes involved in HIV infection. Massively parallel single-cell RNA sequencing will be used for this purpose. They also plan to use the CRISPR-Lentivirus vector to determine phenotype of cells. It also appears that HIV patient PBMC will be used in some experiments. The committee identified that numerous major changes or clarifications are required to conduct a thorough review. Including but not limited to lack of information on experience with live HIV work for the PI and other members of the protocol, IRB information on PBMCs from HIV-infected patients, clarification on the nature of CRISPR work using lentiviral vectors.

Changes/Clarifications Required:
Correction, elaboration or clarification is required for each of the sections indicated below:
Personnel Information: Please add yourself (the PI) in the personnel list and answer all associated questions.
Since the protocol describes work with live HIV, experience with HIV research for the PI and all other personnel listed MUST be clearly stated in the “State how many years experience, when and where” question.
Research Project Description: Q2- Please elaborate further the scientific objectives of the protocol. The current description is too broad and lacks clarity and sentence construction, making it difficult to understand (especially the 2nd line). It was not clear what characteristics of the coding genes will be ascertained by single cell RNA sequencing. Further, elaboration needed on how CRISPR/Cas9 technique will be used to determine cell phenotype.
Q3- Please check typos (‘HIV-LUC or HIVGFP with lack envelope’).
Please clarify the source of replication competent HIV strains. Are you going to transfec HXB2 or HIV-LAI full-length plasmids in HEK 293 cells to get virus supernatant or are you getting the virus supernatant for other sources? How much virus you will be growing at a time? Are you concentrating them for your infection work? Does everyone have experience with HIV work? If not, who will train them?
HIV patient PBMCs will be used in the protocol – are these samples that are already in the PIs laboratory or will there be ongoing shipment of samples from the collaborator Dr Lancioni? If it is the latter, then do you have appropriate IRB approval?
The phrase “Biohazard hood” should be replaced by “biosafety cabinet”.
The project description section only states: 3rd generation lentivirus will be used in CRISPR on PBMC cells to find phenotypes of cells.
PPE and SE: Q3- Check Eye protection. Depending on extent of work with live HIV, other forms of protection may be necessary.
Q5- Biosafety Cabinet (BSC) is required for your work. Please complete this section. Your BSC was last certified on 7/31/2017.
Materials Used in Research: Please check the ‘Other Potentially Infectious Materials’ box.
Hazardous Biological Agent (Section A): HIV-HXB2 and HIV-LAI should be included in this list.
Other Potentially Infectious Material (Section B): Please include HIV patient PBMC in this list and provide IRB information.
Recombinant DNA (Section H): Please complete the donor source in the Prokaryotic Experiments section.
NIH guidelines section for your application should also include and III-E-1 (for viral vectors).
Please NOTE that Dr. Cheng needs to renew BSL1/2 and blood borne pathogen (BBP) training and John needs to renew BBP training.

Lab Safety Training (LST): Lab safety training for the PI and John Cleary are not current.

BUA Site Assessment: Approved.

Recommendation: Deferred.

For: 13
Against: 0
Abstain: 0

3. Bhz  
Title: Role of cigarette smoking, opioid use, and hepatitis C on placental-amniotic function
Primary Reviewer: Robin Ingalls
Secondary Reviewer: John Gonsalves
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: BUMC
Applicable NIH Guidelines: N/A
Protocol Expires: New Application

Layman’s Description: The goal of this project is to understand how maternal cigarette smoking, hepatitis C and opioid use during pregnancy leads to poor fetal growth. Dysregulation of growth factors in the placenta and in the amniotic fluid of smoking mothers may limit lung and brain development. In human studies, we will study how cigarette smoking and maternal opioid use changes the gene and protein expression of the Wnt signaling pathway and other important signaling families in the placenta, amnion and amniotic fluid.

Meeting Comments:
The PI is interested in the effect of cigarette smoking, opioid drug use or hepatitis C infection on the human fetus development. Their working hypothesis is that smoking, drug-addiction or virus infection dysregulate activities of growth factor/s leading to poor development of lung or brain.
The PI proposes to collect cord blood and placenta from opioid-exposed and non-opioid exposed mothers and will analyze expression of opiate receptors in them by immunoblotting and quantitative PCR. The lab will also compare markers of inflammation and drug levels in the amniotic fluid and amniotic membranes from similar study participants collected in the delivery room. The lab will also test the effect of inhibition of Wnt signaling on the proliferation, differentiation and senescence of pluripotent human amniotic epithelial cells and correlate the data with the smoking or addiction status of the participants. Although the protocol objectives and laboratory procedures are well described, the committee indicated that there is insufficient information about how the placenta, cord blood and amniotic fluids are being collected and it is unclear whether the referenced IRB protocol covers all pertinent activities including parental consent.

Changes/Clarifications Required:
Research Project Description: Q3- It is not clear from the laboratory procedure description what is the source of cord blood, placenta, amniotic fluid and amniotic membranes. Please provide appropriate information and describe who are involved in collecting those samples and bringing them to the lab.
Provide IRB approval information for the collection of these material and state briefly the required parental consent necessary for the collection of such materials.
HTR8 cells are listed in the biohazard materials table but their use is not detailed in the scientific project description or in the laboratory procedure section.
PPE and SE: Q3- Do you use all of the checked PPEs in your work? If not, please check only those that you actually use during your work.

Q5- Please update the biosafety cabinet (BSC) certification date. Yours was last certified on 3/31/17.

Materials Used in Research: Please contact Hospital Epidemiologist Dr. Carol Sulis (at 617-414-5037 or csulis@bu.edu) to clarify how hair follicle or oral mucosa samples are being collected safely in the clinic. Please include the date of this communication in your application.

Hazardous Biological Agent (Section A): HTR8 cells do not require an IRB.

Lab Safety Training (LST): Lab safety training is current for the PI (only member in the protocol).

BUA Site Assessment: Approved.

Recommendation: Conditional Approval (Primary and Secondary Member Review)

For: 13
Against: 0
Abstain: 0

4. Bhz

PI:

BUA Tracking ID: 1851

Title: SA1 as a biomarker for early colon carcinogenesis in premalignant mucosa Stem Cells and CRC: Intestinal organoid modeling for field Carcinogenesis

Primary Reviewer: Rosina Georgiadis
Secondary Reviewer: Bob Timmerman

Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: BUMC

Applicable NIH Guidelines: N/A

Protocol Expires: New Application

Layman’s Description: The goal of this experiment is to explore if SA1 can be used as marker and potential driver in colon cancer. Emerging evidence suggests that there are gender and racial differences in the risk of certain types of colon cancer however the molecular underpinnings are unclear. Epidemiological data suggest that African Americans tend to develop tumors in the right side of the colon, where these lesion possess a distinct evolution and phenotype vs left sided CRCs, suggesting that it is biological plausible to have race-specific genetic variations that may increase cancer risk. Our work suggests that the protein SA1 may be a tumor suppressor and an important marker in colon cancer risk/development. Our data have shown that African Americans have a lower expression of SA1 compared to Caucasians. We want to further look into the differences of SA1 in African Americans compared to Caucasians. We will assess these differences through Single nucleotide polymorphism (SNP) studies in biopsies from our patients at BMC undergoing screening colonoscopies as well as established carcinomas from Boston University Archive Specimen Center (BARC). We would also like to study the biological processes that might explain these race and gender based differences in colon cancer risk/development by growing colon cells from patients in cell culture as well as using immortalized cancer cells.

Meeting Comments:
The PI is interested in exploring the possibility of using a distinct epidemiological finding to design a potential biomarker for colorectal cancer screening and treatment. Contrary to Caucasians, African Americans tend to develop tumors in the right side of the colon. The lab discovered that a protein known as SA1, is expressed at a lower level in African American colorectal cancer patients. The lab proposes to investigate SA1 expression and its association with colorectal cancer incidence, and whether SA1 is a real tumor suppressor and can be used as a potential marker for colorectal cancer identification, especially in relation to race. Further, they will isolate colonic stem cells from patient biopsies to develop organoid culture and use them to test chemotherapeutic potential of select chemicals. This is a simple and straightforward application requiring only minor clarifications on the source of rectal biopsy samples and a few other minor issues listed below.

Changes/Clarifications Required:
Personnel Information: Please answer the “rDNA/Infectious Agent/Select Agents” question for Dr. Roy. Please address who will train Mart in the question “State how many years experience, when and where”.

Research Project Description: Q1- Please limit the Lay description to 3-4 sentences avoiding any technical jargon. Explain acronyms at their first use (Such as SA1).

PPE and SE: Q5- Update BSC certification date (should be 11/31/2016).

Materials Used in Research: Please select the highest biosafety level of this protocol to be BSL-2. Please select the highest animal biosafety level for your work (should be N/A).

Please contact Hospital Epidemiologist Dr. Carol Sulis (at 617-414-5037 or csulis@bu.edu) to clarify how rectal biopsy samples are being collected safely in the clinic and are being brought to the lab. Please include the date of this communication in your application.

Other Potentially Infectious Material [Section B]: Please indicate the expiration date for the IRB approval H-34583 (should be 7/10/2018).

Lab Safety Training (LST): Lab safety training for all members is current.

BUA Site Assessment: Approved. BSC last certified on 11/31/16.

Recommendation: Conditional Approval (Administrative Review)

For: 13
Against: 0
Abstain: 0

5. rDNA/Bhz

PI: BUA Tracking ID: 2278

Title: Empirical and computational analyses of striatal MSNs and FSIs and of LS CPNs in the Q175 and DN17 models

Primary Reviewer: Inna Afasizheva
Secondary Reviewer: Rao Varada

Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1

Campus: BUMC

Applicable NIH Guidelines: Section III-E-1

Protocol Expires: New Application

Layman’s Description: This project characterizes the structure and function of nerve cells in a mouse model of Huntington’s disease (HD) that exhibits specific peripheral pathology, and movement disorders. The goal is to fully characterize neurons in these mice and compare these data to those from control mice. Findings will shed insight into how and why motor cortical pyramidal neurons degenerate and die in Huntington’s disease.

Meeting Comments:

This new protocol focuses on characterization of the structure and function of nerve cells in a mouse model of Huntington Disease (HD) that simulate the specific peripheral pathology and movement disorder during the progression of HD. Their research program is based on the knowledge that molecular change in HD is an increase in the number of CAG repeats in the gene causing HD (The \textit{Hd} gene). The Q175 mouse model is a well characterized representative of HD in humans from a genetics perspective as it contains the expanded CAG repeat (~179 repeats). These mice will be used in the electrophysiological assay. Another mouse model Kj18-Cre x Q175 is genetically modified to express Cre topoisomerase only in the pyramidal tract neurons. The injection of AAV-9 viral construct with CAG promoter linked to the red dye dtTomato will be injected into animals, which will identify specific neurons predicted to be vulnerable in HD. The current IBC protocol provides detailed information about procedures involved including, source, transportation, storage and injection into mice the viral vector AAV-9. The PI will purchase ready-to-inject replication incompetent AAV-9 vector that already contains CAG-floxed tdTomato marker (no genetic manipulations with the virus in the lab). The committee noted that the protocol is not using any biohazardous material that would require BSL2 containment and recommended downgrading the protocol to BSL1.

Changes/Clarifications Required:
Materials Used in Research: Since your protocol only involves mouse work with AAV vectors, it is considered as BSL-1/ABSL-1 protocol. Please remove the input in section A first (and save). Then come back to this section IX and uncheck Hazardous Biological Agent box. Please select the highest biosafety level for your work as BSL1. Please note that your (Dr. Luebke) BSL1/2 training needs update for the approval of this protocol.

Lab Safety Training (LST): Dr. Luebke needs to update BSL1/2 training.

BUA Site Assessment: Approved.

Recommendation: Conditional Approval (Administrative Review)

For: 13
Against: 0
Abstain: 0

B. Three-Year Renewal Applications

6. rDNA/Bhz  
PI:    
BUA Tracking ID: 1424
Title: Molecular determinants of RAS dependency in human cancers  
Primary Reviewer: Inna Afasizheva  
Secondary Reviewer: Jim Keeney  
Biosafety Level: BSL2  
Animal Biosafety Level: N/A  
Campus: BUMC  
Applicable NIH Guidelines: Sections III-D-1; III-D-2; and III-D-3  
Protocol Expires: 12/01/2017  
Layman’s Description: Kras is the most frequently mutated oncogene in solid tumors with highest frequencies seen in lung, pancreatic and colorectal cancers. I propose to generate gene expression signatures for lung, pancreatic and colorectal cancers in the hopes of identifying novel therapies for each of these cancers, which are very difficult to treat with current chemotherapeutics.

Meeting Comments:
The PI continues to investigate how the KRAS oncogene can be used to identify potential therapeutic avenues for cancers of the lung, pancreas and colon. Although the KRAS mutation is frequently found in these cancers, pharmacological inhibition of KRAS does not prevent cancer progression. The lab has identified through functional genomics studies that several other genes are also required to maintain the KRAS-dependent state of many of these cancer cells. The PI is interested in investigating whether inhibition of those other genes can be used as therapeutic approaches against KRAS-dependent cancers. For this purpose they will study a number of human cancer cell lines that are either KRAS-dependent or KRAS-independent and manipulate expression of other KRAS-associated genes by using specific si-RNA expressing lentiviral vectors. The committee requested clarification on the lentivirus vector being used in the protocol and the purpose of use of a variety of human cancer cells.

Changes/Clarifications Required:
Overview and Grant Funding Information: Please remove text from the summarize changes box. This is only for amendments and annual renewals. 
Personnel Information: Since you have mentioned possible change of personnel involved in the protocol, please update the list.  
Research Laboratory Facility Information: Please add room K723 to the list.  
Research Project Description: Q3- A large number of human cancer cell lines have been listed in the Biohazard materials list but their use in the protocol has not described. Please clarify. Committee asked if there is any specific need to still use 2nd-generation lentivirus system in your protocol. Use of 3rd generation lentivirus vectors which are safer for the researchers, is recommended wherever possible. It is noted however, that you are using pLKO.1 vector, which is a 3rd-generation SIN vector and tat-independent packing plasmid. Please clarify.
PPE and SE: Q5- Update BSC certification date. Your BSC was last certified on 10/25/2017.
Lab Safety Training (LST): Lab safety training for all members is current.
BUA Site Assessment: Approved. BSC was last certified on 10/25/2017.
Recommendation: Conditional Approval (Administrative Review)
For: 13
Against: 0
Abstain: 0


Title: Exploring the use of adult neural crest stem cells derived from non-ocular sources to treat corneal endothelial disease
Primary Reviewer: Debbie Stearns-Kurosawa
Secondary Reviewer: Rao Varada
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: BUMC
Applicable NIH Guidelines: N/A
Protocol Expires: 12/07/2017

Layman’s Description: Corneal endothelial cells are the cells that line the backside of the cornea, and are critical to keeping the cornea clear. Diseases that affect these cells lead to decreased vision due to swelling of the cornea. Human corneal endothelial cells do not naturally regenerate if they are lost or damaged. The goal of this project is to regenerate corneal endothelial cells by isolating adult (non-embryonic) stem cells from easily accessible sources, such as hair or mouth tissues, and turn them into corneal endothelial cells.

Meeting Comments:
The PI continues to investigate alternate ways to treat corneal diseases. Corneal endothelial cells do not normally regenerate in humans when damaged or lost due to disease or aging. The ability to regenerate these cells would lead to a desirable alternative to corneal transplantation surgery for treating visually significant corneal endothelial disease. Corneal endothelial cells are of neural crest origin. Adult stem cells with neural crest features will be isolated from adult hair follicles and human cadaveric corneas. These multipotent cells have the ability to differentiate into multiple different cell types, guided by the conditions under which they are cultured. The objective of this protocol is to isolate neural crest stem cells from adult hair follicles and/or oral mucosa, and to culture these cells under conditions that will lead to the differentiation of these cells into corneal endothelial cells. Laboratory procedures to be used in the protocol include light microscopy, quantitative RT-PCR, immunohistochemistry and assays of cellular function such as measuring Na/K-ATPase pump function. The biosafety concerns and mitigation plans are described well in the protocol. The committee requested clarification on the use of human cadaveric sample and the percentage of disinfectants for the disinfection of surgical instruments.

Changes/Clarifications Required:
Research Project Description: Q3- Please clarify if collection of human cadaveric cornea is still part of the research plan.
Materials Used in Research: Please contact Hospital Epidemiologist Dr. Carol Sulis to clarify how hair follicle or oral mucosa samples are being collected safely in the clinic. Please include the date of this communication in your application.
PPE and SE: Q7A and 8- What percentage of Wescodyne will be used for the disinfection of surgical instruments?
Other Potentially Infectious Material (Section B): Please indicate that IRB protocol H-33522 is an exempt protocol.

Please note that now on all lab safety trainings are to be renewed annually. You (Dr. Lee) are required to complete the BSL1/2 and BBP training.
Lab Safety Training (LST): Lab safety training for all members is current.
BUA Site Assessment: Approved.
**Recommendation:** Conditional Approval (Administrative Review)

**For:** 13  
**Against:** 0  
**Abstain:** 0

8. rDNA/Bhz  

**PI:**  
**BUA Tracking ID:** 936

**Title:** Early diagnostics and therapeutics for Neurodegenerative diseases  
**Primary Reviewer:** Debbie Stearns-Kurosawa  
**Secondary Reviewer:** Erin Sawyer  
**Biosafety Level:** BSL2  
**Animal Biosafety Level:** ABSL-1  
**Campus:** BUMC  
**Applicable NIH Guidelines:** Section III -D-1 Appendix B-V, B-II, Appendix G II B  
**Protocol Expires:** 12/04/2017

**Layman’s Description:** Amyloid-beta and alpha-synuclein are proteins that tend to form clumps. In the brains of people who have Alzheimer’s and Parkinson’s disease, these clumps build up and become toxic resulting in death of brain cells. The goal of this project is to develop a method for producing these clumps in tissues maintained in the laboratory and study them. Once we can generate these clumps, we can search for molecules that can prevent formation of these clumps. We hope that these molecules can be used to treat patients with Alzheimer’s and Parkinson’s disease and delay the progression of the illness.

**Meeting Comments:**  
The PI continues investigation on ways to regenerate plaques found in brain cells of patients with Alzheimer’s and Parkinson’s disease. Amyloid-beta and alpha-synuclein are thought to contribute to Alzheimer’s and Parkinson’s disease respectively by forming toxic aggregates. PI’s group will use plasmids containing the relevant cDNA driven by appropriate promoters or the Lentiviral expression system to introduce genes relevant to Alzheimer’s and Parkinson’s disease into cell lines, rat or mouse brain slices, rat or mouse primary neurons or C. elegans. Genes to be introduced include amyloid-beta, alphaA crystallin, alphaB crystallin, alpha-synuclein, parkin, and several other MAP-kinase or other signaling pathway members. They will transfect or infect cells in an effort to generate high level expression of amyloid-beta, alpha-synuclein, LRRK2 or TDP-43, because higher expression generally drives more aggregation. Aggregates will be detected by lysing the cells and analyzing the lysates for appropriate proteins listed above in immunoblotting experiments. Once the system is optimized, they will test the ability of various chemicals (e.g., cerium oxide, rotenone, MG132 or NH4) to inhibit protein aggregation, with the goal of identifying novel tools for therapy of Alzheimer’s and Parkinson’s disease. The PI has provided extensive detail of each and every laboratory procedure that will be carried out in the lab. Risks and mitigation plans are also described in excessive detail. The committee suggested trimming some of the procedural details and asked for clarification of the source of human tissues.

**Changes/Clarifications Required:**  
**Research Project Description:** Q3- Some of the procedural details may be shortened as the IBC Chair in person has suggested to the lab. However, the details of the biohazardous materials such as, human eye and brain samples, are very important for the risk assessment and should stay as such.  
Please provide more information on tissue banks and hospital sources of human tissues. Are these from commercial banks? If from local hospitals, how are the samples transported to the laboratory? Are they tested for viruses or prion? How is equipment exposed to human brain-eye tissues decontaminated?  
PPE and SE: Q1- Please check plating, colony counting (for E. coli transformation work).  
Q5- Update BSC certification date (should be 10/31/2017).

**Lab Safety Training (LST):** Lab safety training for all members is current.

**BUA Site Assessment:** Approved. BSC was last certified on 10/31/2017.

**Recommendation:** Conditional Approval (Administrative Review)
C. Amendments & Annual Renewals for Committee Review

None.

IV. Approved Amendments & Annual Renewals

A. Amendments

1. BUA Tracking ID: 756  
   Title: The role of pheomelanin in melanoma development  
   Biosafety Level: BSL2  
   Animal Biosafety Level: ABSL-1  
   Method of Review: Expedited, Administrative Review  
   Modification: To add lenti-CRISPR vector to the protocol and all associated information

2. BUA Tracking ID: 1409  
   Title: Replication and Transcription of Filoviruses Early Host Immune Response in Protection against Filovirus Infection  
   Biosafety Level: BSL2  
   Animal Biosafety Level: N/A  
   Method of Review: Expedited, Administrative Review  
   Modification: To add one personnel and change language related to transport of VSV

3. BUA Tracking ID: 650  
   Title: Growth of laboratory-adapted, vaccine and wild-type negative strand RNA viruses (NSRVs), expression of virus proteins and generation of recombinant laboratory-adapted, vaccine and wild-type negative strand RNA viruses  
   Biosafety Level: BSL2  
   Animal Biosafety Level: ABSL-2  
   Method of Review: Expedited, Administrative Review  
   Modification: To add one personnel, to provide IACUC approval information and to add laboratory room NEIDL 622D.

4. BUA Tracking ID: 756  
   Title: The role of pheomelanin in melanoma development  
   Biosafety Level: BSL2  
   Animal Biosafety Level: ABSL-1  
   Method of Review: Expedited, Administrative Review  
   Modification: To add one and delete one personnel

5. BUA Tracking ID: 2248  
   Title: Artificially manipulating memories in healthy and maladaptive states  
   Biosafety Level: BSL2  
   Animal Biosafety Level: ABSL-2  
   Method of Review: Expedited, Administrative Review  
   Modification: To add three personnel and to address the new DURC question

6. BUA Tracking ID: 1643  
   Title: Mechanisms of Autoimmune Disease  
   Biosafety Level: BSL2  
   Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add one personnel

7. BUA Tracking ID: 2012
Title: Phase 2, Multi-Center Trial of Lorcaserin in the Treatment of Cocaine Use Disorder
Randomized, Double Blind, Placebo-Controlled Trial of the Safety and Efficacy of
HORIZANT (Gabapentin Enacarbil) Extended-Release Tablets for the Treatment of
Alcohol Use Disorder
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add one personnel

8. BUA Tracking ID: 1820
Title: NIH R01 EB00262 Local regulation of angiogenesis by microenvironmental cues
NIH R01 EB008396 Engineering Multicellular Tissue Structure, Function, and
Vascularization NIH R01 HL73305 Stiffness, Cadherins, Integrons, and Mechanochemical
Signaling 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 "Building a Human Adipose Depot" Pilot Program:
Engineered human fat depots on a chip HFSP Architecture/force relationship and
migration mechanics of macrophage podosomes NIH ApoE Arterial Biomechanics and
Cardiovascular Disease NSF Collaborative Research: The Effects of Extracellular Matrix
Alignment of Cellular Mechanotransduction in 3D Architectures PharmAkea Evaluation
of LOX(L) Family Inhibitors on Matrix Remodeling in an Engineered 3D Microtissue
Mechanical Testing
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: IBC Office Review
Modification: To add tamoxifen in the protocol

9. BUA Tracking ID: 844
Title: Gene regulation in muscle development
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Method of Review: IBC Office Review
Modification: To add two and delete four personnel and to add new adenoviral vectors

10. BUA Tracking ID: 1804
Title: Regulation of Gene Expression in the Immune System
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: IBC Office Review
Modification: To add modified dCas9 to the protocol

11. BUA Tracking ID: 1554
Title: NIH R01 DK33765, Cytochrome P450-Endogenous Substrate Metabolism NIH R01
ES024421, Epigenetic Actions of Environmental Chemicals
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: IBC Office Review
Modification: To add AAV vector to deliver Cas9 and dCas9 to mouse cells

12. BUA Tracking ID: 793
Title: Bacterial lysis on a microfluidic device Protozoa lysis on a microfluidic device
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add one personnel and to add language in infectious materials used

13. BUA Tracking ID: 2248
Title: Artificially manipulating memories in healthy and maladaptive states
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add one personnel

14. BUA Tracking ID: 2248
Title: Artificially manipulating memories in healthy and maladaptive states
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add one personnel

15. BUA Tracking ID: 935
Title: Lens-Amyloid: Biochemistry and Diagnostic Imaging Effects of Space Radiation on Hippocampal-Dependent Learning and Neuropathology in Wild-Type and Alzheimer’s Disease Transgenic Mice Clinical validation of a laser eye scanner for AD Preclinical evaluation of non-invasive PEMF therapy in a blast neurotrauma mouse model Effects of Blast Neurotrauma on Alzheimer’s Disease Pathogenesis CTE and posttraumatic neurodegeneration: neuropathology and ex vivo imaging Mechanisms of Repetitive Neurotrauma and Chronic Traumatic Encephalopathy (CTE): Pathways to Diagnosis, Treatment, Protection, and Prevention Visual and Retinal Correlates of Traumatic Brain Injury (TBI): Biology and Behavior Gadolinium Distribution in Rat Brain After Systemic Administration of Gadolinium-Based Contrast Agents Assessed by High-Resolution Metallomic Imaging Mass Spectrometry (MIMS)
Biosafety Level: BSL2+
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add three and delete one personnel

B. Annual Renewals

1. BUA Tracking ID: 2092
Title: Analysis of small RNA processing during vertebrate embryogenesis
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Method of Review: Expedited, Administrative Review
Modification: To add one personnel

2. BUA Tracking ID: 1889
Title: Corneal epithelial adhesion: morphology and biochemistry; Role of purinoreceptors in diabetes, role of purinoreceptors and EGFR in corneal scarring
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Method of Review: Expedited, Administrative Review
Modification: No changes

3. BUA Tracking ID: 1879
Title: Plasmid & virus construct preparation and use for studies on the regulation of skeletal muscle wasting and pathology
Biosafety Level: BSL2
4. BUA Tracking ID: 2152
Title: A Rapid and Sensitive Antibiotic Susceptibility Test for Urinary Tract Infections
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: No changes

5. BUA Tracking ID: 1031
Title: Genome Analysis Based on the Integration of DNA Sequence and Shape; Chemical Probing of RNA Tertiary Structure in a Whole Transcriptome at Single-Atom Resolution
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To remove three personnel

6. BUA Tracking ID: 2063
Title: Lung injury and sepsis
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Method of Review: Expedited, Administrative Review
Modification: No changes

7. BUA Tracking ID: 633
Title: Immunopathology in a murine model of pulmonary infection following traumatic brain injury
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: No changes

8. BUA Tracking ID: 602
Title: Plasma Amyloid-Beta Peptides, Depression and Alzheimer's Disease in the Homebound Elderly: Name Longitudinal Study of a Subset
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Method of Review: Expedited, Administrative Review
Modification: To add two and delete two personnel

9. BUA Tracking ID: 681
Title: Microchip to detect HIV viral RNA in whole-blood samples using branched-DNA hybridization
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To delete one personnel and to include waste management information for virus contaminated material

10. BUA Tracking ID: 874
Title: DEREGULATED MIRNA EXPRESSION IN BIPOLAR DISORDER
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: No changes

11. BUA Tracking ID: 1670
Title: Systems/synthetic biology and microfluidics
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add 5 and delete 9 personnel, to add 6 laboratory rooms in CILSE and to add commercially available human cell lines and 5 new bacterial strains from ATCC

12. BUA Tracking ID: 897
Title: Ah Receptor, Androgen Receptor and Estrogen Receptor: Controlling Receptor Activation and Breast Cancer Growth
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To remove High Throughput Screening Core

13. BUA Tracking ID: 1528
Title: 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
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add one and delete one personnel and to update activities in room 720

14. BUA Tracking ID: 891
Title: Actomyosin-Based Podocyte Contractility and Glomerular Pathobiology
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To delete three personnel

15. BUA Tracking ID: 2127
Title: Physiology and Structure of Prefrontal Projections to Memory and Motor Circuits
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add language in procedures and to add language with animal work

16. BUA Tracking ID: 2094
Title: New Molecular Tools for High Resolution Imaging of Cells and Tissues
Biosafety Level: BSL1
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add 6 new personnel, to add a new laboratory room in CILSE 521 to address new DURC question

17. BUA Tracking ID: 635
Title: Biospecimen Archive Research Core
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Method of Review: Expedited, Administrative Review
Modification: To add four personnel
18. BUA Tracking ID: 1537
Title: Engineering T cells response for cancer adoptive immunotherapy using synthetic genetic and signaling networks
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Method of Review: Expedited, Administrative Review
Modification: To add 5 personnel, to add CILSE Laboratory Rooms 415, 419b, 421 and to delete previous 11 laboratory rooms