IBC Meeting Minutes
Boston University

Location: E-720, 72 East Concord Street

May 17, 2016

Start time: 12:00 PM

End time: 3:15 PM

Present: D. Stearns-Kurosawa (Chairperson), R. Ingalls (left at 2:45 PM), J. Barbercheck, R. Morales (left at 2:00 PM), E. Muhlberger (left at 3:00 PM), B. Slack, K. Tuohey (left at 2:00 PM), J. Barton (left at 2:00 PM), T. Winters, C. Sulis, K, R. Georgiadis, A. Kocsis (left at 3:00 PM), J. Keeney, R. Timmerman, E. Sawyer.

Guests: T. Killeen, M. Auerbach, P. Sundaresh, R. Jordan, D. Corlosquet and E. Beyrent.

Staff: S. Ghosh.

Absent: N. Broude, E. Helmerhorst, V. Britton, F. Gibson, N. Bhadelia.

I. Review of April Minutes

Recommendation: Approved
For: 15
Against: 0
Abstain: 0

II. New Business

A. IBC Training Session: Overview of Zika virus - Dr. Robin Ingalls

Dr. Robin Ingalls, Associate Professor in the Department of Medicine presented on the Zika virus. Dr. Ingalls explained that Zika virus belongs to the flaviviridae family, which include pathogenic viruses such as Dengue, West Nile, and Japanese encephalitis, all of which are mosquito borne (or arbovirus). The genetic composition and replication mechanism of Zika virus is also related to Chikungunya or Rubella virus. Although the virus was identified in 1947 in the Zika forest of Uganda and sporadic infection has been noted in Pakistan and Malaysia, no large scale outbreaks were reported until 2007 in Yap Island and 2013 in French Polynesia. Since 2015, the infection has spread to South America and Central America, particularly affecting Brazil. Phylogenetic relationship has documented that Zika viruses found recently are different from those found in Central Africa.

Dr. Ingalls stated that the reasons we are concerned about Zika virus is because not only does it cause severe rash, fever, conjunctivitis and joint pain in infected individuals, but microcephaly in newborns from Zika virus-infected pregnant women are quite common, as is the incidence of neurological syndromes and Guillain-Barre syndrome. The virus is usually transmitted by mosquito bites (particularly by *Aedes aegypti* and *Aedes albopictus*). It is not contracted by casual contacts with an infected individual. However, Zika virus has been found to survive in human semen up to 17 days, suggesting sexual transmission is a mode of virus transmission.

Dr. Ingalls also addressed the biosafety procedures to be followed when working with Zika virus in laboratories. The Center for Disease Control has recommended and posted guidelines indicating BSL-2 level practice with standard infection control precautions must be used while working with Zika virus. Risk assessment should be performed if specimens or procedures may require higher level of biocontainment. If animal work is planned, it must be done in ABSL-2 facilities. Work with infected mosquitos should be done in an Arthropod Containment Level 3 (ACL3) where Zika virus presence has not been reported in mosquitos. In areas where Zika is already present, ACL2 may be used. The recommendation also included minimization of pregnant workers or those individuals (female or male) that are considering conception.

B. Chairperson Report:

1. Inclusion of BSL1 level work in maneuvers section

Dr. Stearns-Kurosawa informed reviewers that procedures for all biosafety levels should be included in the maneuvers section and in other relevant areas. This should be brief for BSL1, but more detailed for BSL2 and higher. All recombinant DNA work must include a brief statement on bacterial culture and plasmid extraction.

2. Notes on Harvard-Yale Symposium on CRISPR/Cas-9

In May, Harvard University and Yale University organized a symposium on CRISPR/Cas-9 technology at the Harvard Medical School. Presentations focused on the rapidly evolving technology of gene editing with the CRISPR-Cas9 technology. Dr. Stearns-Kurosawa explained that there is no international agreement on how the technology is applied. Some countries have approved use in otherwise nonviable human embryos; the US does not allow this sort of application. There is no agreement for how to monitor laboratory accidents with personnel (e.g., needle sticks with a CRISPR/Cas-9 reagent that targets a tumor suppressor gene). An increasing number of researchers are using single-mode delivery of all the gene editing components for higher efficiency and rapidity, rather than the delivery of individual components separately. The latter procedure although less efficient, protects against harmful consequences of cell line contamination or accidental release of engineered cell lines. The application of the technology in Gene Drives could have global consequences.

Dr. Stearns-Kurosawa reported she will put together a training program for this topic, including suggested guidelines for the IBC. This should help IBC reviewers identify potential biohazards in our protocols.

C. Safety Committees Report:

1. Approved Applications/Amendments

This month 1 new application, 5 three-year renewals, 7 amendments and 16 annual renewals have been approved.

2. Training and Health Clearance Requirement Policy Revised

The revised policy was reviewed and approved unanimously. The revised policy now includes a rDNA/IBC Policy training requirement for all individuals engaged in any recombinant and synthetic nucleic acid work. Further, this training will now be valid for three consecutive years.

3. Incident Reporting Requirements for Research Involving Recombinant or Synthetic Nucleic Acid Molecules Policy

The new policy, reviewed and approved unanimously, sets forth the incident reporting requirements for research involving recombinant or synthetic nucleic acid molecules.

D. Biosafety Report:

1. Research Occupational Health Program Incident Report

Two incidents were reported in this meeting:

i. A research assistant sustained a splash exposure of a droplet of buffered EDTA (Ethylenediamine Tetraacetic Acid) solution in her eye while disposing of unused syringes which contained a mix of EDTA/buffered Saline. She flushed her eye for 15 min. and contacted her supervisor. The physician on call spoke with the researcher who reported her eye was not irritated and the physician confirmed correctness of treatment. The researcher was certain that no other substances were inside syringe. The researcher was instructed that if eye irritation occurs, she should go to the nearest emergency room. A call and email was sent to the researcher to follow up with ROHP the following day.

ii. A PhD student sustained a ¾ cm cut to her right index finger pad while getting ready to use a cryostat machine. As she tried to reach into a box that contained pens and metal pieces for the machine, she accidentally cut her finger on a microtome blade. She was wearing one pair of gloves at the time. She reports there were about 6 loose blades in the container and she is not sure if the blades were ever used. She did not see any visible blood on the blades. This researcher washed the site immediately with soap and water, followed by hand sanitization with 66.5% ethyl alcohol. She was evaluated and treated in ROHP. Baseline lab work was done and a follow up with ROHP was scheduled next day.

2. Updates from Environmental Health & Safety

Biosafety Officer Joe Barbercheck presented on the new OSHA standard that aligns the US with the Globally Harmonized System (GHS) of classification and labeling of chemicals. Mr. Barbercheck explained how the new labeling system would work. All participating countries will now use universal labels and pictograms. New GHS labels will have symbols, signal words, hazard statements, precautionary statements, product identifier, and supplier information. Pictograms must contain a red outer square, a white background and a black hazard symbol. All secondary containers of chemicals must adhere to the GHS format. EHS will provide GHS labels to each laboratory but they will also be available for purchase from the FedEx/Kinko office on the BU campus. For small secondary containers, when the circumference of the container is less than the width of the label, the container can be labeled with the sample number or other identifier correlating to a key. The label can then be placed on a nearby reference sheet.

III. Protocol Review:

Meeting is not closed

A. New Applications

1. rDNA/Bhz **Protocol 2117**

"Novel Recombinant Chlamydia Antigens"
Primary Reviewer: Robin Ingalls
Secondary Reviewer: Jim Keeney
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: NEIDL
Applicable NIH Guidelines: Section III-D-2-a. Experiments in which DNA from Risk Group 2 or Risk Group 3 agents (see Section II-A, Risk Assessment) is transferred into nonpathogenic prokaryotes or lower eukaryotes may be performed under BL2 containment.
Section III-F. Exempt Experiments
Section III-F-3. Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.
Protocol Expires: New protocol
Layman's Description: The experiments in this study seek to express the immunogenic variable regions (VDs) of Chlamydia muridarum major outer protein (MOMP) into a recombinant carrier protein, structurally similar to MOMP and suitable for refolding. This will permit presentation and immune recognition of the VDs for a Chlamydia vaccine formulation.

Pre-Meeting Comments:

Reviewer 2:

Protocol #2117 from Dr. Madico is a new BSL-2 study from the Medical School designed to produce an antigen related to Chlamydia. The purpose is to lead to an eventual vaccine for Chlamydia. In my opinion, the PI's comments provide a better description of the study than what is contained in the Layman's Terms. Other than the PI, no other lab personnel are identified, which brings up the question whether the PI can do all this by himself. I would like more review

as how proteins can be transported into the NEIDL for study. Then the protocol mentions that "constructs" will be sent out for purification - to where, and how secured for transport? BSC is up-to-date.
I think these points need to be explained more fully before I could sign off the study as the community representative.
Reviewer 1:
I am looking at this protocol and I actually wonder if it is a rDNA/BSL2 protocol or if it is just rDNA? Seems like Guillermo is designing plasmid constructs and expressing them in lab strain *E. coli* (Top10 and BL21 which I think are BSL1). He does not seem to be growing *C. muridarum* or *N. lactamica* in the lab, just cloning by PCR from C.m. MOMP and N.l. PorB genomic DNA. My guess is that he has stocks of bacterial DNA to use as a template already in his freezer and that he is not planning to grow these bacteria in the lab, but he should clarify that.
By the way, *C. muridarum* is a mouse pathogen and *N. lactamica* is a non-pathogenic human oral colonizer, so even if he is growing these BLS2 bacteria I would not have any major concerns.
Shipping plasmid DNA or *E. coli* containing your recombinant plasmid to a company for protein purification is pretty standard and does not involve shipping a pathogen since these *E. coli* are BSL1, but it is rDNA. Guillermo did not note any shipping training although I would bet that he has completed it.
This type of work is appropriate for one person to do since it is mainly "dry lab" work for designing the primers and then PCR for cloning.
Meeting Comments:
This simple straightforward application is just for construction of a plasmid that will express recombinant *Neisseria lactamica* major outer membrane protein (MOMP) that contain an immunogenic variable region of Chlamydia MOMP. PI will PCR amplify required region of the bacterial genome from genomic DNA isolated from these bacteria that has been stored in PI's laboratory for years. Only concern that the reviewers had was that it was not clear whether the PI is growing these bacteria in the lab before isolation of genomic DNA. NIH guidelines recommend that cloning of genes from RG2 agents must be done under BSL2 laboratory facilities. Therefore the protocol remains to be in the BSL2 category.
The PI needs to:
Personnel Information: Please specify your shipping training date.
Research Project Description: Q1- Please simplify the layman's term without scientific jargon. Q3- Please clarify how the genomic DNA for *Chlamydia muridarum* and *Neisseria lactamica* were prepared.
Hazardous Biological Agent: *E. coli* TOP10 and BL21 are not biohazard material. Please remove them from the list. Instead, if you have grown Chalmydia or Neisseria to get the genomic DNA, include them in the list and provide brief description of their growth in project description question 3.
LST: All clear for the PI (only person in the protocol).
BUA Site Assessment: Laboratory safety manual should be in place but otherwise lab is in good shape.
Recommendation: Conditionally Approved/Pending (Reviewers don't want to see it unless growth of Chlamydia and Neisseria is added in the revision).
For: 14
Against: 1
Abstain: 0

2. rDNA **Protocol 2088**
"A bioassay for antimicrobial drug identification"
Primary Reviewer: Rosina Georgiadis
Secondary Reviewer: John Gonsalves
Biosafety Level: BSL1
Animal Biosafety Level: N/A
Campus: CRC
Applicable NIH Guidelines: Section III-F (exempt)

Protocol Expires: New protocol

Layman's Description: E. coli cells will be grown with varying amounts of antimicrobial drugs to assess for drug interactions (i.e., cell growth under drug combinations differs from expected growth changes based on individual drug outcomes).

Pre-Meeting Comments:

Reviewer 2:

No major issues with the protocol; Item 16. Layman's Terms: Layperson's Terms adequate (USAID project funded). PI is Prof. Zaman; however, Grad student identified under Personnel Information as experienced. ROHP status cleared 05.10.20 for Z. Weinstein.

Reviewer 1:

Didn't have any major concern with this simple and straightforward application.

Meeting Comments:

In this simple and straightforward application PI is transforming nonpathogenic E. coli with a luciferase expression plasmid. The transformed bacteria will then be used for assaying resistance profile against novel antibiotics. No concern noted but the lab safety training of the PI was not complete yet.

The PI needs to:

PI needs to complete his safety trainings.

LST: PI's lab safety trainings are not complete yet.

BUA Site Assessment: No issue with the lab.

Recommendation: Conditional Approval/Pending (Reviewer's don't want to see it again).

For: 15

Against: 0

Abstain: 0

3. rDNA/Bhz **Protocol 2110**

"PTRF(Cavin-1), ribosome biogenesis and adipocyte biology"

Primary Reviewer: Barbara Slack

Secondary Reviewer: Erin Sawyer

Biosafety Level: BSL2

Animal Biosafety Level: ABSL1 or 2 (?)

Campus: BUMC

Applicable NIH Guidelines:

Prior to the initiation of an experiment that falls into this category, the Principal Investigator must submit a registration document to the Institutional Biosafety Committee which contains the following information: (i) the source(s) of DNA; (ii) the nature of the inserted DNA sequences; (iii) the host(s) and vector(s) to be used; (iv) if an attempt will be made to obtain expression of a foreign gene, and if so, indicate the protein that will be produced; and (v) the containment conditions that will be implemented as specified in the NIH Guidelines. For experiments in this category, the registration document shall be dated, signed by the Principal Investigator, and filed with the Institutional Biosafety Committee. The Institutional Biosafety Committee shall review and approve all experiments in this category prior to their initiation. Requests to decrease the level of containment specified for experiments in this category will be considered by NIH (see Section IV-C-1-b-(2)-(c), Minor Actions).

Protocol Expires: New protocol

Layman's Description: Diabetes is a disease characterized by high blood sugar (glucose) and has many causes although over nutrition (overeating) and obesity seems to be the major reasons for the high incidence of type 2 diabetes. My lab studies the molecular mechanism for adipocyte healthy adaptive changes upon excess lipid loading. We believe ribosome, which is the machinery for protein synthesis plays critical role on adipocyte quality control. Adipocyte metabolic capacity can be improved through the modification of key factors in this pathway.

Pre-Meeting Comments:

Reviewer 1:

This is a straightforward proposal. There are only a few minor issues to address.

1. Liquid wastes- indicate that after treatment with bleach liquid wastes will be disposed of down the sink.
2. Solid wastes- include a reference to human cell lines (HEK293 cells) as well as virus in your description.
3. Please check ABSL1 under table IX.
4. Section H-rDNA: Please add the pSuper vector to table, as it is mentioned in the Lab Procedures section. Please provide some additional information about the virus packaging systems, including commercial source, and which generation of packaging system will be used.

Reviewer 2:
This is an ABSL-1 proposal.

Meeting Comments:
PI is interested in understanding the molecular mechanism of obesity-induced diabetes. In particular, PI wants to study how the metabolism of adipocytes is altered in presence of high blood sugar (as in the case of excess dietary lipid load). They will test the hypothesis that ribosome biogenesis and their activity are altered in presence of excess sugar or lipid. PI will isolate primary adipocytes from normal mice or rats and stimulate them with hormones like insulin to simulate high fat diet load. They will then analyze the fate of ribosome transcription factors to understand the mechanism of adipocyte quality control. They also plan to use primary adipocytes from specific knockout mice. Retroviral vectors will also be used in some cases to induce expression of specific genes that may alter ribosome functions. Review of animal work suggested that it is an ABSL-1 protocol. Nicely written straightforward protocol. Only few minor issues as described below need to be addressed.

The PI needs to:
PPE and SE: Q7A- Liquid wastes- indicate that after treatment with bleach liquid wastes will be disposed of down the sink.
Q7B- include a reference to the particular virus and human cell lines (HEK293 cells) in your description of solid waste. Check typos here and throughout the application.
Materials Used in Research: Please select the highest animal biosafety level for your work (should be ABSL-1).
Recombinant DNA (Section H): Please add the pSuper vector to table, as it is mentioned in the Lab Procedures section. Please provide some additional information about the virus packaging systems, including commercial source, replication competence, and which generation of packaging system will be used. ALSO, your response to question 17 in the section H (rDNA section) should be "yes" and then answer the two associated questions.
In question 19 please indicate only the name of the sections of NIH Guidelines that are applicable for your work. Remove all additional texts. Your response should be "Sections III-D-2-a and III-D-3-a".

LST: PI is clear for all trainings.
BUA Site Assessment: Lab is all set.
Recommendation: Conditional Approval/Pending (Reviewer's don't want to see it again).
For: 15
Against: 0
Abstain: 0

4. rDNA **Protocol 2118**

"Genetic modification of Zebrafish"
Primary Reviewer: Barbara Slack
Secondary Reviewer: Bob Timmerman
Biosafety Level: BSL1
Animal Biosafety Level: ABSL-1 (Zebrafish)
Campus: BUMC
Applicable NIH Guidelines: rDNA section not completed
Protocol Expires: New protocol
Layman's Description: Problems in formation of the skeleton and skull are common human birth defects. Using the zebrafish as an experimental model system, we hope to better understand

what causes these defects, and eventually to test potential treatments. To create accurate zebrafish models of the human diseases, we will introduce mutations into the zebrafish genes equivalent to those found in some human patients.

Pre-Meeting Comments:

Reviewer 1:

1. Section III-Personnel Information-Please add PI's name and requested information to list of personnel.
2. Section VIII. PPE: part 1. If plasmids will be propagated in bacteria, please check related procedures such as vortexing, centrifugation, culture stirrers, and plating. Part 2. check "use of centrifuges with sealed rotors or sealed cups, if applicable.
3. Lab Procedures: Please add a brief section describing how mutated fish will be analyzed. Please briefly describe how fish are euthanized and disposed of.
4. Section VIII-PPE question 8. re: disinfectant- Please add that 10% bleach will be used, as described under liquid wastes.
5. Section IX. Materials used in research- please check rDNA
6. rDNA table should be filled out if plasmids will be propagated in bacteria.

Reviewer 2:

This protocol covers research using Zebrafish to create a model of birth defects in the skull and spine. Zebrafish are well understood, and are used for biological research.

They are tropical, fresh water fish, thriving at water temperatures between about 25°C and 28°C. The Charles River is generally colder than this, with only a few days per year in the 25°C to 26°C range [MWRA data for 2015, other years similar]. Boston Harbor is salt water, and in the author's experience, hardly ever exceeds 24°C. Accidentally released Zebrafish would not thrive in either environment, save for shallow pools at the River's edge where the water could be heated by sunlight. Lower temperatures surrounding these pools might confine the fish to the pools. Accidental release of fish would not appear to constitute a public health hazard.

The protocol is classified as BSL-1, the hazard data confirms this.

There are a number of minor edits necessary to put the protocol into form for approval, to wit:

1. Please clarify the name of the Principal Investigator. The PI is listed variously as Mary Fisher, and Shannon Fisher.
2. Please complete the section on education and experience for the PI
3. Please complete the section on safety training for the PI.
4. Will the centrifuge employ sealed rotors? This is not stated in safety procedures.
5. Will lab coats be employed for handling animals?
6. How will the Zebrafish be disposed of?

Meeting Comments:

PI wants to study molecular mechanisms of common human birth defects using zebrafish as experimental model. They will genetically alter zebrafish in two ways. First, Tol2 transposable element-based vector will be used to create transgenic fish expressing fluorescent markers in specific cell types. Second, recently developed approaches based on CRISPR/Cas9 technology will be used to introduce mutations into specific genes, with the goal of creating models for human genetic diseases. Brief but nicely organized application with complete description of biohazard issues and their mitigation. It was not clear though how the effect of all those mutations in zebrafish will be analyzed. Few other minor clarifications are also needed for the approval of the protocol.

The PI needs to:

Investigator Contact Information: Please use only one name for the PI. Mary Fisher has been replaced by Shannon Fisher in some places.

Personnel Information: Please Include yourself (the PI) in the personnel list and all associated questions as has been done for the other members of the protocol (the “rDNA/Infectious Agent/Select Agents” question and the “State how many years experience, when and where” question).

Research Project Description: Q3- Please add a brief statement in the laboratory procedure section describing how mutated fish will be analyzed. Please also briefly describe how fish are euthanized and disposed of.

PPE and SE: Q1- If plasmids will be propagated in bacteria, please check related procedures such as vortexing, centrifugation, culture stirrers, and plating.
Q2- Check "use of centrifuges with sealed rotors or sealed cups", if applicable.
Q8- Please add that 10% bleach will be used, as described under liquid wastes and 70% ethanol as a general disinfectant.
Materials Used in Research: Please check the recombinant DNA box.
Recombinant DNA (Section H): Please complete this section. Complete Box 1 for prokaryotic rDNA manipulation work and answer questions 3-19 as appropriate. Your response to question 19 should be Section III-F.
LST: All clear for both members in the protocol
BUA Site Assessment: No issues with this new lab. EHS is helping them to set up everything that they need.
Recommendation: Conditional Approval/Pending (Reviewers don't want to see it again).
For: 15
Against: 0
Abstain: 0

5. Bhz Protocol 2121

"1. R21 MH106796:02 (ends March 31, 2017)
Visualizing Cortical Microstructures by Optical Coherence Tomography (OCT)
2.R21 MH107456-01 (ends August 31, 2017)
Regional diversity of cortical white matter neurons in adult and infant rhesus monkey"
Primary Reviewer: Frank Gibson
Secondary Reviewer: James Keeney
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: BUMC
Applicable NIH Guidelines: N/A
Protocol Expires: New protocol
Layman's Description: 1. An exciting new, cellular resolution imaging technique (optical coherence tomography, OCT) is being applied to postmortem human brain. The project entails validating that what appear to be cells in OCT-imaged tissue sections in fact correspond to cells. Overlay comparisons are made between digitised histological images (photomicrography) and OCT images of the same section.
2. A small but important number of neurons are scattered in the cerebral white matter and are particularly numerous in humans and nonhuman primates. We will investigate the organization and function of these neurons, in normal and pathological conditions.
Pre-Meeting Comments:
Reviewer 1:
Overall this new application appears fairly straightforward; however, there is a general lack of clarity regarding what is actually going on, and what the proposed work is to be accomplished and what is the status of the tissues regarding hazard risk. Also there is some lack of attention to details. Minor point - request that the PI change "under the fume hood" to "in the fume hood" throughout the application. Semantic matter, but does more accurately reflect where the procedures are occurring.
Principle Investigator Comments section: New Protocol - Is this a new investigator? Has BIO been obtained? Not clear what this is being indicated in regard to Dr. Medalla? Not sure if needed.
PI (Page 3): Unclear in summary of changes what this is referring to. If new application, then simply indicate this. Proper training is a key element in conducting research, and must be listed for each individual on the application (trained, or who will perform training of individuals that require it).
BU LST needed for couple of team members.
Lay description: Description of project 1 should be simplified. Project 2 description is OK.

Scientific maneuvers: any evidence of prion-associated disease in the individuals from which the brain tissue samples are to be used in these studies? Please detail maneuvers so that it is clear what is occurring and what risks/hazard management procedures are to be implemented. Delete references to literature. Any sense of B-virus status in NHP samples?
Section: Tissues from Dr. Rosene Lab: This section is not clear. Please delineate what will occur in the proposed studies. If sectioned materials will be obtained, then indicate this. If this lab will be performing tissue sectioning, then this needs to be clear. Regarding the tissues from the Rosene lab, what is/are species of origin? Are these only brain tissues, or are there other tissues to be examined as well? Are these fixed? For human brain tissues are prion diseases/exposure possible?
Last sentence of maneuvers section: Please clarify. This will be its own free-standing protocol. As such it needs to stand on its own descriptions and not cross-reference other applications.
PPE Q3: Are both forms of eye protection needed? If there are specific maneuvers that require one form of eye protection over another, please indicate where each form of eye protection is needed in the maneuvers section. Also, please check "other". Osmium is a high hazard chemical. Please detail in the maneuvers section where this and the other molecules will be used. Also, please clarify if this is a biosafety cabinet or a fume hood.
PPE Section Q6. Knives for tissue sectioning? PPE for these? Decontamination?
Q7A: Any chemical concerns regarding DAB+H2O2 treatment with 50% bleach and discarded? Possibly down the sink, but not defined. What about osmium?
Q11: Don't understand what "N.A. Ordered materials" are. Please clarify.
Section IX (page 15): Unclear why this is BSL-2. If all the material to be studied is fixed, then this should not be hazardous, unless there is use of unfixed tissues, or concerns related to the handling of tissues. If some material is not fixed, it is possible this could still be BSL-1 - say if unfixed material is rodent. However, with the BSL-2 level identified by the PI, then clarification as to why this BSL is chosen is needed. For example, maybe it could be appropriate to check off "Other Potentially Infectious Materials". In this event, greater clarification would also need to be placed in the maneuvers section.
Reviewer 2:
After seeing Dr. Gibson's extensive view of this application, I have only a few comments to make. This new BSL-2 study seeks to compare the results a new scanning technique of optical coherence tomography (OCT) to more conventional scans of histological tissue in order to clearly identify certain brain structures. I would like to be assured that the brain tissues being obtained from humans, monkeys and rodents are free of any infectious contaminants. The application makes mention that such processed tissue will be delivered to the lab - but how, and under what safeguards?
Also, why is no BSC not required for this lab work; that is not checked off in the application. And, since osmium is a dangerous substance, please clarify methods whereby it is introduced and disposed of from the lab.
Training of personnel involved in the study appears complete although one member is scheduled to depart in June.
If these assurances can be obtained, then I have no further community-related concerns about the study.
Meeting Comments:
It seems like PI is trying to develop new techniques of imaging brain tissues by Optical Coherence Tomography (OCT) and then compare the data with standard histology and immunocytochemistry. Techniques such as *in vivo* MRI images fall short of cellular-level resolution, whereas traditional histology, despite better resolution, is prone to processing distortions and is labor-intensive at a large scale. OCT is a novel application for postmortem analysis of brain tissue and is being considered a new bridge approach that produces histology-level images and can facilitate higher-resolution interpretation of MRI images. There were multiple issues with this application, the most important ones being unclear presentation of what exactly is going to be done and what will be the source material for various experiments. Description suggests that fixed brain samples from both human and non-human primates obtained from collaborators will be used but a lot more clarification on those issues are needed.

Reviewers wanted to see a revised application where these issues have been addressed.
The PI needs to:
Overview and Grant Funding Information: Please remove text from the summarize changes box. This is only for amendments and annual renewals. Your application should be stand-alone and there is no need to describe your previous association.
Research Project Description: Although the protocol seems to be straightforward, it was not clear what is actually going on in this particular protocol and what is to be accomplished. There is lack of coherence between scientific objectives and the procedures described.
Q1- Lay description is too technical. Please describe your work and your goals in simple non-technical language. Please make sure that the statement is consistent with the description in other sections.
Q2- Please describe what you do and what are your immediate future plans? The OCT imaging work, the source of material, the procedure, etc. are not described in the procedure section. It does not appear that a NHP model will be developed. Please clarify if use of live NHPs will be part of the work.
Q3. Please detail maneuvers so that it is clear what is occurring and what risks/hazard management procedures are to be implemented. Is there any evidence of prion-associated disease in the individuals from which the brain tissue samples are to be used in these studies? Take out reference to human tissues until you start working on human brain tissues.
Any sense of B-virus status in NHP samples? If the tissues are free of infectious agents, please clarify how that determination has been made. Delete references to literature.
Tissues from Dr. Rosene Lab: This section is not clear. Please delineate what will occur in the proposed studies. If sectioned materials will be obtained, then indicate this. If this lab will be performing tissue sectioning, then this needs to be clear. Regarding the tissues from the Rosene lab, what is/are species of origin? Are these only brain tissues, or are there other tissues to be examined as well? Are these fixed?
Please describe the use of Osmium tetroxide in the procedure section.
Last sentence of maneuvers section: Please clarify. This will be its own free-standing protocol. As such it needs to stand on its own descriptions and not cross-reference other applications.
PPE and SE: Q3- If both forms of eye protection are used, please indicate where you use one over the other.
Q6- Please indicate precautions used in using sharps and the type of container (hints available in RIMS next to the question).
Q7A- Is hydrogen peroxide and 50% bleach mixture approved by the EHS for treatment of liquid waste?
Materials Used in Research: Please check the high hazard chemical box.
High Hazard Chemical (Section F): Please complete this section for Osmium tetroxide
Unclear why this is a BSL-2 application. If all the material to be studied is fixed, then this should not be hazardous, unless there is use of unfixed tissues, or concerns related to the handling of tissues. If some material is not fixed, it is possible this could still be BSL-1 - say if unfixed material is rodent. However, with the BSL-2 level identified by the PI, then clarification as to why this BSL is chosen is needed. For example, maybe it could be appropriate to check off "Other Potentially Infectious Materials". In this event, greater clarification would also need to be placed in the maneuvers section.
LST: All clear.
BUA Site Assessment: New laboratory but now concern noted.
Recommendation: Conditionally approved (Reviewers want to see it again).
For: 15
Against: 0
Abstain: 0

6. Bhz **Protocol 2111**

"Behavior, Physiology, and Genomics of Development in South African vervet monkeys (*Chlorocebus pygerythrus*)"
Primary Reviewer: Debbie Stearns-Kurosawa

Secondary Reviewer: Andrew Kocsis
Biosafety Level: BSL2
Animal Biosafety Level: ABSL1 (Field Study)
Campus: CRC
Applicable NIH Guidelines: N/A
Protocol Expires: New protocol
Layman's Description: Obesity is a growing biomedical concern in the United States, but current research with rodent and human models are insufficient for understanding how obesity is influenced by long-term development and growth. My research group studies growth, development and obesity both in captive and wild vervet monkeys (the genus Chlorocebus) to get a better understanding not only of how diet and body size at different ages affect obesity, but also to better characterize and understand how the genetic factors that may underlie obesity function and evolve in the wild.

Pre-Meeting Comments:

Reviewer 1:

1. Section III, include PI. Description of PI experience is particularly relevant since he will be training undergraduate students.
2. Please clarify precisely and in some detail what work will be done by the PI and by the BU students. Will student perform lab work with samples at BU or will they accompany the PI on the field studies? Risk assessment is very different.
3. The PI comments that captive work at another institution is no longer active. Is this the work at Wake Forest? If so, please remove this description of animal sampling and measurements. If you are using stored samples from these animals, a statement to that effect is sufficient.
4. Please remove the details of DNA isolation, PCR and agarose electrophoresis, and provide brief summaries. Only a few sentences are needed. These are standard, fairly universal methodologies. Providing details in the protocol is a balance of providing enough to assess risk while allowing sufficient flexibility for experimental purposes.
5. Manipulation of fecal samples are described, but there is no description of manipulation of the other samples- hair, CSF, blood, ear tissue, or other microbiome collections (vaginal, penile, nasal, buccal, tongue swab). Please provide description of how/where these samples will be processed.
6. This is a BSL2 protocol and use of a biosafety cabinet is needed for manipulation of vervet biological fluids and tissue.
7. Liquid waste- please re-phrase to state that fresh bleach will be added to final 10%, let sit for 15-20 minutes, then flushed down the drain with water. Please remove disposal by solid waste. I think you mean this to be used for small spills- it is better to state that small spills will be decontaminated with 70% ethanol, wiped up and disposed in solid biological waste container.
8. Solid waste- please state that when the biohazard waste box is about 75% full, it will be sealed for disposal.
9. Disinfectant- suggest you add 70% ethanol to this list. Bleach is very corrosive and may not be a good choice for all situations.
10. Please check ABSL2 for the animal biosafety level
11. Section IXB- please add CSF, nasal/vaginal/penile/buccal/tongue swabs,

Reviewer 2:

Here are my thoughts for 2111. It was a very well written protocol, but I do have some comments.

Section VIII.4.

- Please check the PPE that will be worn during animal manipulations.

Section VIII.5

- Will BSCs be used for processing the samples brought back to the lab?

Section VIII.6.

- This should be checked yes as there is injections and blood sampling in this protocol.

Section VIII.7.

- Is this the procedure for field liquid waste as well?

Section VIII.8.

- How is solid waste handled in the field?

Section E.2.

- Please list the ABSL level of working with this animal in the field. Based on the zoonoses potentials listed, it appears that ABSL-2 would be appropriate.

Meeting Comments:

PI wants to compare growth, development and obesity in wild type and captive vervet monkeys to determine how genetic factors and diet influence obesity. Peripheral blood, microbiome, and morphometric measurements will be acquired from approximately 500 wild-caught vervets in South Africa. Each of these animals will be humanely trapped while in its social group, briefly anesthetized, sampled from, then re-released once its health status is confirmed to be good. Important laboratory procedures include isolation and preparation of genetic samples for sequencing genomic and mitochondrial DNA. PI provided clear description of sample collection procedure and excessive detail laboratory procedures. However, it was not clear whether students will participate in field studies and if so, whether PI will accompany them. Some of the objectives of the protocol will be done in other institutions but it was not clear which of the laboratory procedures will be done in Boston University. Some of the sample collection procedures also require further clarification as described below.

The PI needs to:

Personnel Information: Please Include yourself (the PI) in the personnel list and all associated questions as has been done for the other members of the protocol (the "rDNA/Infectious Agent/Select Agents" question and the "State how many years experience, when and where" question).

Please clarify precisely here and in some detail in section VII.3 what work will be done by the PI and by the BU students.

Research Project Description:

Q3- Will student perform lab work with samples at BU or will they accompany the PI on the field studies? Risk assessment is very different.

Manipulation of fecal samples are described, but there is no description of manipulation of the other samples- hair, CSF, blood, ear tissue, or other microbiome collections (vaginal, penile, nasal, buccal, tongue swab). Please provide description of how/where these samples will be processed.

Please remove the details of DNA isolation, PCR and agarose electrophoresis, and provide brief summaries. Only a few sentences are needed. These are standard, fairly universal methodologies. Providing details in the protocol is a balance of providing enough to assess risk while allowing sufficient flexibility for experimental purposes.

PPE and SE: Q1- Check animal handling and cage changing.

Q2 and Q5- This is a BSL2 protocol and use of a biosafety cabinet is needed for manipulation of vervet biological fluids and tissue. If the biological materials are already inactivated or processed with SDS-buffer (as the Biosafety Officer indicated in the meeting), the information must be stated clearly in the laboratory procedure section.

Q6- This should be checked 'yes' and described, as there is injections and blood sampling in this protocol.

Q7A-Liquid Waste: please re-phrase to state that fresh bleach will be added to final 10%, let sit for 15-20 minutes, then flushed down the drain with water. Please remove disposal by solid waste. I think you mean this to be used for small spills- it is better to state that small spills will be decontaminated with 70% ethanol, wiped up and disposed in solid biological waste container. Also, is this the procedure for field liquid waste as well?

Q7B- Solid waste- please state that when the biohazard waste box is about 75% full, it will be sealed for disposal. How is solid waste handled in the field?

Q8- We suggest that you add 70% ethanol to this list as well. Bleach is very corrosive and may not be a good choice for all situations.

Materials Used in Research: Please select the highest animal biosafety level for your work. Based on the zoonoses potentials listed, it appears that ABSL-2 would be appropriate for your study.

Other Potentially Infectious Material (Section B): Please also add in this section the CSF, nasal, vaginal, penile, buccal and tongue swabs.

LST: Lab safety training are clear for all members. Students will not be exposed to any blood and serum. Local veterinarian will take care of the processes. These details need to be in the protocol.
BUA Site Assessment: No issues with the site assessment. All manipulations will be done in the field – will be mixed with SDS buffer (DK: those details are not there in the protocol).
Recommendation: Conditionally Approved (Reviewers want to see it again).
For: 15
Against: 0
Abstain: 0

C. 3-Year Resubmissions

7. rDNA/Bhz **Protocol 639**

"The Role of B Cells and B Cell Toll-like Receptors in Glucose Intolerance; The Role of T cells in the Transition to Type 2 Diabetes; Origin and Function of an Inflammatory T cell Subset Balance in Type 2 Diabetes; Immune system in obesity-associated periodontal disease; Breast tissue immunophenotyping"
Primary Reviewer: Debbie Stearns-Kurosawa
Secondary Reviewer: Andrew Kocsis
Biosafety Level: BSL2
Animal Biosafety Level: ABSL2
Campus: BUMC
Applicable NIH Guidelines: Sept. 2009; Section III D, Appendix BII A, D (risk group 2); BV1 (risk group 1); no special practices
Protocol Expires: 6/10/2016
Layman's Description: The project will determine how cells change the ways they use their DNA and proteins during disease states, and how to manipulate the cells so that these altered traits may be returned to normal to alleviating disease. The work is with cell lines that have been used in labs for 20 years, with primary human cells and tissues from healthy individuals or diabetic patients, or women undergoing elective breast reduction, and from lean and obese mice from a commercial vendor or bred at BUSM.
Pre-Meeting Comments:
Reviewer 1:
3 year renewal review May 2016. Well organized and methods described. Only a few comments:
1. Please complete training information for Belkina, Cappione, Zhu; update training, ROHP for lab members and PI
2. In maneuvers section, please state that the lentiviral system is replication incompetent. I suggest inserting the following, which was taken from the PI's description of the vector packaging system on page 22: "The use of a five plasmid transfection system in which the viral genome is split between the helpers, ensure that no replication competent particles are generated, as the only RNA that get packaged is the one containing the packaging signal which contains the transgene of interest."
3. In maneuvers section, please provide some brief information about sources of human tissues. Are these surgical samples?
4. VIII #1- not clear how razor blades will have the potential to produce aerosols or droplets. Please clarify in the maneuvers section VII.3. Or- remove from this table. Use of razor blades is described later in the sharps section.
5. Liquid waste- please include decontamination of liquid waste; e.g., addition of fresh bleach to 10% final, let sit for 15-20 minutes, then discard down drain.
Amendment to add *P. gingivalis*:
1. Complete/update Section III, tables 1 and 2 for DeFuria, Zhu and PI
2. What will be done with the *P. gingivalis*? How will it be grown, processed, stored, disposed, decontaminated? There is no information to judge what will be done with the bacteria other

than used as oral gavage in mice.
3. Complete VIII-5 for BSC information
4. Section IX B- move the *P. gingivalis* to section A and complete table. This is bacteria- not cells or bugs

Reviewer 2:

I have looked over Dr. Nikolajczyk's renewal and I only have a couple minor comments.
Section VII.3

- What generation of lentivirus construct is being used? It appears maybe a fifth, but I am unsure.
- For the mouse IP injections, is this done with an infectious agent or with some non-hazardous experiment compound?

Section VIII.1

- Please clarify where razor blades are being used, it is not clear in section VII.3 what their use on this project is.

Section VIII.2.

- Please indicate if gasket blenders/homogenizers are being used.

Section VIII.7.

- Expand on how the liquid waste will be treated and disposed, this currently only describes collection of the waste.

Meeting Comments:

PI in this protocol is trying to understand how changes in the extracellular environment or stimulation affect gene expression and function of immune cells which play important role in diseases, such as type 2 diabetes, periodontal disease or breast inflammation. They will treat cell lines or primary cells obtained from human and mouse blood or tissues with stimulants. Cells will also be subjected to lentiviral vectors or siRNAs for the purpose of overexpression or downregulation of specific genes. In some experiments wild type or genetically engineered mice will be treated with high-fat diet and tested for blood and adipose tissue chemistry. To test the role of obesity in periodontal disease some of the high-fat diet fed mouse will also be treated with *Porphyromonas gingivalis* (the bacteria associated with gum disease). The protocol is well organized and the procedural descriptions were nice. Handling of biohazardous material and waste management sections are well described. However, few technical clarifications and corrections as described below are needed.

The PI needs to:

Overview and Grant Funding Information: Please remove text from the summarize changes box. This is only for amendments and annual renewals.
Investigator Contact Information: Please provide the name of the lab safety coordinator. In the absence of a designated LSC, PI himself can serve as LSC.
Personnel Information: Please answer the "rDNA/Infectious Agent/Select Agents" question for Jennifer and Min. Please answer the question "State how many years experience, when and where" for Anna.
Research Project Description: Q3- Although you have detail description of retroviral and lentiviral vectors to be used in your study, reviewers suggested that please also insert in the laboratory procedure section part of that description to indicate that they are replication incompetent – "The use of a five plasmid transfection system in which the viral genome is split between the helpers, ensure that no replication competent particles are generated, as the only RNA that get packaged is the one containing the packaging signal which contains the transgene of interest".
Please provide some brief information about sources of human tissues. Are these surgical samples?
Is mouse IP injection done with an infectious agent or with some non-hazardous experiment compound?
PPE and SE: Q1- Not clear how razor blades will have the potential to produce aerosols or droplets. Since razor blade is already mentioned in Q6, please remove razor blade from Q1 response. Also, indicate the purpose of razor blade in your study.
Q7A- Liquid waste- please include decontamination of liquid waste; e.g., addition of fresh bleach to 10% final, let sit for 15-20 minutes, then discard down drain.

Other Potentially Infectious Material (Section B): Please move the *P. gingivalis* to section A and complete the table. This is bacteria- not any primary or unfixed human or NHP cells.
LST: All clear.
BUA Site Assessment: Fume hood ordered. Otherwise lab is OK.
Recommendation: Conditionally Approved/pending (Reviewers don't want to see it again).
For: 15
Against: 0
Abstain: 0

8. rDNA/Bhz Protocol 618

"A system biology approach to tuberculosis-Gene regulation in Mycobacterium tuberculosis"
Primary Reviewer: Robin Ingalls
Secondary Reviewer: Jim Keeney
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: NEIDL
Applicable NIH Guidelines: Section III-D-1, Appendix B-11-A, Appendix G-II-B-1
Protocol Expires: 6/26/2016
Layman's Description: The overall goal of this research is to better understand how bacteria related to tuberculosis turn their genes on and off and how this affects the microbe's ability to adapt host environment. By studying these relatives of the tuberculosis bacterium, we hope to gain a better understanding of the disease-causing bacterium itself.
Pre-Meeting Comments:
Reviewer 2:
This is a 3-yr, renewal BSL-2 study from the School of Engineering. My records show that this study or a version of it has been reviewed by IBC on at least three prior occasions, in 2012, 2013, and 2014. It seeks to use non-pathogenic versions of the infectious TB organism to better understand how transmission of the disease occurs. In two cases, the word "grown" is misspelled. Training of personnel seems up-to date. In my opinion, transport techniques for bacteria from Harvard could be better explained. However, disposal techniques seem adequate. The BSC certification is old, dating back to 3/12.
As the community representative, I have no further objections to the study continuing.
Reviewer 1:
Clearly written protocol, adequate precautions for handing these agents.
Additional comments:
Remove PI comments from the beginning of the protocol -- these seem to be related to prior versions?
Some of the columns in the personnel tables (training, title, etc.) are missing or misplaced.
Solid and liquid waste should be separated.
Lots of typos but it is clear what he is doing.
Meeting Comments:
PI in this protocol uses non-pathogenic relatives of *Mycobacterium tuberculosis*, such as *M. bovis BCG, M. smegmatis* and others to understand how these organisms control their own gene expression. PI's group will clone and characterize transcription factors from these organisms and will determine experimentally to which promoters these transcription factors bind to. PI will utilize knowledge gained from these studies to design better therapeutics using system biology approach. The protocol will use variety of molecular cloning work as well as standard molecular biology work. PI provided detailed description of all laboratory procedures to be used in the protocol and addressed biosafety concerns and waste management. Only few minor issues as listed below need to be addressed.
The PI needs to:
PI Comments: Please delete old comments or else date them, so that IBC office can find the change in the current submission.
Personnel Information: Please provide title of yourself and Patricia. Please answer the "rDNA/Infectious Agent/Select Agents" questions for yourself.

Research Project Description: There are several typos throughout the application that needs to be corrected.
Q3- Reviewers want to know how the bacteria have been transported from Harvard to your lab.
PPE and SE: Q5- Please provide recent certification date for your biosafety cabinets.
Q7A- Please remove the description of solid wastes from Q7A (Should go to Q7B).
Q12- Please answer this question.
Recombinant DNA (Section H): Q5 – Make a selection.
Agreement Policy: Please check the last box regarding ROHP clearance requirement.
Please NOTE that BUA site assessment must be completed before this protocol may be approved. Please contact Joe Barbercheck (617-638-8842) to have this assessment done. Also, your own lab safety training and rDNA/IBC Policy training must be updated.
LST: Except for the PI, all clear.
BUA Site Assessment: BUA not done yet.
Recommendation: Conditionally Approved/pending (Reviewers don't want to see it again).
For: 12
Against: 0
Abstain: 0

9. rDNA/Bhz Protocol 648

"Role of ACLP in Vascular Smooth Muscle Biology; Regulation of fibroblast and myofibroblast transitions"
Primary Reviewer: Elke Muhlberger
Secondary Reviewer: Erin Sawyer
Biosafety Level: BSL2
Animal Biosafety Level: ABSL1
Campus: BUMC
Applicable NIH Guidelines: Sections III-D-2, III-D-3, III-D-4 and III-E-4; Appendices B and G.
Protocol Expires: 6/26/2016
Layman's Description: The primary goal of our research is to understand the mechanisms of fibroproliferative diseases (organ fibrosis, vascular disease, and cancer). This work may lead to the discovery of proteins that contribute to, or inhibit the development of these disease processes.
Pre-Meeting Comments:
Reviewer 1:
VII.3. Laboratory Procedures
Please rephrase the following sentence "*These experiments will not use sharps and will aerosolization such as aspiration*." as follows: "*These experiments will not use sharps and will not lead to aerosolization by aspiration*."
Will animals be injected with plasmid DNA? If this is the case, please add to procedure section.
VIII, PPE
ad 7A. Move solid waste part to section 7B.
ad 11. Some of the sentences seem to be incomplete. Please fix.
IX. Materials Used in Research
Check ABSL1
Reviewer 2:
Would isoflurane be used in hood or on bench? What is the fixative?
Meeting Comments:
The PI is interested in the study of regulation of gene expression in vascular smooth muscle cells and fibroblasts *in vitro* and *in vivo.* In particular, his interest is to identify molecular mechanisms of the functional regulation of an extracellular matrix protein called aortic carboxypeptidase-like protein (ACLP) that promotes smooth muscle cell proliferation and fibrosis. They are using several molecular biology techniques to study the transcription of genes *in vitro* using transient transfection as well as adeno- and retroviral vector-mediated gene expression in a variety of rodent and human smooth muscle and fibroblast cells. They will overexpress these factors to define their roles *in vitro*. They will also use a mouse femoral injury and fibrosis model to study

the interaction of ACLP with other proteins and its ability to alter the phenotype of cells *in vitro* and *in vivo* as it relates to vascular disease and fibrosis. The protocol is nicely written with well-described sections of management and disposal of biohazard materials. Reviewers only asked for few minor edits and clarifications as described below.

The PI needs to:

Research Project Description: Q3- Please rephrase the following sentence "*These experiments will not use sharps and will aerosolization such as aspiration*." as follows: "*These experiments will not use sharps and will not lead to aerosolization by aspiration*."

Will animals be injected with plasmid DNA? If this is the case, please add this to the procedure section.

Would isoflurane be used in hood or on bench? What histological fixative will be used for the animal work?

PPE and SE: Q7A- Please remove the description of solid wastes from Q7A (Should go to Q7B).

Q11- Some of the sentences seem to be incomplete. Please fix.

Materials Used in Research: Please select the highest animal biosafety level for your work (should be ABSL-1).

LST: All clear

BUA Site Assessment: Lab is in good shape.

Recommendation: Conditionally Approved/pending (Reviewers don't want to see it again).

For: 12

Against: 0

Abstain: 0

10. rDNA/Bhz **Protocol 642**

"Dynamics of the Vascular Smooth Muscle Cytoskeleton
The Role of the Cytoskeleton in Vascular Aging"

Primary Reviewer: Elke Muhlberger

Secondary Reviewer: Bob Timmerman

Biosafety Level: BSL2

Animal Biosafety Level: N/A

Campus: CRC

Applicable NIH Guidelines: Guide from September 2009: SECTION III-D-1-A, APPENDIX C-II, APPENDIX GII-B

Protocol Expires: 6/12/2016

Layman's Description: We are studying the proteins that are responsible for regulating the degree of narrowing of blood vessels. It is hoped that the new proteins we identify may eventually lead to the identification of new candidates for drug development. Our work has relevance to cardiovascular diseases such as stroke and hypertension.

Pre-Meeting Comments:

Reviewer 2:

This protocol is investigating the loss of flexibility of the smooth muscle cytoskeleton of the proximal aorta. This vessel acts to smooth pressure pulses from the heart, to reduce the effect of those pulses downstream. This is a general problem with all pumping equipment where the pumping takes place in discrete steps, such as the heart, but also large piston pumps for pumping liquids in industry. Many fire engines used piston pumps up into the 1930s, and they featured beautiful, nickel plated air domes next to the pumps, to produce a smooth discharge.

Dr. Morgan is attempting to develop an explanation for the loss of elasticity of the smooth model, in the hope of preventing it or reversing it.

There do not appear to be any problems with this Level 2 protocol. The potential hazards appear to be confined to the Biosafety cabinet, which has up to date approval. The PI has up to date safety training.

There are some insignificant omissions of safety procedures in the Site Assessment.

As there does not appear to be any hazard to the community, I recommend that this protocol be approved.

Additional comments from Reviewer 2:

This protocol concerns the deterioration of the smooth muscle of the proximal aorta, which functions as a shock absorber to smooth the pulsations of the heart muscle.
The need for smoothing pulsations in pressure waves from the heart is analogous to filtering a rectified voltage in electrical engineering. This is a *very* well studied problem. I wonder if a future collaboration between the present PI and an electrical of biomedical engineer would produce useful insights.
Reviewer 1:
VII.3. Laboratory Procedures
Please briefly describe experimental procedures that will be done using the various cell lines.
VIII, PPE
ad 1. Check *Pipetting infectious liquid* (NHP cell culture)
ad 2. Check *Work that produce/or potentially produce aerosols are done in the Biological Safety Cabinet or other containment equipment*
ad 7A, liquid waste. Describe how liquid waste will be disposed. Red bags cannot be used to dispose liquids.
ad 7B, solid waste. Describe how sold waste will be disposed. Use the blurb provided by IBC.
ad 11, transport of material. Please rephrase as follows: "*Cells are kept in a freezer in room 426A. The area is kept locked at all times. Frozen material is transported to the tissue culture lab (402C) in a leak-proof, shatter-proof container. After transport to 402C, the container is opened in the biosafety cabinet for use."*
IX, Section H. Recombinant DNA
ad 1. Remove explanation in Vector Packaging System Box. N/A is sufficient.
Meeting Comments:
PI is this protocol is interested in understanding the role of vascular smooth muscle cells in regulating the flexibility of blood vessels. The broad objective of this study is to define molecular mechanisms of aging-associated malfunction of actin cytoskeleton structure and its relationship with the function of proteins associated with focal adhesion complex in vascular tissues. In representative cell culture models they will analyze the effect of small molecule inhibitors and peptide mimics together with other biomechanical approaches to test the cause-and-effect relationship between changes in cytoskeleton and aortic tissue stiffness. Reviewers felt that the description of laboratory procedures, particularly the use of the various cell lines mentioned in recombinant DNA section is either very brief or absent. In addition, several sections of the application are not completed carefully.
The PI needs to:
Personnel Information: Biosafety Officer indicated that more individuals are possibly working in your lab. If so, please include them in the personnel list and respond to all associated questions.
Research Project Description: Q3- Please describe briefly the experimental procedures using various cell lines to understand how different protocol objectives mentioned in question 2 are investigated.
PPE and SE: Q1- Check *Pipetting infectious liquid* (NHP cell culture)
Q2- Check *Work that produce/or potentially produce aerosols are done in the Biological Safety Cabinet or other containment equipment*.
Q7A- Liquid waste. Describe how liquid waste will be disposed. Red bags cannot be used to dispose liquids.
Q7b- Solid waste. Describe how sold waste will be disposed. Use the hints provided in RIMS next to the question.
Q11- Please rephrase as follows: "*Cells are kept in a freezer in room 426A. The area is kept locked at all times. Frozen material is transported to the tissue culture lab (402C) in a leak-proof, shatter-proof container. After transport to 402C, the container is opened in the biosafety cabinet for use."*
Recombinant DNA (Section H): Remove explanation in Vector Packaging System Box. N/A is sufficient.
LST: Clear.
BUA Site Assessment: No problem with the lab. But more personnel are possibly working in the lab. Protocol only lists the PI.
Recommendation: Conditionally approved (Reviewers want to see it again).

For: 12
Against: 0
Abstain: 0

11. rDNA/Bhz **Protocol 1781**

"Regulation of HIV transcription and Latency by Cellular Mechanisms"
Primary Reviewer: Elke Muhlberger
Secondary Reviewer: Bob Timmerman
Biosafety Level: BSL2+
Animal Biosafety Level: N/A
Campus: BUMC
Applicable NIH Guidelines: These experiments would fall under NIH guidelines section III-D-1, appendix B-IIID, Appendix G-II-C-II
Protocol Expires: 6/11/2016
Layman's Description: The primary goal of this research is to gain a better understanding of how HIV is controlled in different cells. Our work will identify new ways to make HIV more susceptible to current antiretroviral treatments.

Pre-Meeting Comments:

Reviewer 1:

VII.3. Laboratory Procedures
Please provide brief description of *E. coli* work.
VIII, PPE
ad 1. Check *Culture stirrers, shakers* and *Plating, colony counting* (BSL1 cloning work)
ad 5. Add BSC certification date
IX, Section A. Hazardous Biological Agents
Remove blood and tonsil from list
IX, Section H. Recombinant DNA
Not clear why heat-killed *Porphyromonas gingivalis* is listed here.

Reviewer 2:

I have but a few comments:

7. Dr. Henderson's training appears to be almost expired.
8. Training for some other members of his staff seems to be past due
9. It appears that two different emergency contacts are to be provided, only one is furnished.
10. Certification date of Biosafety cabinets is not given.
11. In the PI's introduction, several additional members of his team are listed who are not listed in the protocol. Please explain.

These are minor edits; the protocol can be approved upon completion of the edits.

Meeting Comments:

PI is interested in characterizing how cellular gene transcription mechanisms regulate replication of HIV in target cells such as in T-cells and macrophages. Specifically, PI will study how transcription elongation represses HIV transcription and initiates chromatin remodeling events. Role of specific signaling molecules and kinases in controlling HIV entry and release will also be studied. Virus receptors and down-stream signaling molecules are either overexpressed or downregulated using siRNA or hnRNA to understand their contribution in regulating HIV expression. In addition to commercially available cell lines, primary macrophages, T-cells or tonsils obtained from healthy donors (from IRB exempt sources) will be infected with HIV clones and then treated with cytokines or phorbol esters. In some cases commercially available replication-incompetent lentiviral vectors will also be used. HIV transcription and replication are then monitored by standard molecular biological assays. All live HIV work will be performed in specially secured BSL2 suites where BSL3 practices are followed. Culture supernatants or infected cells will be inactivated by detergents or by paraformaldehyde before bringing them on to the general BSL2 lab bench or for imaging work. Biosafety issues have been described well throughout the application. PI marked 'yes' to one of the DURC questions for making VSV-G-pseudotyped viruses for wider cell line specificity. Reviewers considered that as a standard

approach and not a DURC issue. Only minor clarifications as described below, was requested by the reviewers.

The PI needs to:

Research Project Description: Q3- Please provide brief description of E. coli K12 work (example: we grow 500 ml liquid cultures of nonpathogenic E. coli K12 for plasmid isolation using standard plasmid extraction methods).

PPE and SE: Q1- Please check *Culture stirrers, shakers* and *Plating, colony counting* (BSL1 cloning work).

Q5- Please add Biosafety Cabinet Certification dates.

Hazardous Biological Agent (Section A): Remove Blood and Tonsil from this list.

Recombinant DNA (Section H): Prokaryotic Experiments: Not clear why the statement "In collaboration with Gibson lab we have used heat killed Porphyromonas gingivalis." Is here.

LST: Clear for all members.

BUA Site Assessment: All clear.

Recommendation: Conditionally approved/pending (Reviewers don't want to see it again).

For: 12

Against: 0

Abstain: 0

12. Bhz **Protocol 661**

"Biocompatibility of Dental Materials"

Primary Reviewer: Frank Gibson

Secondary Reviewer: John Gonsalves

Biosafety Level: BSL2

Animal Biosafety Level: N/A

Campus: BUMC

Applicable NIH Guidelines: N/A

Protocol Expires: 6/12/2016

Layman's Description: This project is designed to develop the biocompatible materials for dental root canal fillings and implants. The ceramic materials will be compared with titanium materials for their biosafety and efficacy. The effects of these materials on cell attachment, proliferation, and differentiation will be tested using normal primary osteoblasts and dental pulp cells as well as fibroblasts purchased from ATCC.

Pre-Meeting Comments:

Reviewer 1:

This appears to be a fairly straightforward application. Some concerns related to the need for updated trainings. Admin Point: IRB approval is indicated for this project and a number is listed in the maneuvers section. I do not know the IRB approval date listed in this application. Would like it if IBC could confirm that this IRB is in good standing.

Interactions with BU Cores: Is there potential for infectious material to be contained in the growth medium? Need to consider treatment or neutralization?

Description of scientific maneuvers: Rather than citing literature for pulp cell extractions/handling, please provide sufficient detail of the procedures for cell isolations and other maneuvers to be performed. Include PPE, safety/risk, and procedures necessary to reduce risk of exposure. Also include aspects of waste stream management. As human samples are to be used, suggest addition of language to indicate that individuals will perform studies using universal precautions.

PPE: In the maneuvers section, please describe how each of the checked items in VIII Q1 will be employed and PPE used.

Are all of the PPE listed in Q3 required? If not, please revise, if so, please define in the maneuvers section where each form of PPE will be employed.

Update BSC recertification needed.

PI resubmitted on 5/12/16 to update BSC certification date.

Reviewer 2:

Simplify the layman's term.

Meeting Comments:
PI of this protocol wants to investigate biocompatibility of dental materials used for root canal filling and implants. Human fibroblast cell lines obtained from ATCC will be cultured on ceramic or titanium dental materials to test cell attachment, cell proliferation and cell differentiation. Additionally normal primary dental cells (osteoblasts and dental pulp cells) isolated from waste bone chip or waste teeth obtained through IRB approved protocols will also be tested similarly. Reviewers wanted actual description of the procedure for isolation of dental cells from primary human tissues instead of cited references. Few other minor issues as listed below also need to be addressed. However, there was no major concerns with the protocol.
The PI needs to:
Personnel Information: Majority of personnel listed are identified as "Students". All but one person indicated as having experience. Not sure what level these students are at? Ph.D. or Masters-level, or undergraduates?
Core Facility Utilization Form: Is there potential for infectious material to be contained in the growth medium? If yes, please state they are disinfected before bringing to the core or clarify.
Research Project Description: Q3- Rather than citing literature for pulp cell extractions/handling, please provide sufficient detail of the procedures for cell isolations and other maneuvers to be performed. Include PPE, safety/risk, and procedures necessary to reduce risk of exposure. Also include aspects of waste stream management. As human samples are to be used, suggest addition of language to indicate that individuals will perform studies using universal precautions.
PPE and SE: Q3- Are all of the PPE listed required? If not, please revise, if so, please define in the maneuvers section where each form of PPE will be employed.
Q8- Please mention that the bleach will be 'freshly made 10%'. Also include 70% ethanol as a general disinfectant.
Q10- Please describe the security of room X220 (card key or such).
Materials Used in Research: Please check the Other Potentially Infectious Material box and complete section B.
Hazardous Biological Agent (Section A): Remove normal human osteoblasts and primary human pulp cells from this list. They should go to section B.
Other Potentially Infectious Material (Section B): Complete this section for normal human osteoblasts and primary human pulp cells.
LST: Clear for all members.
BUA Site Assessment: Recent certification date for the biosafety cabinet is 12/22/15.
Recommendation: Conditional Approval/Pending (Reviewers don't want to see it again).
For: 12
Against: 0
Abstain: 0

13. Bhz **Protocol 1788**
"Provide services related to the use of Flow Cytometer analyzer and cell sorting instruments"
Primary Reviewer: Frank Gibson
Secondary Reviewer: Rosina Georgiadis
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Campus: BUMC
Applicable NIH Guidelines: N/A
Protocol Expires: 6/26/2016
Layman's Description: Our goal is to take mixtures of cells and try to understand what proteins are present in and on the surface of the cells. This helps understand the cell's biology and functions. Also we separate heterogeneous mixtures of cells into purified populations. This will allow researchers to work with them in their labs under controlled situations. The hazards associated with this separation procedure are not applicable to the community but do apply to people that are in the room at the time. Several precautions and safeguards are in place to reduce the risks to below reasonable levels
Pre-Meeting Comments:

Reviewer 1:
Overall this application is in very good shape.
Personnel: Little bit of info on experience for all individuals would be helpful
BU LST needs to be confirmed for all folks.
Maneuvers: please clarify that IBC approval is obtained as part of the project review with the Core users.
BSC recertification needed.
Page 15. Highest BSL: The check-off of BSL-2 does not align with the ID in the protocol where studies that are designated BSL-2 with special precautions are permitted. Please clarify.
Agreement Policy: Reason why last box is not checked off?
Reviewer 2:
I don't have more to add on Frank's comment.
Meeting Comments:
This is the Flow Cytometry core facility IBC protocol application. This core provides service to the BU researchers who want to analyze proteins on the surface or inside of a cell. The core also provide service for separating cells on the basis of identifiable cellular marker protein. Because of the nature of the service, the core depends on investigator's own IBC approval of the work. The PI of the core detailed variety of biosafety issues that they encounter and how they handle them. PI marked it as a BSL2+ protocol, although the reviewers felt that the BSL2+ designation is not necessary.
The PI needs to:
Personnel Information: Please answer the "rDNA/Infectious Agent/Select Agents" questions for yourself and Anna. Please answer the question "State how many years experience, when and where" for all personnel.
Research Laboratory Facility Information: Please clarify the BSL designation of the room X324. Is BSL2+ appropriate?
PPE and SE: Q7A- Please remove the description of solid wastes from Q7A.
Materials Used in Research: Highest BSL remains a point of confusion: The check-off of BSL-2 does in this section not align with the marking in section IV in the protocol where studies that are designated BSL-2 with special precautions are permitted as indicated in the maneuvers. Please clarify. Please consult with Biosafety Officer Joe Barbercheck.
Agreement Policy: Please check the ROHP clearance related box.
Please NOTE that your (PI) rDNA/IBC Policy training has expired and must be updated for the approval of this protocol.
LST: PI's lab safety training (rDNA/IBC Policy) is not complete yet.
BUA Site Assessment: No problem with the core facility. BSL2+ is not necessary.
Recommendation: Conditional Approval/Pending (Reviewers don't want to see it again).
For: 10
Against: 0
Abstain: 0

IV. Approved Amendments & Annual Renewals

AmE1. Protocol 679

"1. Development of Klotho enhancers as novel therapeutics for AD. Start date: 6/1/2013. End date 5/31/2016 2. Development of novel APP dimerization inhibitors that lower Abeta levels. Start date: 9/1/2015. End date 8/31/2016"
Biosafety Level: BSL2
Animal Biosafety Level:
Type: Expedited Amendment
Modification: To include CRISPR/Cas9 gene editing plasmid

AmE2. Protocol 1459

"Uremic vascular disease and cancer biology"

Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Expedited Amendment
Modification: To add 4 new personnel and delete two personnel

AmE3. Protocol 1643

"Mechanisms of Autoimmune Disease"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Expedited Amendment
Modification: To add a common NEIDL room for microscopy

AmE4. Protocol 1203

"1) Exosome-mediated Dissemination of Tau Aggregation in Alzheimer's Disease 2) Invention and Clinical Application of Protein Kinase Inhibitors 3) Clinical evaluation of LRRK2 inhibitors on inflammatory responses in Crohns and Parkinsons diseases 4) The cellular mechanism of tau dissemination 5) Exosome pathway as a novel therapeutic target of tauopathy 6) Characterization of Microglial Wnt signaling in maternal immune activation-related autism"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Type: Expedited Amendment
Modification: To update personnel training detail

AmE5. Protocol 1459

"Uremic vascular disease and cancer biology"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Expedited Amendment
Modification: To include sharp use and add one personnel

AmE6. Protocol 2012

"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: ABSL-2
Type: Expedited Amendment
Modification: To add one new personnel

AmE7. Protocol 935

"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 Alzheimers 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"
Biosafety Level: BSL2+
Animal Biosafety Level: ABSL-2

Type: Expedited Amendment
Modification: To add one personnel and change funding information

AmR1. Protocol xxxx

"xx"
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Type: Amendment Review
Modification: To add *xx*

AnR1. Protocol 964

"Molecular Systematics and Population Genetics of Birds"
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: To delete personnel

AnR2. Protocol 1605

"Cell Wall Integrity Signaling in Yeast Control of Transcriptional Attenuation of Stress-induced Genes in Yeast"
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: To delete personnel

AnR3. Protocol 826

"Use of expression plasmids for protein production and site-directed mutagenesis"
Biosafety Level: BSL1
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: To change personnel

AnR4. Protocol 1996

"AMPA receptor tracking and synaptic plasticity"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To add personnel and modify adenovirus use protocol

AnR5. Protocol 1805

"Suppression of genomic instability by tuning the DNA damage response at telomeres"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To add a personnel and add several human cell lines

AnR6. Protocol 1362

"Characterization of *Escherichia coli* infection and Shiga toxin type-2 in vitro and in vivo models"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To change personnel

AnR7. Protocol 1261

"Bacteria studies relevant to 1) Nonhuman Primate model and pathogenesis of anthrax sepsis; 2) Translation of immunologic technologies from basic research into pre-clinical nonhuman primate (baboon) models to evaluate protection from B. anthracis; 3) Shiga-toxins: Pre-clinical animal model development and therapeutic testing; 4) Development and Treatment of Pre-Clinical EHEC Models with HUS"
Biosafety Level: BSL2+
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To change personnel

AnR8. Protocol 2024

"Molecular pathomechanism of hereditary pancreatits Pancreatic elastases Chymotrypsin C in pancreatitis Mouse models of human hereditary pancreatitis"
Biosafety Level: BSL2
Animal Biosafety Level:ABSL-1
Type: Annual Renewal
Modification: To add two personnel

AnR9. Protocol 1285

"Insulin regulation of cell nutrition Secretion from adipose cells Regulation of lipolysis"
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: To add two personnel

AnR10. Protocol 1231

"PPARs and Periodontal Disease - Innate immunity, lipid signaling and chronic infection - Interactions of *Porphyromonas gingivalis* with adipocytes: pathogen-specific modeling of blood microbiome and inflammatory change in obesity - Oral macrophage function in the context of periodontal disease and HIV infection"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Type: Annual Renewal
Modification: To remove ABSL-2 work

AnR11. Protocol 793

"Bacterial lysis on a microfluidic device"
Biosafety Level: BSL2
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: To add 4 new personnel and modify sharp disposal procedure

AnR12. Protocol 1214

"Next Generation Therapeutics for Hemoglobinopathies, and Novel Globin Gene Modulators, and Oral agents to stimulate neutrophils, Oral therapeutic to promote healing of refractory wounds"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-1
Type: Annual Renewal
Modification: Minor changes in wording

AnR13. Protocol 1339

"Restoration of Immune Homeostasis by Nuclear Receptors During HIV Infection Oral Macrophage Function in the Context of Periodontal Disease and HIV Infection"
Biosafety Level: BSL2+
Animal Biosafety Level: N/A
Type: Annual Renewal
Modification: No change

AnR14. Protocol 1299

"Toxin Studies relevant to: Shiga-toxins: Pre-clinical animal model development and therapeutic testing; Development and Treatment of Pre-Clinical EHEC Models with HUS"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To change personnel

AnR15. Protocol 998

"Control of TNF Alpha Gene Expression"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL-2
Type: Annual Renewal
Modification: To delete a person

AnRR1. Protocol 896

"Environmental PPAR Agonists Accelerate Aging of Bone and Impair Lymphopoiesis"
Biosafety Level: BSL2
Animal Biosafety Level: ABSL2
Type: Annual Renewal Review
Modification: To add one personnel and add PCB-126 in the protocol