



Date: Tuesday, July 11, 2017 4:21:11 PM

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View: UPitt SF: Basic Information

Basic Information

*** 1. Title of IBC research project:**

Transmission, resistance, treatment, and persistence of human immunodeficiency virus

*** 2. Short title:**

HIV pathogenesis

*** 3. Project Summary:**

Our lab performs research to study the HIV-1 in the context of transmission, development and persistence of drug resistance, and therapeutics to prevent infection or to treat infection.

We use plasmids and lentivirus transduction for expression of wild-type and mutant forms of human proteins and reporter proteins. We also transfect cells with siRNA for knock down of proteins. We infect mammalian cells with replication defective and replication-competent retroviruses and lentiviruses.

To understand the mechanisms of HIV-1 drug resistance and persistence, known or potential drug resistance-conferring mutations are 1) cloned into viral vectors and may arise during replication of viruses in cell culture in the presence of antiretroviral drugs. Small coding regions (<20% of the total viral genome) of the virus genome (i.e. reverse transcriptase or capsid) are sometimes amplified, and sometimes subcloned into a bacterial expression plasmid, for sequencing purposes.

In addition, HIV-1 is administered to humanized, transgenic mice.

*** 4. Is this application for a Core Facility; that the mission or activities described are to produce and distribute materials under IBC oversight to the broader research community?** Yes No*** 5. Principal Investigator:**

Tyrion Lannister

*** 6. Principal Investigator Biosketch:**

Document Name	Date Modified
Lannister Biosketch.docx	7/11/2017 3:18 PM

7. Select a Primary Contact to receive all communications from the MyIBC support office:*** 8. Is this MyIBC submission intended to replace a currently existing paper (legacy) IBC protocol?** Yes No**8a. Identify the legacy IBC protocol number(s) to be replaced:**

View: UPitt SF: Protocol Team Members

Protocol Personnel

1. List research study contact personnel:

Name	Roles	Additional Roles	Involved With Procedures	E-Mail	Phone
Sansa Stark	Supervisory technical	Graduate student	yes	sss3@pitt.edu	624-1234
Theon Greyjoy	Laboratory manager		yes	reek@pitt.edu	624-2345
Lord Varys	Supervisory technical	Postdoctoral fellow	yes	varys@pitt.edu	624-3456

View: UPitt SF: Funding Sources (not integrated with Grants)

Funding Sources

*** 1. Is the source of funding:** Internal Only (e.g. departmental or start-up funding)

External (e.g. sponsored research)

1a. Select an Organization:

Funding Organization

Grant Identifier/Award#

There are no items to display

View: UPitt SF: Biosafety Summary

Biosafety Summary

* 1. Select any items involved in the protocol:

- Tissues, Blood, or Body Fluids**
- Primary Cells or Cell Lines**
- Bacteria, Yeasts, Fungi, Parasites, Invertebrates, or Insects**
- Viruses or Prions (Wild-type or Recombinant)**
- Toxins
- Recombinant or Synthetic Nucleic Acids**
- Human Subjects used in experiments (clinical trial; HGT)
- Live animals used in experiments**
- Genetically Engineered Animals**
- Plants, Plant Pathogens, or Plants with Genetically Engineered Insects
- Other

2. If other, describe items:

View: UPitt SF: Tissues, Blood, or Body Fluids

Tissues, Blood, or Body Fluids

* 1. List category, type, and source of all tissues, blood, and body fluids:



Tissue/Blood/Fluids - Mouse (murine) (Lymphatic Tissue, Digestive Tissue, Blood)

BSL: BSL-2+ **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** Mice in BST3

Description of Usage: Blood and tissues will be obtained from uninfected and HIV-infected mice for cellular and molecular assays

2. Describe any tissues transplanted between species:

N/A

View: UPitt SF: Primary Cells or Cell Lines

Primary Cells or Cell Lines

* 1. Identify the category and source of all primary cells or cell lines by species:



Cell/CellLine - Other Human cells or cell lines (HeLa, Jurkat, 293T)

BSL: BSL-2+ **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** ATCC, my colleague Jon Snow at the U. of Castle Black

Description of Usage: In vitro experiments for transfection of plasmids or transduction with viruses; imaging; isolation of RNA and DNA.



Cell/CellLine - Non-human primate (COS)

BSL: BSL-2+ **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** my colleague Daenerys Targaryen at Meereen Univ.

Description of Usage: In vitro experiments for transfection of plasmid/siRNA or transduction with viruses; imaging; isolation of RNA and DNA.



Cell/CellLine - Mouse (murine) (3T3 cells)

BSL: BSL-2 **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** ATCC

Description of Usage: Transfection with plasmids and siRNAs

View: UPitt SF: Bacteria, Yeasts, Fungi, or Parasites

Bacteria, Yeasts, Fungi, or Parasites/Invertebrates

* 1. Identify microorganisms or invertebrates by category and strain:



Escherichia coli, non-pathogenic strains - DH10

(Bacteria & Rickettsia)

BSL: BSL-1 **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** Invitrogen

Description of Usage: Propagation of plasmids

2. Describe other microorganisms or invertebrates:

View: UPitt SF: Viruses and Prions

Viruses, Prions, or Vectors

* 1. Identify viruses, prions, or vectors used by strain and source:



Human Immunodeficiency Virus (HIV, Types 1 and2) - NL4-3, clinical isolates (Viruses and Prions)

BSL: BSL-2+ **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** my colleague Brienne of Tarth College

Description of Usage: Replication-competent HIV-1 will be expanded and characterized for infectivity and replication in cell culture. In addition, humanized mice will be challenged with replicationcompetent HIV-1.

Additional Virus Information: Agent **CAN** enter or infect human cells, Agent **IS NOT** replication-defective, Investigator IS NOT requesting biosafety containment level downgrade



Human Immunodeficiency Virus (HIV, Types 1 and2) - NL4-3 (Viruses and Prions)

BSL: BSL-2 **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** Invitrogen

Description of Usage: Replication-defective viruses will be used to express shRNA and genes in cells.

Inserted Nucleic Acids Information: GFP, luciferase, actin, tubulin, shRNA

Additional Virus Information: Agent **CAN** enter or infect human cells, Agent IS replication-defective, Investigator IS NOT requesting biosafety containment level downgrade



Murine Leukemia Virus (MLV or MuLV, Retrovirus family) - MLV (Viruses and Prions)

BSL: BSL-2 **Storage :** Biomedical Science Tower (Starzl) - 100 **Use :** Biomedical Science Tower (Starzl) - 101 **Source :** Addgene

Description of Usage: Transduction of 3T3 cells.

Inserted Nucleic Acids Information: GFP, luciferase, insulin gene

Additional Virus Information: Agent **CAN** enter or infect human cells, Agent IS replication-defective, Investigator IS NOT requesting biosafety containment level downgrade

2. Describe other viruses or prions:

View: UPitt SF: Recombinant or Synthetic Nucleic Acids Usage

Recombinant or Synthetic Nucleic Acids Usage

* **1. Does research with recombinant or synthetic nucleic acids involve the use of:** (select all that apply)

- NIH Section The deliberate transfer of drug resistance into organisms that do not acquire them III-A-1-a or naturally Section III-B-2
- NIH Section The deliberate transfer of recombinant or synthetic nucleic acids into humans III-C-1
- NIH Section Genes that produce vertebrate toxins with LD50 less than 10ng/kg of bodyweight III-B-1 and Appendix F
- NIH Section III-D-1 Use or cloning of human or animal pathogens used as host-vector systems**
- NIH Section Use or cloning of pathogen DNA or RNA in a non-pathogenic prokaryote or lower eukaryote III-D-2
- NIH Section III-D-3 Infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of a helper virus in tissue culture**
- NIH Appendix Q Animal research involving recombinant or synthetic nucleic acids not in standard laboratory containment housing
- NIH Section III-D-4 Administration of any recombinant or synthetic nucleic acid molecules to whole or living animals, such as transduced or transformed cells, genetically engineered tissues and/or organs, morpholinos, or engineered DNA or RNA, siRNA, shRNA, etc**
- NIH Section Genetic engineering of plants, or plants with microorganisms or insects containing recombinant or synthetic nucleic acids III-D-5 and Appendix P
- NIH Section Experiments involving more than 10 liters of culture at one time III-D-6 (Large Scale)
- NIH Section Experiments involving any influenza viruses from this special classification III-D-7
- NIH Exempt: Sections III-E or III-F Use of recombinant or synthetic nucleic acid molecules for: detection purposes (markers), genomic library creation, basic cloning, vector construction, or expression in organisms, cell cultures, or breeding of genetically engineered rodents.**
- Other / None of these apply

2. If other or none of these apply, describe:

View: UPitt SF: Recombinant or Synthetic Nucleic Acid Work Description

Recombinant or Synthetic Nucleic Acid Work Description

* **1. Describe the procedures and techniques to be used with the nucleic acid molecules in the project:**

- For example - if the research involves a recombinant virus, bacteria, or other organism
- Describe the vectors and the transgenes being used
 - Describe how the vectors are used in the research project

E. coli for plasmid production
 plasmids for expression of genes in mammalian cells
 siRNA for knockdown of genes in mammalian cells
 retroviruses for infection of mammalian cells and for qRT-PCR detection
 lentiviruses for infection of mammalian cells
 transgenic mice for HIV-1 transmission studies

* **2. List any known oncogenes or toxins that will be expressed and identify the expression system(s) used for expression:**

None

* **3. Does the research include any oligonucleotides, or any gene drive technology used to edit or change the gene function, such as siRNA/shRNA, CRISPR/Cas9, TALENS, etc.?**

Yes No

3a. What genes will be involved in the experiments?

actin, GFP

3b. What type of vector or delivery system is used for the experiments?

siRNA transfection and transduction of lentiviruses containing shRNA

* **4. Is there any potential for increased virulence by manipulation of any of the nucleic acid molecules or genes listed above with respect to the vector or organism?**

Yes No

4a. Explain the details regarding the potential for increased virulence and provide the steps taken to mitigate the risks involved with the increased virulence:

* **5. Does the project involve the use of Lentiviruses or Lentiviral vectors?**

Yes No

View: UPitt SF: Lentivirus and Lentiviral Vectors

Lentivirus and Lentiviral Vectors

* **1. Is the lentivirus/lentiviral vector generated/produced in your laboratory at the University of Pittsburgh?**

Yes No

* **2. Is the lentiviral vector produced from a multi-component system? (e.g., separate plasmids for packaging, envelope and gene transfer)**

Yes No

2a. Please describe the safety features of each different lentivirus or lentiviral vector system that is used in this research:

Some of the lentiviral vectors we use are replication-defective using 3 plasmids (2nd generation), consisting of an expression vector, a gag-pol packaging plasmid, and VSV-G envelope.

* **3. Will lentiviruses be used to generate stable cell lines**

Yes No

3a. Provide the number of passages of the transduced cell lines prior to experimental use (e.g., administration into *in vivo* models)

5

View: UPitt SF: Animals (IBC)

Live Animals

1. Related IACUC Protocols:

ARO ID	Protocol ID	Protocol Title	PI First Name	PI Last Name	Status	Species	Expiration Date
IS00000001	12345678	HIV transmission studies	Tyrion	Lannister	Approved	Mouse	7/16/17

* **2. Will this research involve any non-IACUC regulated animals (invertebrates) that may be exposed to recombinant or synthetic nucleic acid molecules?**

Yes No

* **3. Will tissues, cells, or organs from animals be used in *in vitro* experiments?**

Yes No

* **4. Are the animals used in the experiment immunocompromised?**

Yes No

4a. If yes, describe how immunocompromised animals will be used:

* **5. Will transgenic, knockouts, gene-targeted, or other genetically engineered animals be used?**

Yes No

* **6. Will recombinant or synthetic nucleic acid molecules be administered to live or intact animals?**

Yes No

View: UPitt SF: Genetically Engineered Animals

Genetically Engineered Animals: Source

* **1. Will you be purchasing, breeding, or obtaining transgenic animals from an external source?**

Yes No

* **2. Will transgenic, knockouts, gene-targeted, or other rodents be bred at an on-site facility?**

Yes No

2a. Does the project involve rodents (parental or offspring) that contain more than 50% of the genome of an exogenous eukaryotic virus from a single virus family?

Yes No

2b. Does the project involve rodents where a transgene is under the control of a gammaretroviral long-terminal repeat (LTR) and where the LTR is functional?

Yes No

* **3. Will any tissues, organs, or cells from genetically engineered animal be transplanted into another animal?**

Yes No

3a. If yes, describe the transplantation experiments. Be sure to include the materials, species, and strain of the donor and the species and strain of the recipient animals if different.

View: UPitt SF: Animal Gene Transfer

Animal Gene Transfer

* **1. Do the experiments involve formation of vectors containing more than 50% of the genome of any eukaryotic virus?**

Yes No

* **2. Do the experiments involve the use of infectious human or animal viruses?**

Yes No

* **3. Do the experiments involve the use of a replication-defective human or animal virus in the presence of a helper virus?**

Yes No

* **4. List proposed biosafety level:**

ABSL-1

ABSL-1+

ABSL-2

ABSL-3

* **5. Identify animal species (and strain if applicable) receiving the experimental agents; recombinant/synthetic nucleic acid molecules or materials:**

NOD/SCID/gamma null (NSG) mice transplanted with human cells

*** 6. Describe the route of administration for each experimental agent used in *in vivo* and per species as applicable:**

Intravenous

*** 7. What are the target cells/tissues/organs for the recombinant/synthetic material?**

CD4+ cells

View: UPitt SF: Risk Group and Containment Practices

Risk Group and Containment Practices

*** 1. What is the highest risk group level of the biological agents and materials you will use in the proposed research?** (If you are unsure about the risk group designation of an agent and/or material please refer to the [NIH Guidelines Appednix B](#)).

RG-1

RG-2

RG-3

RG-4

*** 2. What is the highest biosafety containment practices required for the research activities covered by this protocol?**

Biological Research Standards

BSL-1

BSL-2

BSL-2+

BSL-3

RBL

Biological Research Involving Animals

ABSL-1

ABSL-1+

ABSL-2

ABSL-3

Clinical Research Standards

BSL-2 (Universal Precautions)

3. Handlers:

Name	Organization
Tyrion	U of Pgh School of Medicine
Lannister	Medicine

4. Other Handlers not in the list above:

Cersei Lannister

View: UPitt SF: Exposure Assessment and Protective Equipment (Biosafety)

Exposure Assessment and Protective Equipment

*** 1. Describe whether the agent(s) used in the course of this research may be infectious to humans: (i.e. replication-competent vector vs. single-round of infection; potential for integration of vector into host chromosomes; use of human cells or cell lines that may harbor unknown infectious agents; use of known human pathogens)**

Yes, HIV is infectious to humans and may cause disease if replication competent. If replication-defective, HIV should not cause disease.

MLV can infect human cells but will not replicate.

Primary cells and cell lines used in the lab may contain unknown infectious agents.

*** 2. Describe any procedures that may increase risk for accidental exposure to personnel via percutaneous or mucous membrane exposure routes or environmental release: (e.g. use of needles, centrifugation, in vivo studies)**

HIV1 infection can occur by direct inoculation through skin or mucous membranes. Sharps are not used

unless absolutely necessary, which is typically when performing intravenous inoculations of mice or dissection of infected mice/mouse tissues.

*** 3. Does the research involve any potential for airborne transmission of agent(s)?**

No

*** 4. Please describe procedures, work practices, and/or engineering controls (such as a Biological Safety Cabinet) that will be used to mitigate potential risks identified in question 2 and 3 above:**

HIV-1 is only used in a BSL2+ laboratory. Personnel have all been trained by Dr. Lannister and have read the laboratory manuals. In the BSL2+, personnel must wear a Tyvek or cloth gown, booties, 2 pairs of gloves, and eyewear. Face masks and safety goggles/glasses are available for cell culture and are required for mouse work. All infectious (or potentially infectious) materials must only be used in a certified biosafety cabinet. Use of syringes or needles with EHS approved safety features is only allowed when needed. No glassware is used during BSL2+ lab procedures.

*** 5. Indicate the personal protective equipment that will be used:**

Bite/scratch resistant gloves/sleeves

- Disposable sleeves
 Double gloves (latex or nitrile)

Face shield

- Facility-dedicated scrubs
 Facility-dedicated shoes/booties

Gloves (latex or nitrile)

- Hair bonnet
 Laboratory coat

Liquid-barrier coverall suit

- N-95 respirator
 Other
 Powered Air-Purifying Respirator (PAPR)

Safety glasses

Safety goggles

Shoecovers

- Solid-front wrap around gown
 Surgical mask
 UV resistant face shield

6. If other, specify:

View: UPitt SF: Dual Use Research of Concern

Dual Use Research of Concern

*** 1. Does any of the research directly involving nonattenuated forms of 1 or more of the agents listed in the US Government Policies for oversight of Life Sciences Dual Use Research of Concern produce, aim to produce, or may be reasonably anticipated to produce 1 or more of the following experimental effects: (select all that apply)**

None of the above

*** 2. Please explain why you believe this protocol does or does not involve Dual Use Research of Concern:**

My research will not pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

3. I understand and agree that if there is a change in this research with respect to the applicability of any of the seven experimental effects listed above, or if the Investigator, for any reason, thinks the research needs to be reconsidered for DURC potential, the Investigator must immediately notify the IBC Office, and modify/resubmit the information above.

View: UPitt SF: Waste Management (Biohazard)

Waste Management

Describe the methods used for proper decontamination (e.g. specific disinfectant or physical decontamination method used) and disposal of the following (if applicable):

For additional information on decontamination, see [Environmental Health and Safety Guideline #05-006](#)

*** a. Solid Waste:**

All solid waste is decontaminated with 1:10 bleach solution in the biosafety cabinet for at least 20 minutes and doublebagged prior to autoclaving.

*** b. Liquid Waste:**

All liquid waste is decontaminated with 1:10 bleach solution (final concentration) in the biosafety cabinet for at least 20 minutes prior to disposal down the drain.

*** c. Animal Carcass(es):**

Animals are NOT removed from the ABSL2 facility and they are placed in labeled biohazard bags at the animal facility for disposal by DLAR.

2. Autoclave Location:

Building	Floor
Biomedical Science Tower (Starzl)	1st

*** 3. Describe plans for decontamination in response to a biological spill:**

Biological aerosols or bioaerosols refer to airborne suspensions of biological agents either solid particles such as bacterial spores, or liquid particles such as droplets of blood, body fluids, bacteria, viruses, or other biological materials. Many laboratory activities have the potential to generate aerosols. Any process performed in the BSL2+ suite with a potential to form biological aerosols shall be performed only in safety equipment, such as a biosafety cabinet or centrifuge equipped with sealing safety lids. The processes shall be performed carefully to minimize the creation of splashes, sprays, and aerosols. Centrifugation can create aerosols. For this reason, all potentially infectious or biohazardous samples (whether known or suspected to contain HIV or other blood borne pathogens) must be centrifuged in sealed safety cups that include caps with an O-ring to seal the cap to the centrifuge cup. Samples to be centrifuged in the lowspeed, tabletop Sorvall Legend RT must be placed in plastic centrifuge tubes with a screw cap (preferably flanged seals), balanced, and decontaminated with 70% ethanol prior to removal from the hood. All centrifuge tubes should be inspected for cracks prior to centrifugation, and it is important not to overfill centrifuge tubes to avoid spills or leakage of fluids during centrifugation. Tubes should be placed into centrifuge buckets and sealed before centrifugation. After centrifugation, the sealed buckets must be opened in the BSC to prevent exposure of aerosols or liquids. In the event of leakage during centrifugation, the centrifuge buckets and caps should be thoroughly decontaminated in the BSC before removal. Finally, inspect the inside of the centrifuge after each run for signs of leakage, and decontaminate when appropriate.

Centrifugation can place personnel at risk for exposure to infectious agents or for physical harm. The process of centrifugation may result in creation of aerosols and if the centrifuge tube or vial is compromised, aerosols can be released. If a centrifuge load is not properly balanced, the centrifuge may rock enough to move. An unbalanced centrifuge rotor can crack and break apart within the unit, causing heavy pieces to fly at high speeds within the unit. Finally, incompatible rotors and accessories may malfunction if used in the wrong centrifuge.

- In order to prevent spills and leakage, centrifuge tubes and vials should not be overfilled.
- Transport the rotor or centrifuge buckets with caps to the BSC, load tubes or vials, seal the safety lid or cap, and transport the rotor or capped bucket to the centrifuge. Rotors and buckets must only be loaded and unloaded within the BSC and sealed prior to removal.
- The rotors or buckets shall be wiped with a CaviCide prior to removal from the BSC and after use.
- In the event of a centrifuge malfunction, balance issue, or compromised tube, the centrifuge should be turned off and unplugged. The centrifuge must not be opened until 30 minutes have passed, so that aerosols formed within the unit settle out of the air. Upon opening the centrifuge, sealed rotors or capped buckets should only be opened in the BSC and disinfected appropriately. The interior of the centrifuge should be disinfected with an appropriate disinfectant if a tube has become compromised or if the centrifuge has malfunctioned.
- The centrifuge should be disinfected routinely (e.g. surface disinfect rotors/safety cups/interior on a weekly basis).

Biological Spills Inside of a BSC:

- Remove contaminated outer gloves, discard in the biohazard bag in the BSC, and remove hands from BSC. Disinfect and discard any other personal protective equipment (PPE) that may have become contaminated.
- Close the sash and allow the cabinet to operate for at least 5 minutes before proceeding with the spill cleanup.
- Notify others in the lab that a spill has occurred in the BSC.
- If any material has been splashed onto you, follow the procedure for Reporting Exposure to Potentially Infectious Material found in the University Safety Manual (EH&S Guideline #05005). See Appendix A.
- Don clean PPE.

- Cover the spill with paper towels to prevent further aerosol formation.
- Pour a 1:10 dilution of bleach gently over the covered spill, working from the outside inwards.
- Wait at least 15 minutes for the disinfectant to penetrate through the contained spill and achieve the required contact time for disinfection.
- Wipe up the spill working inward to the center of the spill. Avoid excess spraying of disinfectant as this can create more splashes and aerosols. Change gloves as needed. Do not use hands if glass or other sharps are involved in the spill. Use a tool (e.g. shovel or forceps) to remove the absorbent material and debris.
- Place all materials in a biohazard bag and repeat application of disinfectant. Allow for the appropriate contact time.
- Wipe off contaminated reusable supplies. Discard disposable contaminated supplies into the biohazardous waste.
- If the material spilled into the front or rear grille, lift the grille and disinfect both it and the waste basin underneath.
- Notify supervisor or PI.

Biological Spills Outside of a BSC:

A Major Biological Spill involves the release of BSL2 or higher materials outside of a biological safety cabinet or involves excessive splashing or aerosol formation and requires assistance of EH&S and/or external emergency personnel.

- Alert personnel in the laboratory of the spill and direct additional personnel away from the spill area.
- If any material has been splashed onto you, follow the procedure for Reporting Exposure to Potentially Infectious Material found in the University Safety Manual (EH&S Guideline #05005).
- Remove and disinfect any contaminated clothing.
- Notify supervisor, PI, and the Department of Environmental Health and Safety (EH&S) at 412624-9505 of the incident.
- If the situation involves an imminently lifethreatening injury, a release outside the building, or has other catastrophic potential, call 4126242121.
- Personnel knowledgeable of incident and laboratory should be available to assist EH&S and/or emergency personnel.

*** 4. I acknowledge that investigators are required to report accidental exposures, spills, or loss of containment to the IBC.**

View: UPitt SF: Supporting Documents

Supporting Documents

Thank you for completing the information required to submit this protocol to the appropriate safety review. Remember to upload the supporting documents before submitting.

1. Attach additional supporting documents:

Document Name	Date Modified
There are no items to display	

Please take this opportunity to review the information you have provided. It is very important that the responses in this protocol be thorough and specific. Failure to respond to all requested items, to submit all required documents, or complete all personnel requirements will result in a delay in the review of this protocol and may result in the protocol being returned to the protocol team for correction or completion.

Please note that this protocol has not yet been submitted for review. Upon completing the information in this protocol and clicking the "Finish" button below, the Principal Investigator must also click the "Submit" activity from the protocol workspace in order to forward this submission for review.