

Vitalant Research Institute (VRI)

Institutional Biosafety Committee (IBC) Meeting Minutes

Thursday, March 21, 2024, 1:00 PM to 2:00 PM PDT

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- **Members Present:** Graham Simmons, Satish Pillai, Clara Di Germanio, Marcus Muench, Jing Jin, Mohamed Bouzidi, Rachel Martinelli, and Steve Sweet (non-voting VRI member).
 - **Members Online:** Krystyna Kozakiewicz (Community Member), Laura L. Flores (Community Member)
 - **Members Absent:** Patrick Roberts (non-voting VRI member).
 - **Public Present:** NA

Start Time: Dr. Graham Simmons, IBC Chair, called the meeting to order at 1:05 AM PT, and quorum was noted.

1. **Announcements:** Dr. Graham Simmons reported the following to the IBC Members...

- a. **Public Posting of March 21, 2024, IBC Meeting:** Dr. Graham Simmons noted that the IBC Meeting of the meeting was publicly posted.
 - b. **Biosafety Officer Update Announcement:** Rachel Martinelli - accepted Biosafety Officer position: Dr. Graham Simmons announced that Rachel Martinelli is currently training to take over as the IBC Officer for the VRI SF Site, final stage will take place in the next six months.
 - c. **IBC CITI Certification updates for NIH Submission:** Dr. Simmons noted that all IBC Members will need to recertify their yearly annual CITI Certification for our NIH IBC Registration that will be due soon.
 - i. Patrick Roberts will submit the annual membership report to bring the VRI IBC to current good standing with the NIH starting in Jan. 2025.
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2. **Old Business**

- a. **SP-002-2023.** Discovery and Development of SARS-CoV-2 Therapeutics. Proposed NIH Guidelines section: III-D-3. Principal Investigator, Satish Pillai
 - i. Per the October 9, 2023, meeting notes, this application is returned to the PI for revisions, and the PI's responses will need to come back before the Full Committee for further review.
 - ii. **Committee unanimously approved this application, March 21, 2024.**
- b. **SP-003-2023.** Characterization of HIV Latency and Reactivation. Proposed NIH Guidelines section: Principal Investigator, Satish Pillai
 - i. **The Committee unanimously approved this application, March 21, 2024.**

3. New Business / New IBC Applications

- a. **JJ-001-2024. Screen for antivirals against Alphaviruses by targeting viral replication complexes.**
Principal Investigator, Jing Jin / Co-Investigator, Marcus Muench

Protocol Review: This protocol looks on developing antiviral drugs that stop the virus by targeting its replication process. Dr. Jin and staff will test new agents already identified in lab studies for their ability to block CHIKV and Mayaro virus (MAYV) in both cell cultures and mice. This is a project that builds on ongoing work funded by the NIH and uses specialized mouse models that mimic both mild and severe infections. Promising drugs will be tested to see if they can stop virus spread, reduce joint inflammation, and prevent chronic symptoms.

Lab Safety & Risks:

- i. Work involves live Togaviridae family, Alphavirus genus, Chikungunya virus and Mayaro virus.
- ii. Source of agent(s): Made in house from full-length clones obtained from Scott Weaver, UTMB, and Stephen Higgs, Kansas State and a provide a copy of the Material Transfer Agreement (MTA) is provided.
- iii. Experiments are done under strict biosafety protocols with protective gear.
- iv. Risks to researchers are minimized through training, lab design, and use of a CHIKV vaccine.
- v. Virus samples are fully deactivated before disposal. Work surfaces and equipment are cleaned with Opticide or 10% bleach, followed by 70% alcohol. All waste in biohazard bags is autoclaved before disposal. All supernatants/liquids from bacterial cultures and from plasmid DNA preparations will be either autoclaved or treated with a final concentration of 10% bleach for 30 minutes before being disposed down the drain. Stocks of virus will be inactivated using 1% vesphene followed by autoclaving.

Animals & Cell Lines Used:

- i. Mice are used for testing drug effects during infection.
- ii. Human and monkey cell lines are used to grow and study the virus in the lab.
- iii. All animal work is done under approved biosafety conditions.

All the biosafety cabinet certifications are attached and are current. All Lab staff CITI certification has been reviewed and are current. Dr. Jin provided a provided a copy of the Material Transfer Agreement (MTA).

- i. **Committee unanimously approved this application, March 21, 2024.**

- b. **MB-001-2024. Enhancing anti-HIV gene therapy through epigenetic modulation.**
Principal Investigator, Mohamed Bouzidi / Co-Investigator, NA

Protocol Review: Because HIV hides in the body by staying dormant in infected cells, making it hard to completely cure with current treatments - improved gene-editing strategies to fight HIV by using drugs that change how genes are turned on or off (epigenetics). Dr. Bouzidi will use the CRISPR-Cas9 gene editing to try to cut out the virus's DNA from infected cells. However, this tool doesn't always work well because the virus can hide in tightly packed DNA or be masked by chemical tags (like DNA methylation) that block access.

(continued)...

The study aims to make CRISPR more effective by using drugs that loosen up the DNA or remove those chemical tags, making it easier for CRISPR to find and cut the virus. The study will test these approaches in HIV-infected immune cells in the lab to understand how DNA packaging and chemical tagging affect CRISPR's success. The researchers will use drugs to loosen the virus's DNA or remove its gene-silencing markers, test how well CRISPR works when these changes are made, and study different versions of HIV-infected cells to see which DNA conditions are best for editing.

The agents used in the study, Modified HIV viruses that glow to help track infection and editing; Lentiviruses (virus-based tools) to deliver gene-editing systems, and HEK-293T cells (a lab-grown cell line) to produce the viruses safely under controlled lab conditions.

Lab Safety & Risks:

- i. **Toxic Drug Exposure:** Some of the drugs (like romidepsin or decitabine) are harmful if touched or accidentally consumed
- ii. **Biosafety Level:** BSL-2, and BSL-2+. Room Number for BSC: 211/N, 214/ Y/ Baker SG403 S/N 64684; S/N 83116; S/N 74094; Thermo Scientific S/N 300509257
- iii. **Risk management includes** using biosafety cabinets, regular equipment checks, proper PPE, disinfection procedures, and staff training. All viral tools and cells will be handled in approved BSL-2+ labs using protective protocols. Some of the drugs to be used in this project (romidepsin, prostatin, decitabine, etc.) can be toxic to humans through ingestion or contact with mucosal sites. The risk of exposure will be minimized by diluting and aliquoting stock concentrations to safer working concentrations (20 uL at 5mM) in a fume hood located in the BSL-2, utilizing appropriate personal protective equipment (PPE) such as gloves and lab coats. These working concentrations will be stored in a -20°C freezer within the BSL-2+ facility.
- iv. Non-commercial obtained from NIH AIDS reagent program and collaborator, BSL-2. HEK-293T cells will be used to generate single round infectious virus in BSL-2+. The virus quantification assay (p24 ELISA) will be performed at least once per month. The virus will be used to infect primary CD4+ T cells. Lentivirus vectors, BSL-2. HEK-293T cells will be used to generate single round virus in BSL-2+. The virus quantification assay (p24 ELISA) will be performed two to six times over the course of this project. This virus will be used to infect Jurkat and J-Lat cells. Dr. Bouzidi provided a provided a copy of the Material Transfer Agreement (MTA).

All the biosafety cabinet certifications are attached and are current. All Lab staff CITI certification has been reviewed and are current.

- i. **Committee unanimously approved this application, March 21, 2024.**