IBC Meeting Minutes

Meeting Minutes
7/10/2025

Voting Members Present
Biana Godin, PhD Chair
Daniel Kiss,
Sasha Azar, PhD Vice Chair
Chas Gray, RPh
Jillian Chahal
Nagendran Tharmalingam, PhD
Edward Graviss, PhD, MPH
Vicente Zuno
Jiangyong Shao,
Tanya Herzog, PhD
Wenhao Chen, PhD
Tamara Steele
Joan Nichols, PhD

Other Non-Voting Attendees:
Shehla Barlas
Malissa Mayer-Diaz
Mary Brugger
Leola Griffin
Joy Jerlin
Prince Agyapong
Kimberly Marquez
Shane Wilson
Michael Smith
Perla J. Rodriguez
Wanda Quezada
Leticia Cano
Claudia Pacheco
Israel Ramirez
Joana Espinosa
Rebecca Corrigan
Dalia Hamza

Voting Members Absent:
Francesca Taraballi
Sachin Thakkar
Anjana Tiwari

Non-Voting Members Present:
Leon Brown,
Brenda Hartman, B.S
Tiffany Gunter
Gretchen Gotlieb

Call to Order:

The Institutional Biosafety Committee convened via Microsoft Teams on July 10, 2025, and the meeting was called to order at 10:40 a.m. with 13 members in attendance, exceeding the quorum requirement of 9 members.

Education:

- Dr. Joan Nichols and the biosafety officer, Vicente Zuno, provided training regarding gain-of-function research.

Reports:

- **Biosafety Officer Report**
    - The final report for Dr. Graviss's Import Permit has been received from the CDC. It included only two minor observations, both of which can be easily addressed.
    - CV Sciences, Orthopedics, and RNA Therapeutics now have access to a courier service for the transport of biological hazardous materials to and from Dynamic One. Preliminary training for the primary contacts was conducted last week, and test runs are scheduled for next week.

Conflict of Interest:

Committee members were reminded by the IBC Chair to recuse themselves in the event of any conflicts of interest.

Old Business:

- A list of approved protocols was shown to committee members during the meeting.

New Business:

- A list of approved amendments via designated member review was shown to the committee members during the meeting.
- A list of approved administrative amendments was shown to the committee members during the meeting.
- A list of approved continuing reviews was shown to the committee members during the meeting.

Minutes Review:

- The meeting minutes from June 5, 2025 and June 13, 2025, were reviewed. It was requested that an additional statement be added to each item to reflect the specific actions taken by the IBC.
- **Motion: Approve, pending the implementation of the clarification**
    - Yes votes: 13
    - No votes: 0
    - Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002198
Title: Phase 3 Study of Adjuvant Pembrolizumab +/- V940 in Resectable Stage II–IIIB
Principal Investigator: Min Kim

- **Study Overview**: This clinical trial evaluates the safety and efficacy of V940 (mRNA-4157), an investigational individualized neoantigen therapy, in combination with pembrolizumab (Keytruda) following surgical resection of non-small cell lung cancer (NSCLC). V940 is a personalized mRNA-based treatment encoding up to 34 tumor-specific neoantigens, tailored to each patient's tumor DNA profile. The administered dose of V940 is 1 mg.
- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL1
- **Risk assessment and Discussion**:
    - As an mRNA molecule with a large molecular weight, little to no systemic absorption is expected to occur in a workplace setting. It is also expected to rapidly degrade in the digestive tract following accidental ingestion. V940 is not known to cause disease in healthy adults and presents minimal potential hazard to laboratorians and the environment. V940 may be handled on open bench.
    - Acronyms were not defined. It was also unclear who was administering V940 and if another pharmacist needs be included in the case that the listed pharmacist is not available
- **Comments sent to the PI for clarification**:
    - **Staff Identification**: Please clarify whether an additional pharmacist will be involved in the study. If so, include their relevant experience, education, and training related to this agent. Additionally, regarding the staff member listed as the 'back-up research nurse,' is a different nurse responsible for administering the agent? Please provide clarification.
    - **Summary of Proposed Research**: Please define all acronyms - FFPE (formalin-fixed paraffin-embedded), pCR (pathologic complete response), etc.
- **The motion to approve the study by designated member review was seconded and passed.**

Motion: Approve after Designated Member Review

- Yes Votes: 13
- No Votes: 0

- Abstained: 0

IBC00002306
Title: Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial of Descartes-08 in Patients with Generalized Myasthenia Gravis
Principal Investigator: Sheetal Shroff

- **Study overview**
  Aim: A multi-center randomized, double-blind placebo-controlled Phase 3 trial to evaluate the efficacy, safety and tolerability of autologous T-cells expressing a chimeric antigen receptor (CAR) directed to B-Cell maturation antigen (BCMA) ("descartes-08") in patients with acetylcholine receptor antibody-positive (AChR+) generalized myasthenia gravis (gMG). The agent will be administered weekly for 6 weeks at a dose of 52.5e6 CAR+ cells/kg with the maximum dose capped at 52.5e8 per infusion.
  Agent/target/gene to be expressed: The agent is "Descartes-08", which is an autologous T cell therapy. CAR T transiently expresses an antigen against B-cell maturation antigen (BCMA) for targeting BCMA+ cells.
  Packaging system: To minimize toxicity, the agent is based on transient mRNA transfection and not permanent viral transduction. mRNA CAR T-cells can be expected to have self-limited proliferation in vivo and potentially may show dose-linear pharmacokinetics.
- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**:
  - Descartes-08 and its donor-matched Thawing Solution are autologous cell therapy products. CAR is delivered via transient mRNA transfection, not viral vectors, to reduce toxicity. As such, they may pose a risk of transmitting infectious agents to healthcare personnel during handling. Standard universal precautions must be followed to minimize this risk. The therapy involves CAR-T cells with transient expression and requires Biosafety Level 2 (BSL-2) containment.
  - The use of enhanced personal protective equipment (PPE), such as double gloves, full face splash shields, and solid-front gowns, is not required for this protocol. Standard universal precautions are considered sufficient. Additionally, the protocol does not clearly specify who is responsible for thawing the product prior to administration. The provided transport SOP lacks detailed instructions on how the agent is transported to the patient's room.
- **Comments sent to the PI for clarification**:
  - **Exposure Management Laboratory**: Double gloves, full face splash shield

and solid front gown are not required. Please remove these selections from the required PPE. Additionally, the attached transport SOP pertains to the shipment of patient-derived T cells to the manufacturer for CAR-T cell production and does not address the transport of the Descartes-08 CAR-T product to the patient's room. Please provide the appropriate SOP covering this step. Lastly, clarification is needed regarding who is responsible for thawing the product prior to administration—please confirm whether this is performed by nursing staff or by KJCCT personnel.

  - **Exposure Management Clinic/Hospital:** According to "Exposure Management - Clinic/Hospital"- "The agent will be delivered to the patient's room and handed to the nurse who will begin the thawing process.". However, in all other places- KJCCT is mentioned as a responsible entity for thawing. If the nurse is indeed responsible, the procedure and safety measures must be clearly documented and communicated. Please include KOP-004 if this is the procedure that is followed.

- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0

IBC00001798
Title: IBC for prophylactic mRNA Vaccine
Principal Investigator: Junhua Mai

- **Study Overview**: This study aims to address the challenge of mRNA instability, which currently necessitates costly ultralow-temperature storage. The proposed approach seeks to develop broadly applicable strategies to protect mRNA from degradation throughout its lifecycle—including manufacturing, storage, formulation, transport, and administration—while also enhancing its expression efficiency in target cells. As a proof-of-concept, the study will develop stable COVID-19 prophylactic vaccines using mRNA encoding the Spike protein, including formulations targeting the Omicron variant. These vaccines will be administered to healthy C57BL/6 mice via subcutaneous injection in the footpad on Day 0 and Day 21. Blood samples will be collected at various time points post-vaccination to assess anti-Spike antibody titers, cytokine and chemokine responses, and potential liver and kidney toxicities. All virus-related studies will be conducted at the collaborator's facility at UTMB. At HMRI, only immune response evaluations in healthy mice will be performed to support characterization and optimization of the vaccine formulations.
- **Training**: All staff members are currently up to date with their training.
- **Applicable NIH Guidelines**: Section III-D-1
- **Containment Conditions to be implemented**: BSL2

- **Risk Assessment & Discussion**:
    - The handling and containment procedures described in the protocol are appropriate. SARS-CoV-2 spike omicron variant protein and mRNA are not RG2 agents. They are RG1, however it is wise to follow BSL-2 practices with nanoparticle delivery systems.
    - Transport protocol does not clearly state where material will be moved from or to. Potentially UTMB transfer? The Transport form, under "Originating Areas" states "Nanomedicine department, Mai Lab RIB8th floor Laboratory" as the starting point. The starting point of lab areas and transfer points need to be clearly stated. Since animal studies are planned the protocol needs to describe transfer to CMP areas

- **Comments sent to the PI for clarification**:
    - **Exposure Management- Laboratory**: Transport protocol does not clearly state where material will be moved from or to. Potentially UTMB transfer? The Transport form, under "Originating Areas" states "Nanomedicine department, Mai Lab RIB8th floor Laboratory" as starting point. The starting point of lab areas and transfer points need to be clearly stated. Since animal studies are planned the protocol needs to describe transfer to CMP areas.
- **The motion to approve the study after designated member review was seconded and passed.**

Motion: Approve after designated member review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0

IBC00002296
Title: H-23574-CHARKALL: Phase I Study of CAR T-Cell Therapy Targeting Kappa Light Chain in CLL, B-Cell Lymphoma, and Multiple Myeloma
Principal Investigator: Carlos Ramos

- **Study overview**: Dr. Carlos Ramos resubmitted a three-year renewal for a continuing clinical trial that was previously tabled during the IBC meeting held on June 5, 2025. Progress reported: To date, the study demonstrated that T cells engineered with a CD28-Containment chimeric antigen receptor (CAR) targeting the kappa light chain expand effectively in vivo. Among 19 patients treated (20 total infusions), no cell-related side effects were observed. While most patients showed limited response, one achieved a complete response after two infusions, and another had a transient complete response after three. Four patients experienced stable disease. Incorporating lymphodepleting chemotherapy prior to CAR-T infusion enhanced CAR-T cell expansion, and early results suggest potential for improved antitumor activity, with one patient maintaining a complete response for 21 months and another now disease-free. The risk of exposure to personnel is low-

utilizing replication deficient viral vectors to produce the CAR-T cells in a BSL2 GMP facility using BSL2 practices while wearing BSL2 PPE. **Training**: All staff members are currently up to date with their training.

- **Applicable NIH Guidelines**: Section III-C
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment and Discussion**:
    - As requested during the IBC meeting on June 5, 2025, the study team addressed the prereview clarifications. No further clarifications required.
    - Furthermore, the clinical trials team administering the CAR-T cells to patients are wearing the appropriate PPE to mitigate the risk of exposure to the drug or bloodborne pathogens and have been trained to prevent accidental needlestick injury. Shedding of retroviral vectors from the patients is low, due to the replication deficient characteristics of the vectors. Transport of the therapeutic from the GMP facility to the clinical patient clinic within the building follows the proper packaging and labeling to prevent a spill or release.
- **The motion to approve the study was seconded and passed. The IBC subsequently approved the study.**

Motion: Approved

- Yes Votes: 13
- No Votes: 0
- Abstained: 0

IBC00002337
Title: Understanding molecular and cellular mechanisms in cancer to discover new therapeutic targets and personalized treatment approaches.
Principal Investigator: Jenny Chang

- *Voting Member Nagendran Tharmalingam was not present during the discussion of this amendment and did not vote. Quorum was maintained.*
- **Study Overview**: The research focuses on understanding mechanisms of therapy resistance, immune response, and metastasis in Triple Negative Breast Cancer (TNBC) and Ovarian Cancer (OC). This includes identifying and validating candidate genes and pathways as potential therapeutic targets and prognostic indicators. The team employs xenograft and syngeneic mouse models using human and murine cell lines to study tumor biology and treatment responses.
- Additional aims include: Developing a personalized mRNA-based neoantigen vaccine for TNBC using liposomal and leukosomal nanoparticles, utilizing bioluminescence imaging (BLI) to monitor tumor progression and drug efficacy, modulating gene expression to analyze protein function and its role in therapy resistance, evaluating the effectiveness of immunotherapies, chemotherapies, targeted inhibitors, and RNA-based therapies, investigating upstream open

reading frames (uORFs) to understand translational regulation in TNBC, conducting bacterial transformation using DH5α *E. coli* for plasmid propagation in molecular biology protocols.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-D-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment and Discussion:**
    - This lentiviral vector system includes multiple biosafety features to minimize risk. It lacks oncogenic inserts and is replication-deficient due to the deletion of essential viral genes. The vector and packaging components are split across multiple plasmids to reduce recombination risk. Third-generation plasmids eliminate Tat expression by using a chimeric 5' LTR with a heterologous promoter. Lentiviral particles will be produced at a laboratory scale, not exceeding 100 ml, to further limit exposure and environmental release.
    - The protocol outlines appropriate safety measures and PPE for handling human recombinant cell lines, which are deemed adequate for the proposed work.
    - The laboratory will utilize a replication-deficient adenovirus (Ad5) vector, engineered with a deletion of the E1a gene, which is essential for viral replication. This modification renders the virus replication-incompetent. The adenovirus vector, carrying the IL-12 gene, is produced by a GLP Core Facility. These vectors are commonly used in vaccine development and gene therapy, presenting minimal biosafety risk under standard laboratory containment procedures.
    - A note was made regarding the listing of DH5α *E. coli* in the documentation. Since these are common cloning strains and are exempt when derived from *E. coli* K-12, comments were added to clarify this exemption. It was recommended to explicitly state that the strains used are K-12 derivatives to ensure appropriate handling and compliance
    - In the summary of proposed research, siRNA is mentioned as covered under the IBC application of a collaborator. This needs to be confirmed by the study team.
    - The doses mentioned for human ovarian cancer cell lines in the linked animal use protocol are not consistent with what is listed in the IBC protocol.
    - The transport SOP from the collaborator needs to be updated after the move to their new location is completed.
- **Comments sent to the PI for clarification**:
    - **Hazard Identification**: If these are standard cells for cloning, then please indicate that they are K12-type E coli. If they are K12, they are exempt.
    - **Summary of Proposed Research**:
        - If the DH5-alpha are commercially sourced, then mention that the E.

coli are K-12 subtype. If the E. coli are not K-12 type, then add additional appropriate safety measures.

- In the statement "siRNA is a gene therapy with a great potential for treatment of cancer and other diseases. Clinical success of siRNA treatment is dependent on its efficient delivery to target tissues. Lipid nanoparticles (LNPs) and Leukosome nanoparticles have proven effective in delivering siRNA into tumor tissues. We will use this technology to deliver specific siRNAs targeting RPL39 into TNBC/MpBC tumors. LNPs and Leukosome nanoparticles carrying siRNA against RPL39 (Horizon Discovery) will be synthetized by a collaborator." siRNAs are not mentioned in the collaborator's protocol. If siRNAs encapsulated using the described methods will be used in the current study, please ensure the correct protocol is referenced or update the collaborator's protocol to include these agents.

- **Animal Section:**
  - Agent: mRNA-LNP cancer vaccine encoding 20-30 HLA-A2 restricted tumor neoantigens - In the mentioned animal use protocol, the dose is 5-30 µg. Please make sure it is congruent with the animal use protocol
  - Agent: Human Ovarian Cancer Cell OVCAR8 was genetically modified with a silenced iNOS gene - In the animal use protocol the dose is mentioned as up to 10e7, please make sure that these are congruent.
- **Exposure Management- Laboratory:** Please have the transport SOP updated with the PI's signature

- **The motion to approve after designated member review was seconded and passed.**

Motion: Approve after Designated Member Review

- Yes Votes: 12
- No Votes: 0
- Abstained: 0

IBC00002237
Title: IBC for Aptamer function in tumor study
Principal Investigator: Youli Zu

- *Voting Member Nagendran Tharmalingam was not present during the discussion of this amendment and did not vote. Quorum was maintained.*
- **Study Overview**: This new IBC protocol involves the use of PDL1 and PDGC21-T aptamers conjugated with doxorubicin (DOX) for targeted tumor therapy. The study includes an in vivo component utilizing an NSG-MHC I/II double knockout (DKO) tumor mouse model. The experimental procedure encompasses aptamer-

DOX conjugation, characterization of the conjugates, in vivo administration, and subsequent monitoring of therapeutic efficacy and toxicity in the animal model.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-F
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**
    - Containment procedures and PPE described are appropriate for the experimental procedures.
    - The study team needs to confirm if radioactive isotopes will be utilized in this study.
    - Given that the agent is being transported to animal areas, a transport SOP is required.
- **Comments sent to the PI for clarification**:
    - **Exposure Management:** Please include a Transport SOP - it is indicated that the aptamers will be transported from the laboratory to the animal areas.
    - **Summary of Proposed Research:** Are radioactive isotopes being utilized in these studies? Please provide clarification. If so, an RSC application needs to be created and submitted.
    - **Animal Section:** The containment procedures on the animal use protocol need to be updated to reflect that the cage will be marked with a yellow chemical hazard sticker to alert the staff the waste needs incineration.
- **The motion to approve the study after designated review was seconded and passed.**

Motion: Approve the study after designated member review

- Yes Votes: 12
- No Votes: 0
- Abstained: 0

IBC AMENDMENTS

IBCA00001269
Title: Hazard Amendment 3 for IBC for Role of very Long-Chain fatty acids in neuroinflammation
Principal Investigator: Hyunglok Chung

- *Voting Members Tanya Herzog and Nagendran Tharmalingam were not present during the discussion of this amendment and did not vote. Quorum was maintained.*

- **Amendment Overview**: This amendment includes the addition of experiments involving human iPSC-derived neural organoids. These studies will incorporate the use of human iPSCs (induced pluripotent stem cells) to generate 3D organoid cultures for modeling neurodegenerative disease mechanisms. Recombinant DNA technology will be utilized to introduce disease-associated mutations via plasmid transfection, adeno-associated viral vector transduction, or CRISPR-based genome editing. In addition, RNA interference (RNAi) techniques will be employed to suppress the expression of specific genes (ACER1, ACER2, ACER3, ASAH1, ASAH2) relevant to disease pathways. These changes involve the introduction of human cells/tissues, recombinant DNA, and synthetic or recombinant nucleic acids into the protocol.
- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-D-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion:**
    - AAV is nonpathogenic and not known to cause disease in humans. However, BSL2 handling and containment is appropriate. Universal precautions will be used when handling iPSCs.
- **The motion to approve the amendment was seconded and passed. The IBC subsequently approved the amendment.**

Motion: Approve

- Yes Votes: 11
- No Votes: 0
- Abstained: 0

IBCA00001277
Title: Hazard Amendment 2 for IBC for Effect of over-expression of antioxidant enzymes in brain cells on spin oscillating magnetic field (sOMF) induced toxicity
Principal Investigator: Santosh Helekar

- *Voting Member Nagendran Tharmalingam was not present during the discussion of this amendment and did not vote. Quorum was maintained.*
- **Amendment Overview**: To evaluate the effects of oncomagnetic treatment in animal models, including large animal models, a lentiviral system carrying the gene of interest will be used to achieve stable expression of genes or shRNAs in human, mouse, and pig cells. These modified cells will be used to mimic gene expression profiles characteristic of human glioblastoma
- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-D-1-3

- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion:**
    - The purpose of the amendment is unclear. The committee is unable to proceed with discussion until further clarification is provided
- **Comments sent to the PI for clarification**:
    - **Hazard Amendment Summary**: Requirement 2 below states, "provide a summary of the changes to the research protocol". The PI and team have provided a statement, which is not a summary of the changes, nor has the study team provided a summary of the study progress to date, which is also requested.

      It looks like the original study was focused on understanding the mechanisms of oscillating magnetic fields (sOMF)-induced oxidative stress, DNA damage and cell death in glioblastoma multiforme (GBM) cells and obtain an explanation for the lack of toxicity in normal neurons and glia. From the statement provided, it is unclear where the study is going. Please explain in a summary paragraph.

    - **Summary of Proposed Research**
        - **Revise the Amendment Summary Title**
          The current title in the "Summary of Proposed Research" section incorrectly references only "Amendment 1." Please update the title to reflect that this is **"Hazard Amendment 2"**
        - **Clearly Separate Amendment Descriptions**
          The summary must clearly describe the procedures and changes introduced in **Amendment 1** and **Amendment 2** as **distinct sections**.
            - *Amendment 1* was approved for the addition of **human cortical neurons** and **normal human astrocyte cell lines**.
            - *Amendment 2* should be described separately, with a clear explanation of what is being added or changed.
        - **Describe New Processes or Methods**
          For Amendment 2, provide a detailed explanation of any **new processes, procedures, or methods** that differ from what is currently being done under the approved protocol.
- **The motion to table the amendment was seconded and passed. The IBC subsequently tabled the amendment.**

Motion: Tabled

- Yes Votes: 12
- No Votes: 0
- Abstained: 0

Adjournment:

- The meeting adjourned at 12:01 pm.
