Houston Methodist Research Institute IBC Meeting Minutes

2/5/2026

Meeting Time Records

Meeting start time: 10:00 am

Meeting end time: 11:15 am

VOTING MEMBER ATTENDANCE				
Name of Member	**Status (member or alternate)**	**IBC role**	**If Voting Alternate, Member Substitution**	**Present in Person or Virtually (TEAMS)?**
Biana Godin, PhD, M.Sc. Pharm	Chair	Scientific, affiliated		Yes, Virtually
Sasha Azar, PhD	Vice Chair	Scientific, affiliated		Yes, Virtually
Vicente Zuno, BS, RBP	Member	Biosafety Officer, affiliated		Yes, Virtually
Joan E. Nichols, PhD	Member	Scientific, affiliated		Yes, Virtually
Chas Gray, RPh	Member	Scientific, affiliated		Yes, Virtually
Tanya Herzog, DVM	Member	Animal Expert, affiliated		Yes, Virtually
Edward Graviss, PhD	Member	Scientific, affiliated		No
Wenhao Chen, PhD	Member	Scientific, Affiliated		Yes, Virtually
Daniel Kiss, PhD	Member	Scientific, affiliated		Yes, Virtually
Tamara Steele, BS	Member	Community member, Non-affiliated		Yes, Virtually
Jillian Chahal, MPH, CSP	Member	Community member, Non-affiliated		Yes, Virtually
Francesca Taraballi, PhD	Member	Scientific, Affiliated		Yes, Virtually
Jiangyong Shao, MS	Member	Scientific, Affiliated		Yes, Virtually
Nagendran Tharmalingam, PhD	Member	Laboratory representative, Affiliated		Yes, Virtually
Anjana Tiwari, PhD	Member	Laboratory representative, Affiliated		Yes, Virtually
Dimitrios Wagner, MD PhD	Member	Human gene transfer expert, Non-affiliated		No

Sachin Thakkar, PhD	Member	Scientific, Non-affiliated		No

NON-VOTING MEMBER ATTENDANCE		
Name of Member	**IBC Role**	**Present in Person or Virtually (TEAMS)?**
Brenda Hartman BA	Ex-officio, Director, Central Laboratory Operations	Yes, Virtually
Gretchen Gotlieb, MS	Ex-officio, Safety Representative, Chemical Hygiene officer, Central Laboratory Operations	Yes, Virtually
Enid Burns	Ex-officio, Central Laboratory Operations Safety Representative	Yes, Virtually
Michael Smith	Ex-officio, Legal Counsel	Yes, Virtually
Michael Metcalf	Ex-officio, Environmental Safety	No
Tiffany Gunter	Ex-officio, Employee Health Representative	No
Astrid Marcela Quiroga	Ex-officio, Employee Health Representative	Yes, Virtually
Leon Brown, MS	Ex officio, Radiation safety officer	Yes, Virtually

QUORUM INFORMATION

Number of IBC members on the roster: 17

Number required for quorum: 9

All members present by TEAMs received all pertinent material before the meeting and were able to actively and equally participate in all discussions.

ATTENDANCE OFFICE OF RESEARCH PROTECTIONS STAFF
Malissa Mayer-Diaz, Safety Committees Manager
Perla J. Rodriguez, Sr. Analyst
Shane Wilson, Analyst
Prince Agyapong, Analyst
Rebecca Corrigan, IACUC Manager
Joylise Mitchell, IACUC Analyst

ATTENDANCE STATUS AND VOTING KEY	
ABSTAIN:	Present for the vote, but not voting "For" or "Against."
ABSENT:	Absent for discussion and voting for reasons other than a conflicting interest.
RECUSED:	Absent from the meeting during discussion and voting because of a conflicting interest.
SUBSTITUTION:	When regular members and their alternate(s) are listed in the ATTENDANCE table above and an alternate member substitutes for the regulator member this identifies the name of the alternate to indicate which individual is serving as the voting member for this vote. May be deleted if there are no substitutions.

CALL TO ORDER

The Institutional Biosafety Committee convened a hybrid meeting via Microsoft Teams on February 5, 2026. The meeting was called to order at 10 a.m. with 14 members in attendance, exceeding the quorum requirement of 9 members.

REPORTS

Biosafety Officer Report

- No reports

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 distributed to the committee members one week prior to the meeting and shown during the meeting.
- A list of approved administrative amendments was distributed to the committee members one week prior to the meeting and shown during the meeting.
- A list of approved continuing reviews via designated member review was distributed to the committee members one week prior to the meeting and shown to the committee members during the meeting.
- An annual refresher orientation was presented by Malissa Mayer-Diaz, Safety Committees Manager.

MINUTES REVIEW

The meeting minutes from January 15, 2026, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.

Motion: Approved

- Yes votes: 14
- No votes: 0
- Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002592
Title: IBC for CPRIT-RNAcore for mRNA manufacturing and assessment
Principal Investigator: John Cooke

Study Overview: In this resubmission, the RNAcore will continue to manufacture mRNA constructs for both new and returning clients, as well as for its research consortium partners. The team will also maintain ongoing efforts to optimize and develop manufacturing processes to enhance efficiency and product quality.

To comply with the Executive Order on safe and secure AI, all DNA sequences submitted by clients are screened using the SynScreen program on the HMH HPC system. If a sequence is flagged as potentially concerning, the client is notified and asked to complete an accompanying questionnaire. Program Managers, together with the RNAcore Scientific and Medical Directors, then review the project using the HHS Screening Framework Companion Guide to determine whether work may proceed.

RNA production is carried out using RNAcore's proprietary protocols, which include plasmid design and amplification in *E. coli*, DNA purification and linearization, in vitro transcription with modified nucleotides, DNase treatment, and mRNA purification through lithium chloride precipitation and spin filtration. Product quality is assessed using TapeStation analysis, and mRNA yield is measured with DeNovix instrumentation.

- **Training**: All staff members have completed training.
- **Applicable NIH Guidelines**: Section III- D-2
- **Containment Conditions to be implemented**: BSL2
- **Risk assessment and Discussion**: Handling mRNA constructs in these studies presents minimal risk to staff. mRNA molecules are non-infectious, incapable of replication, and rapidly degraded in biological environments, including on skin and in environmental surfaces. They do not pose risks of infection or transmission.
- **Comments sent to the PI for clarification**:
    - **Section Hazard Identification**: **H5N1 and H3N2** are not Risk Group 1 agents. Please create separate entries for Risk Group 2 and Risk Group 3 derived antigens. *Alternatively,* you may submit an amendment to **IBC protocol IBC00002238** if these materials are intended to be reviewed under the protocol covering Risk Group 4 pathogens. Containment Requirements:

The appropriate containment level for these materials is BSL-2, not BSL-1. Please update accordingly. Influenza Strain Confirmation: Please confirm the specific influenza strains that will be used. Plasmids: Similar to H5N1 and H3N2, because the plasmids encode templates derived from Risk Group 2 and Risk Group 3 agents, please create corresponding entries under Risk Group 2 plasmids and Risk Group 3 plasmids or submit an amendment to IBC protocol IBC00002238.

- **Section Summary of Proposed Research:** Please correct the spelling of "proprietary." Please remove the IBC Exemption Checklist. This document is outdated and is no longer used by the IBC or the Office of Research Protections.

- **Section Risk Assessment**: **Question 6:** *"Does your proposed project include DNA from Risk Group 2, Risk Group 3, Risk Group 4, or Restricted Agents which is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems? (Sec. III.D.2)"* This response should be updated to "Yes" because the project involves DNA derived from antigens of Risk Group 2 and Risk Group 3 agents.

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

Motion: Approvable by Designated Member Review

- Yes Votes: 14
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002585
Title: IBC 2026: Investigation of glioblastoma cell tumorigenicity through viral gene targeting
Principal Investigator: Robert Rostomily

Study Overview: This project utilizes several hazardous biological agents and materials in the development and evaluation of glioma models. **Human and Mouse Glioblastoma Cells:** Includes primary cells isolated from human tumor specimens and established cell lines. Depending on the study, cells may be screened or unscreened for pathogens. Animals receiving screened cells are housed at ABSL-1; unscreened cells at ABSL-2. **Viral Vectors: Lentiviral vectors** (produced in the laboratory) carrying ORFs, shRNA, or CRISPR guide RNA for genetic modification. **AAV vectors** (produced in core facilities) used similarly for gene delivery. Gene targets: p53,p16,NF1, hTERT, EF1A Markers for cell and tumor tracing: GFP, RFP, Luc. All viral work follows institutional SOPs and involves replication-incompetent vectors. **Pig, Mouse, and PDX Tumor Models:** Includes intracranial or subcutaneous implantation of tumor cells for growth and survival studies. **mRNA–Lipid Nanoparticle (LNP) Formulations:** mRNA constructs (commercially synthesized) are encapsulated in LNPs and administered by tail vein,

intranasal, intraperitoneal, or subcutaneous injection. Genes of interest: ORF myrAKT, Ha-RasVII, hTERT, SV40 Tag, EGFRVIII, mutant p53, PDGF.

- **Training**: All staff members have completed training.
- **Applicable NIH Guidelines**: Section III-D-1, 3
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: The agents used in this project present low to moderate biosafety risks, primarily due to the use of viral vectors and human-derived cells. Recombinant AAV, third-generation replication-deficient lentiviral vectors, and retroviral particles produced in Phoenix cells are all replication-incompetent, with potential hazards limited to accidental exposure through aerosols, mucosal contact, or sharps injuries that could result in unintended delivery of genetic material to host cells. HEK293T cells and human glioblastoma cells require BSL-2 precautions due to their human origin and, when transduced, may contain integrated genetic constructs or residual vector particles. mRNA–LNP formulations are non-infectious and non-replicating, with risks primarily associated with chemical handling, aerosol generation, and accidental injection during animal procedures. All materials are managed under established SOPs and appropriate BSL-2 containment practices to minimize risk to personnel.
- **Comments sent to the PI for clarification**:
    - **Section Summary Of Proposed Research** - Please clarify if glioblastoma cells derived from patients and collaborators are screened for common human pathogens. If they are not, mice administered these cells need to be housed at ABSL2 (section 'Animals').
    - **Section Animals** - Retroviral Vector transformed cells: Please clarify whether animals injected with cells transformed using retroviral vectors will be housed at ABSL-1 or ABSL-2 as both levels are indicated. Please note ABSL2 handling and housing is appropriate- mRNA LNP Studies: Animal housing for mRNA LNP work may be updated to ABSL-1. Under the "Housing" section please select "Conventional Rodent Room" and enter ABSL-1 in the text box.- Transduced Human GBM Cells: In the housing description text box, please indicate that tested transduced GBM cells will be housed at ABSL-1, and untested transduced GBM cells will be housed at ABSL-2.
- **The motion to approve the study by designated member review was seconded and passed.**

Motion: Approvable by Designated Member Review

- Yes Votes: 14
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

Title: 3Y resubmit: Research to develop messenger RNAs and circular RNAs that express antigens from Mycobacterium tuberculosis in human cell lines as part of a study to develop vaccines
Principal Investigator: Daniel Kiss

*** Member Daniel Kiss recused himself from both the discussion and the vote due to a conflict of interest*

Study Overview: This project aims to develop messenger RNA (mRNA) and circular RNA (circRNA) constructs that encode Mycobacterium tuberculosis antigens as potential vaccine candidates. The RNAs are designed to direct mammalian cells to produce non-harmful recombinant antigens that can stimulate protective immune responses. Plasmid templates for circRNA constructs will be generated using standard molecular cloning methods, including restriction enzyme cloning, site-directed mutagenesis, Golden Gate cloning, or Gibson Assembly. RNAs will be produced by in vitro transcription and delivered into mammalian cell lines using standard transfection reagents or lipid nanoparticles (LNPs). Transfected cells will be harvested within 24–48 hours and analyzed for antigen expression using techniques such as western blotting, ELISA, or microscopy. Once expression of the intended antigen is confirmed, RNA materials will be transferred to approved collaborators under established MTAs.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-D-2
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: The proposed work involves molecular cloning, in vitro transcription of mRNA and circular RNA constructs, and transfection of mammalian cell lines to assess antigen expression. These activities present minimal biosafety risk and fall within standard BSL-2 practices. The RNA constructs encode *Mycobacterium tuberculosis* antigens but do not contain infectious agents, replicating sequences, or full-length bacterial genomes, and the expressed recombinant proteins are non-toxic. Mammalian cell lines require routine BSL-2 handling due to their human or animal origin, but no work with live *M. tuberculosis* or other infectious materials is performed. With adherence to established SOPs and BSL-2 containment, risks to personnel are low and no significant biosafety concerns are anticipated.
- **Comments sent to the PI for clarification**:
    - **Section Staff Identification**: Recommendation: ESAT-6, Ag85B, and the M72 artificial polyantigen are highly immunogenic and pro-inflammatory M. tuberculosis antigens, commonly used in vaccine research because they elicit strong innate and adaptive immune responses. These antigens are also known to participate in trained immunity, which involves durable epigenetic reprogramming of innate immune cells. The safety concern arises from the potential for excessive or prolonged inflammation, as well as pathogen-driven immune modulation. These effects can contribute to tissue damage, chronic inflammatory states, or impaired pathogen clearance. Because of these risks, all project staff must be trained on the hazards associated with innate immune stimulation, and the specific risks related to the M. tuberculosis antigens being expressed, even when expression occurs solely

in cell culture.

- **Section Summary of Proposed Research**: The protocol describes expression of antigens from BCG, which derives from Mycobacterium bovis, as well as antigens from Mycobacterium tuberculosis. This distinction is not clearly stated in the submission, and the text shifts between the two organisms without clarification. Please clearly specify which antigens originate from M. bovis BCG and which originate from M. tuberculosis to avoid ambiguity in the risk assessment.
- **Section Exposure Management – Laboratory**: mRNA vaccines and vaccine candidates are known to induce significant local inflammation, which is often attributed to the lipid nanoparticle (LNP) delivery system rather than the antigen alone. In this case, the constructs express ESAT-6, Ag85B, and the M72 artificial polyantigen—all of which are highly immunogenic and pro-inflammatory antigens commonly used in vaccine research specifically because they elicit strong immune responses. While the mRNA or circular RNA platforms themselves are generally not considered safety concerns, their ability to encode and produce strongly inflammatory proteins elevates the associated safety risk. This should be reflected appropriately in the risk assessment.
- **Section Risk Assessment**: BCG should be identified as the relevant agent. At minimum, please list Mycobacterium bovis BCG antigens in the risk assessment section by updating the hazard identification section. Because your constructs express M. tuberculosis–specific proteins (ESAT-6, Ag85B, and the M72 artificial polyantigen), these antigens constitute the relevant agent for reporting in Risk Section #6. Please list them accordingly by updating the hazard name in the hazard identification section.

- **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
- Recused: 1, Daniel Kiss
- Absent: 0

IBC00001799
Title: mRNA manufacturing for vaccine development with ARPA-H
Principal Investigator: John Cooke

*** Member Francesca Taraballi recused herself from both the discussion and the vote due to a conflict of interest*

Study Overview: This project involves the production of mRNA constructs encoding CMV and EBV viral glycoproteins for vaccine-development studies conducted by external collaborators.

RNAcore will perform mRNA manufacturing using standard procedures applied to all clients. Collaborators will provide customized plasmids, which will be amplified in *E. coli* and assessed for sequence accuracy, purity, and supercoiled content. Plasmids will then be linearized with restriction enzymes and used as templates for in-vitro transcription incorporating N1-methyl-uridine. Synthesized mRNA will undergo purity and endotoxin testing before release for formulation into lipid nanoparticles. All incoming sequences will be screened for sequences of concern in accordance with NIH guidelines, and completed RNA products will be shipped following institutional transport SOPs under the terms of the collaborative grant.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-D-2
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: The work involves standard BSL-2 molecular biology procedures to manufacture mRNA constructs encoding non-infectious CMV and EBV glycoproteins from collaborator-supplied plasmids. These plasmids contain antigen-encoding sequences only and do not include full viral genomes or elements capable of producing infectious virus. The resulting mRNAs are non-replicating and pose no infectious risk to personnel. Potential hazards are limited to routine handling of *E. coli* cultures, molecular cloning reagents, and mRNA synthesis materials, all of which are mitigated through established SOPs, biosafety cabinet use, and appropriate PPE. All sequences are screened per NIH guidelines, and when conducted under standard BSL-2 containment, the work presents minimal biosafety risk.
- **Comments sent to the PI for clarification**:
    - **Section Hazard Identification**: CMV and Epstein Barr virus are RG2 organisms. Please update to RG2.
    - **Section Plasmid**: E. coli should be downgraded to RG1 from RG3.
- **The motion to approve the study through administrative review was seconded and passed.**

Motion: Approvable by Administrative Review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 1, Francesca Taraballi
- Absent: 0

IBC00002586
Title: RELY-30: Phase I Study of Relapsed CD30 Expressing Lymphoma Treated with Multi-Dose CD30 CAR T Cells
Principal Investigator: Carlos Ramos

Study Overview: This Phase I dose-escalation clinical trial evaluates the safety of autologous activated T lymphocytes (ATL) genetically modified ex vivo to express a CD30-targeted chimeric antigen receptor (CD30.CAR) containing a CD28 costimulatory endodomain. T cells are transduced in vitro using a replication-deficient SFG retroviral vector (Mo-MuLV–based), which delivers the CAR transgene; the retroviral vector itself is not administered to patients. The CAR T-cell product is manufactured in the CAGT GMP facility and administered as a single IV infusion at one of three dose levels: 2×10^7 cells/m², 1×10^8 cells/m², or 2×10^8 cells/m², with cohorts of 3–6 patients per level. Patients who have not recently undergone transplant may receive lymphodepleting chemotherapy (cyclophosphamide with fludarabine or clofarabine) prior to infusion. The study evaluates safety, CAR-T cell persistence, and antitumor activity, with all manufacturing and transport steps performed under established GMP clinical SOPs.

Three-Year Progress Summary:
The RELY-30 study remains active with ongoing enrollment and treatment. To date, 59 patients have been enrolled and 35 treated. During the 2024–2025 review period, one patient underwent T-cell procurement and one received CAR T-cell infusion; 14 participants remain in follow-up. No investigational product–related unanticipated problems or complaints have been reported. Adverse events have primarily been Grade 1–2 constitutional, gastrointestinal, dermatologic, or metabolic effects, with expected Grade 3–4 hematologic cytopenias consistent with lymphodepleting chemotherapy and CAR-T therapy. One Grade 1 cytokine release syndrome event occurred in June 2025 and resolved with standard supportive care. Most adverse events were unrelated or unlikely related to the investigational product; those considered possibly or probably related were anticipated and manageable. The overall safety profile remains consistent with the protocol's expected risk profile.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: There is a low potential for biohazard exposure to personnel. The viral vector is administered to the T cells (ATC) in a protected environment in a designated facility. These T cells are then cultured and cryopreserved in this controlled facility. The final product is administered at HMH and the personnel thawing cells is GMP trained for handling the product and containing spills. In the event of accidental spills of the thawed cells from the syringe, common disinfectants, in the case at HMH, "Sani-master" will be used to inactivate the agent. All personnel are instructed on the safe use and potential biological hazards of the virus and of the recombinant cells before the procedure is performed. Injection Healthcare Workers: There is a low potential for biohazard exposure to personnel. All steps are performed in a biosafety cabinet by GMP trained personnel. The syringes for the transportation of the product outside the biosafety cabinet are free of needles, but will be secured with a safety cap. The syringes are also secured in a biohazard bag. In the event of accidental spills of the recombinant cells from the syringe an HMH approved disinfectant will be used to inactivate the agent. All personnel are instructed on the safe use and potential biological hazards of the virus and of the recombinant cells before the procedure is performed. Retrovirus: It is highly unlikely that the retrovirus will escape the patient via urine, feces, saliva, mucus, tears or other secretions. Exposure to the shed replication defective virus will pose a very limited hazard as the titers will be extremely low. Healthcare workers will be instructed on the safe use

and potential biological hazards of the virus vector before they are allowed to work with patients.

- **Comments sent to PI for clarification**:
    - **Section Exposure Management**: The attached transport SOP, SOP: C05.01.46 – Transportation & Transfer of Non-Cryopreserved Cellular Products, is not appropriate for the CAR T-cell therapy described in this protocol. Please provide an updated or correct SOP that specifically addresses the transport and handling requirements for the CAR T-cell product used in this study.
    - **Section: Hazard Identification:** The protocol states that the product will be thawed on site, but it does not identify the specific laboratory or pharmacy space, nor the biosafety cabinet (BSC) in which thawing will occur. Please update this section to clearly indicate the location and biosafety equipment that will be used for thawing, or provide further clarification.
- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 14
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002591
Title: Research using recombinant DNA and synthetic RNAs including mRNA/circRNA/plasmids/viral vectors to express/deliver reporter proteins and human proteins in human cell lines to study and develop RNA therapeutics for gene rescue therapies
Principal Investigator: Daniel Kiss

Study Overview: This project investigates fundamental mechanisms of RNA regulation and translation, with a focus on cytoplasmic capping, codon-dependent RNA surveillance, the role of PCIF1 in stress responses, and how cellular stress affects translation from both endogenous and exogenous RNAs. The work includes the design, development, and testing of novel mRNA and circular RNA therapeutic candidates in mammalian cell culture systems. Experimental activities include cell culture in BSCs, molecular cloning of expression and reporter constructs, in-vitro synthesis of synthetic RNAs, RNA and protein extraction, and reporter assays using plasmids, synthetic nucleic acids, or stable cell lines generated using lentiviral vectors. All experiments are limited to in-vitro and in-vivo cell culture models.

Over the current review period, the laboratory's work has focused on defining the basic science underlying RNA therapeutic development. Ongoing studies have examined cytoplasmic capping

as a regulatory layer of mRNA metabolism, using Oxford Nanopore sequencing to map full-length RNA isoforms and identify features associated with recapping. Additional experiments have investigated how cytoplasmic capping contributes to early stress-response signaling using targeted assays (e.g., qPCR, 5′ RACE, polysome profiling) and transcriptome-wide methods such as ribosome profiling. The laboratory has generated preliminary findings supporting the role of alternative splicing, polyadenylation, and RNA structural features in marking recapping sites.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-D-1, 3
- **Containment Conditions to be implemented**: BSL2
- **Risk assessment and Discussion**: The scope of work includes mammalian cell culture; cloning of reporter/expression constructs; in-vitro synthesis of mRNA and circular RNA; transfection of external RNAs; reporter assays; generation of stable cell lines (lentiviral vector–mediated). No work with infectious agents, human subjects materials, or in vivo animal models is included. When conducted under standard BSL-2 containment with BSC use, PPE, and established SOPs, the activities present low biosafety risk. The principal biological hazard is exposure to replication-deficient lentiviral vectors during production/transduction; residual risks are effectively mitigated by BSL-2 with enhancements, proper training, and routine decontamination. No significant additional biosafety concerns are anticipated.
- **Comments sent to the PI for clarification**:
    - Risk assessment question #7 "*Does your proposed project include the use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems? (Sec.III.D.3)*" should be updated to "Yes"
- **The motion to approve the study through administrative review was seconded and passed.**

Motion: Approvable by administrative review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 1, Daniel Kiss
- Absent: 0

IBC00002581
Title: IBC for the Testing of the Biodistribution and Protein Expression for Novel Biomimetic mRNA Nanotherapeutics
Principal Investigator: Francesca Taraballi

*** Member Francesca Taraballi recused herself from both the discussion and the vote due to a conflict of interest*

Study Overview: This study aims to evaluate the performance of novel lipid nanoparticle (LNP) formulations for mRNA delivery by assessing both biodistribution and protein expression in vitro and in vivo. Reporter mRNAs (luciferase, eGFP, mCherry) and IL-1Ra mRNA will be used to provide quantifiable readouts of translation through imaging or standard protein-detection methods. Fluorescently labeled LNPs will enable assessment of cellular uptake in vitro and tissue biodistribution in vivo following multiple administration routes, including intravenous, subcutaneous, intraperitoneal, intramuscular, intrathecal, intracerebroventricular, and intra-articular delivery. Imaging-based analyses and downstream protein assays will be performed to compare formulation performance across different biological systems.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-D-4
- **Containment Conditions to be implemented**: BSL2, ABSL-1
- **Risk assessment and Discussion**: This work involves RG1 synthetic mRNAs delivered via non-infectious lipid nanoparticles, presenting minimal biological risk due to the non-replicating, non-integrating nature of the constructs and non-hazardous reporter proteins. Primary personnel hazards relate to accidental parenteral exposure, aerosol generation during handling, and routine chemical/sharps risks. Standard BSL-2/ABSL-1 practices, use of a Class II BSC, appropriate PPE, and established sharps controls effectively mitigate these risks. Environmental and community risks are low given the rapid degradation of mRNA and lack of transmissible agents, with waste managed through standard biohazard procedures. When these containment measures and institutional SOPs are followed, overall residual risk to personnel and the environment is considered low.
- **Comments sent to the PI for clarification**:
    - **Section Study Progress**: Please confirm that the mRNA that were used in the publications cited (e.g. mRNA-based Tc24 vaccines, b-catenin, etc.) are currently not being used in the lab. If yes, please add the respective agents to the protocol.
    - **Section Animals**: In IACUC 8867 (pre-submission), please make sure to use congruent dosages. E.g. it is stated that "Genetic payload (mRNA, mmRNA, siRNA) as nanoparticles payload" at doses of up to 300ug/mouse, which is significantly higher than 2-40ug/mouse. None of the agents require ABSL2 handling. Please update to ABSL1
    - **Section Summary of Proposed Research**: Please make sure that all the attached documents (combined in 1 pdf) are signed by the PI.
    - **Section Recombinant and Synthetic Nucleic Acids**: Please attach current SDS sheets for the materials (some are ~ 10 years old).
    - **Section Exposure Management – Laboratory**: Please sign the documents, including the transport SOP
- **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
- Recused: 1, Francesca Taraballi
- Absent: 0

IBC00002570
Title: Combined Viral and Non-Viral Gene Modulation of Brain Tumor Cells (S100A4, YAP1, CD276) in PDX/Mouse Systems
Principal Investigator: Kyuson Yun

Study Overview: The Yun lab investigates regulators of glioma stem cells using patient derived xenograft (PDX) tissues, primary mouse tumor cells, and established cell lines to identify mechanisms driving therapy resistance and tumor recurrence. Ongoing work includes lentiviral activation or suppression of targets such as S100A4, Yap1, and Cd276—using both constitutive and inducible shRNA systems—along with reporter virus labeling to track cell behaviors. Additional approaches include generating CD276-targeted murine CAR T cells to study tumor–immune interactions and using liposomal nanoparticles for transient nucleic acid delivery (siRNA, sgRNA, mRNA). Over the past three years, the lab has made significant progress: identifying Yap1 as a sex-biased regulator of medulloblastoma stem cells and immune infiltration, developing a novel bispecific antibody targeting S100A4 and TfR, securing two R01 grants related to S100A4 and tumor slice profiling, and characterizing four additional transplantable mouse glioma models with deep immune and single-cell RNA profiling to support immunotherapy research.

- **Training**: All staff members have completed their required training.
- **Applicable NIH Guidelines**: Section III-D-1, 3, 4
- **Containment Conditions to be implemented**: BSL2, ABSL2
- **Risk assessment and Discussion**: This work uses RG2, 3rd-generation SIN lentiviral vectors (VSV-G pseudotyped) to manipulate S100A4, YAP1, and CD276, carrying a risk of stable genomic integration/insertional mutagenesis upon accidental parenteral or mucous-membrane exposure; RCL risk is minimized by split-packaging and SIN design, and vectors are single-round. Transgene/shRNA risks are not expected to cause acute toxicity in healthy personnel, but any unintended genetic modification is a biohazard. Additional agents include mRNA reporters (RFP/GFP/YFP/luciferase; RG1) with minimal hazard; liposomes with sgRNA/siRNA (non-infectious)—note potential gene editing/knockdown only where Cas9 or RNAi machinery is present; human primary cells and PDXs (bloodborne pathogen risk; BSL2 practices); CD276-CAR T cells (murine; bioactive cells posing sharps/accidental exposure risk, negligible community risk); tumor cell lines: MDA-MB-231br/eGFP (human; RG2), 4T1-Br (murine; BSL2), and HEK-293T (RG2, lentiviral packaging). Primary hazards: needlesticks, splashes/aerosols during vector prep/transduction, handling human/animal materials, and exposure to

bioactive CAR T cells; environmental risk is low given non-replicating vectors and contained use. Controls: BSL-2/ABSL-2 containment; Class II BSC for all viral/PDX/CAR-T manipulations; lab coat/gown, gloves, eye/face protection; strict sharps controls; sealed transport/secondary containment; bloodborne pathogen training; surface/equipment disinfection per SOP; and biohazard waste streams for cultures, PPE, and carcasses. With these measures, residual risk to personnel and community is low.

- **Comments sent to the PI for clarification**:
    - **Section Animals**: mRNA targeting RFP, GFP, luciferase, YFP: ABSL-3 appears to have been selected in error for mice injected with these mRNA constructs. ABSL-1 is the appropriate containment level for both handling and housing. CD276-CAR T cells: Please remove ABSL-1 for agent administration. ABSL-2 is the correct containment level for all handling and administration of CAR T-cell products. 4T1-Br (murine breast cancer cell line with GFP/luciferase): For agent administration, please remove ABSL-2. ABSL-1 is appropriate for this cell line.
- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 14
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 0

*** Member Francesca Taraballi left the meeting and did not return for the remainder of the meeting.*

IBC AMENDMENTS

IBCA00001438
Title: Hazard Amendment 1 for Research using nanoparticles to deliver the mRNA of tumor suppressor gene/ immune signaling molecule in animal tumor models to study efficacy of immune therapy and mRNA nano therapy
Principal Investigator: Gabriel Duda

Amendment Overview: This amendment adds the use of Ad5CMVCre, a recombinant adenoviral vector expressing Cre recombinase under the CMV promoter, for inducing loxP-mediated recombination in MST1$^{-/-}$ MST2^F/$^{-}$ mice to achieve conditional knockout of MST2 during the experimental induction phase. The only procedural change is the inclusion of intravenous administration of Ad5CMVCre; no new surgical or invasive techniques are introduced beyond standard injection methods. All adenoviral vector handling will occur under BSL-2 containment, including work within a certified biosafety cabinet, use of appropriate PPE, and decontamination

with approved disinfectants. Injections will be performed in an IACUC-approved procedure room following institutional BSL-2 practices, and all sharps and viral waste will be managed through established BSL-2 biohazard disposal procedures. No changes to animal housing or research objectives are proposed. The addition of Ad5CMVCre is necessary to enable conditional gene knockout within the mouse model.

- **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, ABSL2
- **Risk Assessment & Discussion:** The addition of Ad5CMVCre, a recombinant adenoviral vector used to induce conditional MST2 knockout in mice, introduces minimal new risk beyond standard BSL-2 work with replication-defective adenoviral vectors. The only procedural change is intravenous administration of the vector, performed using routine injection techniques. Potential risks involve accidental exposure to the viral vector through sharps injury, mucous membrane contact, or aerosol generation during handling. These risks are mitigated by conducting all vector preparation and handling under BSL-2 containment, including the use of a certified biosafety cabinet, appropriate personal protective equipment, and approved disinfectants for decontamination. Injections will take place in an IACUC-approved procedure room following institutional BSL-2 practices, and all sharps and biohazardous waste will be disposed of according to established BSL-2 procedures.
- **Comments sent to PI for clarification:**
    - **Section Exposure Management:** The attached transfer protocol appears to be the generic CLO template and does not include specific details such as where the materials will be transported to. Please update with laboratory specific information and transportation details.
- **The motion to approve the amendment through administrative review was seconded and passed.**

Motion: Approvable by administrative review

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1

IBCA00001460
Title: PI Amendment 1 for Phase 3b Trial of Nadofaragene Firadenovec vs.Observation in Subjects with Intermediate Risk Non-Muscle Invasive Bladder Cancer
Principal Investigator: Dharam Kaushik

Amendment Overview: This amendment updates the Principal Investigator on an IBC protocol associated with an IRB-approved Phase 3 clinical trial involving Nadofaragene Firadenovec, a non-replicating adenoviral vector gene therapy that delivers the IFN-α2b gene to the bladder urothelium for the treatment of intermediate-risk non–muscle invasive bladder cancer (NMIBC). The current PI, Dr. Raj Satkunasivam, is leaving the institution and will be replaced by Dr. Kaushik, who has the appropriate qualifications and experience to assume PI responsibilities on both the IRB and IBC protocols. No other changes to study procedures or approved agents are requested.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Not applicable
- **Containment Conditions to be implemented**: Not applicable
- **Risk Assessment & Discussion:** Not applicable
- **Comments sent to PI for clarification:** None
- **The motion to approve the PI amendment was seconded and passed.**

Motion: Approved

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1

IBCA00001467
Title: PI Amendment 5 for IBC for A Phase 2, Multi-Arm, Multi-Cohort, Open-Label Study to Evaluate the Safety and Efficacy of Cretostimogene Grenadenorepvec in Participants with High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC)
Principal Investigator: Dharam Kaushik

Amendment Overview: This amendment updates the Principal Investigator on an IBC protocol associated with an IRB-approved Phase 2 clinical trial. The investigational agent, Cretostimogene Grenadenorepvec ("cretostimogene," formerly CG0070; hAdV-5/E2F/hGM-CSF), is a recombinant, conditionally replicating adenoviral serotype 5 vector engineered to selectively replicate in and lyse cancer cells and to stimulate an anti-tumor immune response through GM-CSF expression. The agent is administered via intravesical instillation for the treatment of subjects with high-risk non–muscle-invasive bladder cancer.
Due to the departure of the current PI, Dr. Raj Satkunasivam, Dr. Kaushik will assume the role of Principal Investigator on both the IRB and IBC protocols. Dr. Kaushik possesses the necessary expertise to serve in this capacity.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Not applicable
- **Containment Conditions to be implemented**: Not applicable
- **Risk Assessment & Discussion:** Not applicable
- **Comments sent to PI for clarification:** Not applicable
- **The motion to approve the PI amendment was seconded and passed.**

Motion: Approved

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1

IBCA00001463
Title: PI Amendment 3 for IBC for Phase2/NadofarageneFiradenovec-GemcitabineDocetaxel-Pembrolizumab_ABLE-22_26349
Principal Investigator: Dharam Kaushik

Amendment Overview: This amendment updates the Principal Investigator on an existing IBC protocol associated with an IRB-approved Phase 2 clinical trial. The study involves Nadofaragene Firadenovec, a non-replicating adenoviral vector–based gene therapy delivering the IFNα2b gene to the bladder urothelium. The investigational agent is administered quarterly as a 75 mL intravesical instillation at 3×10^{11} vp/mL and may be used alone or in combination with gemcitabine, docetaxel, or pembrolizumab. The primary objective is to evaluate the efficacy of intravesical nadofaragene firadenovec, either as monotherapy or in combination with chemotherapy or immunotherapy, in patients with high-grade BCG-unresponsive non–muscle-invasive bladder cancer (NMIBC) with carcinoma in situ (with or without high-grade Ta/T1 papillary disease).
Due to the departure of the current PI, Dr. Raj Satkunasivam, Dr. Kaushik will assume the role of Principal Investigator on both the IRB and IBC protocols. Dr. Kaushik possesses the appropriate expertise to serve in this capacity.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Not applicable
- **Containment Conditions to be implemented**: Not applicable
- **Risk Assessment & Discussion:** Not applicable
- **Comments sent to PI for clarification:** Not applicable
- **The motion to approve the PI amendment seconded and passed.**

Motion: Approved

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1

IBCA00001465

Title: PI Amendment 4 for A Phase 3, Randomized Study of Adjuvant Cretostimogene Grenadenorepvec versus Observation for the Treatment of Intermediate Risk Non-Muscle Invasive Bladder Cancer Following Transurethral Resection of Bladder Tumor

Principal Investigator: Dharam Kaushik

Amendment Overview: This amendment updates the Principal Investigator on an existing IBC protocol associated with an IRB-approved Phase 3 clinical trial. The investigational agent, Cretostimogene Grenadenorepvec ("cretostimogene," formerly CG0070; hAdV-5/E2F/hGM-CSF), is a recombinant, conditionally replicating adenoviral serotype 5 vector designed to selectively replicate in and lyse cancer cells while inducing an anti-tumor immune response through expression of GM-CSF. The agent is administered via intravesical instillation into the bladder at a dose of 1×10^{12} vector particles in a total volume of up to 100 mL. The study population includes subjects with intermediate-risk non-muscle-invasive bladder cancer.

Due to the departure of the current PI, Dr. Satkunasivam, Dr. Kaushik will assume the role of Principal Investigator on both the IRB and IBC protocols. Dr. Kaushik has the necessary qualifications and relevant expertise to serve as PI for this study.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Not applicable
- **Containment Conditions to be implemented**: Not applicable
- **Risk Assessment & Discussion:** Not applicable
- **Comments sent to PI for clarification:** Not applicable
- **The motion to approve the PI amendment was seconded and passed.**

Motion: Approved

- Yes Votes: 13
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1

ADJOURNMENT

The meeting adjourned at 11:15 am