Houston Methodist Research Institute IBC Meeting Minutes

12/4/2025

Meeting Time Records

Meeting start time: 11:00 am

Meeting end time: 12:01 pm

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, in Person
Sasha Azar, PhD	Vice Chair	Scientific, affiliated		Yes, Virtually
Vicente Zuno, BS, RBP	Member	Biosafety Officer, affiliated		Yes, in Person
Joan E. Nichols, PhD	Member	Scientific, affiliated		Yes, in Person
Chas Gray, RPh	Member	Scientific, affiliated		Yes, in Person
Tanya Herzog, DVM	Member	Animal Expert		Yes, in Person
Edward Graviss, PhD	Member	Scientific, affiliated		Yes, Virtually
Wenhao Chen, PhD	Member	Scientific, Affiliated		Yes, in Person
Daniel Kiss, PhD	Member	Scientific, affiliated		No
Tamara Steele, BS	Member	Community member, Non-affiliated		Yes, in Person
Jillian Chahal, MPH, CSP	Member	Community member, Non-affiliated		Yes, Virtually
Francesca Taraballi, PhD	Member	Community member, Non-affiliated		No
Jiangyong Shao, MS	Member	Scientific, Affiliated		Yes, in Person
Nagendran Tharmalingam, PhD	Member	Laboratory representative, Affiliated		No
Anjana Tiwari, PhD	Member	Laboratory representative, Affiliated		Yes, in Person
Dimitrios Wagner, MD PhD	Member	Non-affiliated, Human gene transfer expert,		Yes, Virtually

		Non-affiliated		
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, In person
Gretchen Gotlieb, MS	Ex-officio, Chemical Hygiene officer	Yes, In person
Enid Burns	Ex-officio, Central Laboratory Operations Safety Representative	No
Michael Smith	Ex-officio, Legal Counsel	No
Michael Metcalf	Ex-officio, Environmental Safety	No
Tiffany Gunter	Ex-officio, Employee Health Representative	No
Astrid Marcela Quiroga	Ex-officio, Employee Health Representative	Yes, in Person
Leon Brown, MS	Ex officio, Radiation safety officer	Yes, in Person

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 December 4, 2025. The meeting was called to order at 11 a.m. with 13 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 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 via designated member review was shown to the committee members during the meeting.

MINUTES REVIEW

The meeting minutes from November 6, 2025, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.

Motion: Approved

- Yes votes: 13
- No votes: 0
- Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002381
Title: Phase 2 adaptive, randomized, open-label, blinded study evaluating efficacy & safety of Rapcabtagene Autoleucel vs Standard of Care in patients with system lupus erythematosus with active, refractory lupus nephritis
Principal Investigator: Sarah Kazzaz

Study Overview: Rapcabtagene Autoleucel (YTB323) is a CAR-T cell therapy manufactured by Novartis. During the manufacturing process, patient T cells are collected via leukapheresis and genetically modified using a lentiviral vector to express a chimeric antigen receptor (CAR) targeting CD19 on B cells. The lentiviral vector used for transduction is supplied by Oxford Biomedica and is a replication-defective, third-generation, self-inactivating (SIN) vector derived from HIV-1. Approximately 85% of the native HIV-1 sequence has been removed, resulting in a minimal lentiviral system with negligible risk of replication-competent lentivirus (RCL). All cell products must meet RCL release criteria prior to patient administration.
The study will evaluate the safety and efficacy of YTB323 following a lymphodepletion regimen compared to standard of care in participants with systemic lupus erythematosus (SLE) and active, refractory lupus nephritis. Patients will receive a single intravenous infusion of YTB323 at a target dose of 12.5 × 10^6 CAR-positive viable T cells. Prior to infusion, lymphodepletion will be performed to facilitate CAR-T cell expansion.
The investigational product will be received and processed by the Ann Kimball & John W. Johnson Center for Cellular Therapeutics. The product will be transported in a labeled biohazard container by authorized personnel using designated routes.

- **Applicable NIH Guidelines**: Section III-C-1
- **Containment Conditions to be implemented**: BSL2
- **Risk assessment and Discussion**: The clinical site will not handle the CTL019 (murine) HIV-1 lentiviral vector directly. This vector is used exclusively during the manufacturing process at the Novartis facility to transduce patient T cells and produce YTB323. Therefore, no vector-related exposure is anticipated at the clinical site. No intentional release of YTB323 into the environment is expected other than its administration via intravenous infusion to patients. At the site, the product is thawed and infused under controlled conditions. Theoretical risk of exposure exists if a product bag leaks during handling. In such cases, decontamination should follow institutional biosafety procedures for spills involving human blood and potentially infectious materials. No additional product-specific measures are required because YTB323 consists of autologous T cells that do not survive outside the human body. The product is not an infectious agent and does not persist in spills. Given these characteristics, no immediate or delayed adverse effects on non-target individuals or personnel handling YTB323 are anticipated. Environmental risk is considered negligible.
- **Comments sent to the PI for clarification**:
    - **Summary of Proposed Research:** The attached brochure states "For detailed instructions concerning the preparation, handling and administration of rapcabtagene autoleucel, please refer to the [Novartis T-Charge Product Handling Manual for Clinical Trials]" and mentions the "Novartis T-Charge Product Handling Manual for Clinical Trials" several times, therefore please attach a copy

of this manual in this section. Please provide a safety data sheet for YTB223.

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

Motion: Approve by Designated Member Review

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

IBC00002558
Title: IBC protocols: Research using plasmids/viral vectors to express or inhibit cytokine and protein expressions in human and mouse cell lines to study multiple myeloma
Principal Investigator: Jing Yang

Study Overview: This research focuses on tumor biology, translational research, and immunology in multiple myeloma (MM) and its associated bone disease. MM is the second most common hematologic malignancy in the U.S., characterized by malignant plasma cell accumulation in bone marrow, leading to impaired hematopoiesis and severe skeletal complications. Over 80% of patients experience skeletal-related events such as fractures, bone pain, and hypercalcemia. The study aims to understand interactions between myeloma cells and bone marrow stromal components (e.g., T cells, osteoblasts, osteoclasts, osteocytes, adipocytes) to identify mechanisms and signaling pathways for targeted therapies. Experimental approaches include gene manipulation (introduction or knockdown) using plasmid DNA and viral vectors (lentivirus, retrovirus) delivered in vitro to cell lines or patient-derived cells. Lentiviral CRISPR/Cas9 and shRNA systems will be used for gene editing and knockdown.

- **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**: All viral work will be conducted in a BSL-2 laboratory using biological safety cabinets. Lentiviral and retroviral vectors are replication-defective and self-inactivating; risk of replication-competent virus (RCV) is minimized by using third-generation systems and validated protocols. No virus will be administered directly to animals; only stable cell lines derived from viral transduction will be used in mouse studies. Standard PPE, biohazard labeling, bleach decontamination, and inventory tracking will be enforced. Viral DNA and stocks will be stored in designated freezers with biohazard labeling. All waste will be decontaminated with 10% bleach prior to disposal.

- **Comments sent to the PI for clarification**:
    - **Section Hazard Identification:** Please provide a comprehensive list of all

plasmids and vectors currently in use; avoid using vague terms such as "etc." Any future modifications can be submitted through amendments as needed. For target genes, the current entry under "Lentiviral vector" states: "our target genes will include cytokines, receptors, or others such as ACSS2, NHE6, EZH2, and etc." All target genes must be clearly specified—using "etc." or other non-specific wording to cover potential future work is not acceptable. If additional genes are identified during the course of the study, they should be added through an amendment specifying the exact gene(s). Remove "etc." and any ambiguous language.

- **Section Summary of Proposed Research: E. coli Strains**: List all strains that will be used (e.g., DH5α, One Shot™ TOP10). Avoid "etc." Ensure strains are captured in the hazard identification table, as some may not be IBC exempt. The protocol emphasizes that the third-generation lentiviral system is replication-incompetent and self-inactivating. However, there is concern about accidental recombination or contamination. Please include a plan for periodic evaluation to confirm the absence of replication-competent virus. The protocol notes that viral contamination in animal bedding is rare and manageable with standard disposal. Please provide additional details or justification for this statement.
- **Section Human Cells, Tissue, and Fluids:** Attach the IRB approval letter and informed consent for PRO00022561.
- **Section Animals:** Clearly state all substances or materials administered to animals. Update the Hazard table to include transduced cells. The protocol notes that 5×10^5 to 1×10^6 shRNA-modified cells will be administered; these must be listed.
- **Section RNAi:** The team answered "No" to the question: *Do you expect these molecules to functionally suppress expression of the cognate gene?* Since shRNA is designed to suppress gene expression, please update this response accordingly.
- **Section Exposure Management:** Regarding the transport SOP, attach the updated transport SOP using the new template provided in the "Summary of Proposed Research" section and add specific room numbers and a signature. The Originating Area should not be Central Laboratory Operations. For the question: *If your immediate action post-exposure process is different from above, describe below —* include contacting the biosafety officer as part of the response.

- **The motion to TABLE the study was seconded and passed.**

Motion: Tabled

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

IBC00002496
Title: IBC Protocol for Lentiviral Generation and Delivery of Gene Constructs (e.g, TERT, Cas9) in Vitro

Principal Investigator: John Cooke

Study Overview: The current study involves the generation of reporter cells using a lentiviral vector expressing blue fluorescent protein, resulting in a stable HEK293T cell line exhibiting blue fluorescence. This reporter system serves as a platform to evaluate DNA repair pathways by enabling fluorescence conversion from blue to green following targeted gene modification. These reporter cells will be broadly utilized to examine factors influencing genomic DNA repair, including newly identified functions of TERT.

Additionally, the system will support ongoing research in cellular transdifferentiation and Telo-editing, where precise genomic alterations and lineage transitions require controlled assessment of DNA repair outcomes. Cells will be modified using various lentiviral vectors included in this IBC submission, carrying genes for overexpression or shRNA-mediated knockdown, to investigate molecular mechanisms regulating genome stability and transdifferentiation across multiple project areas.

Transfection followed by FACS sorting will be employed to select green cells and determine system efficiency. Cas9/gRNA will be used to induce site-specific DNA damage. Previous work included generating iPSCs using Yamanaka factors and differentiating them into multiple cell types. Building on insights from the reporter cell system, the team plans to extend these investigations to additional differentiated cell types and related research projects. Other experimental approaches will include immunofluorescence (IF), qPCR, Comet assay, and western blot analysis.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-D-1, Section III-E-1
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: The risk to humans and the environment is considered low. The lentiviral vectors utilized in this study are third-generation, replication-deficient constructs in which all essential viral replication functions have been removed. These functions are supplied only transiently and in trans during the packaging process, enabling the production of infectious but non-replicating recombinant virus. Consequently, the virus cannot propagate following infection of cells or mouse tissues. The probability of unintended integration events is extremely low and consistent with the standard risk profile associated with third-generation lentiviral systems.

- **Comments sent to the PI for clarification**:
    - The National Institutes of Health (NIH) requires a clear description of the genes to be targeted, the proteins produced, and the vectors used for several critical reasons related to scientific safety. There is not enough information in the proposal summary to determine issues related to safety. A clear, brief, and non-technical summary of the research objectives and how the biohazardous or recombinant materials are relevant to those goals needs to be provided. NIH also requires details on the funding source, including the agency name and grant number, if applicable. This is important if accidental exposures occur that need to be reported. There also

needs to be a detailed description of the laboratory procedures, including how biohazards or recombinant materials are used, produced, and transported between locations. The transport protocol that was uploaded is the general central laboratory operations template and does not state where materials are transferred to or from.

- **Section Summary Of Proposed Research** - Please clarify how DNA damage will be induced in the proposed study. While FACS sorting is necessary for working with HEK293T reporter cells, it is unclear how this applies to the other projects. Will previous studies be continued, or is the primary goal to establish HEK293T cells stably expressing blue fluorescence for assessing DNA repair mechanisms? This section should include a clear description of the planned work for the next three years in 1–2 paragraphs. Will all activities described in the previous three years continue? Which specific DNA repair pathways will be targeted, and what methods will be used to induce DNA damage?
- **Section Staff Identification** - Will any of the work described in the previous three-year summary be continued during the next three years? If not, this represents a significant change from the original protocol, and the title should be updated accordingly. Additionally, please clarify whether staff with no experience with be supervised by senior staff with appropriate experience. It is noted that all work described in the protocol will be conducted by staff who currently have only one year of experience working with viral vectors.
- **Hazard Identification** - Will all of these agents be used in the next 3 years or is the work with DNA repair going to be the focus? The title suggests in vivo work, but it's unclear whether these studies involve animals. If they do, please select 'Animals' under 'Please check below all that will be involved in your research' and 'Animal Areas' under 'Where will you work with these agents?'.
- **Sponsor Information -** Please provide the sponsor info. This is required for NIH or other federally funded grants in case of emergency for IBC.
- **Study Progress** - The summary and three-year plan do not clearly identify which genes will be targeted. The protocol title, *"IBC Protocol for Lentiviral Generation and Delivery of Gene Constructs (e.g., TERT, Cas9) in Vitro and In Vivo,"* is too general. All listed genes are proto-oncogenes. For iPSC studies, Oct4, Sox2, Klf4, and c-Myc will be targeted. However, the genes to be targeted in mouse studies are not specified. Please clarify the following: (1) Will Oct4, Sox2, Klf4, and c-Myc continue to be targeted in iPSCs using vectors for overexpression or knockdown? (2) Will the investigation into telomerase and its potential to reverse aging in progeria mice continue? (3) Which genes will be targeted in HEK293T reporter cells? The plan mentions studying DNA repair, but the approach is unclear.

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

Motion: Approvable by designated member review

- Yes Votes: 12
- No Votes: 1

- Abstained: 0
- Recused: 0
- Absent: 0

IBC00002540
Title: 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

Study Overview: The study team aims to develop novel therapies for gastrointestinal (GI) cancers, including pancreatic and liver cancers. The approach proposes evelopment of therapies for gastrointestinal cancers (pancreatic and liver) using mRNA-loaded nanoparticles in murine models. **Target Genes:** p53 and EGFP mRNA. **Delivery System:** Polymer-Lipid Hybrid Nanoparticles (LPHN).

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-D-4
- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: The EGFP mRNA and p53 mRNA nanoparticles are investigational lipid-based formulations intended for murine use. No known human toxicity; however, due to limited safety data, these are classified as Unknown Hazard. Standard BSL-1/2 precautions will be followed during handling and administration.
- **Comments sent to PI for clarification**:
    - **Section Hazard Identification:** It's unclear whether the mRNA is provided to the researcher—by a vendor or collaborator—already encapsulated in nanoparticles, or if encapsulation occurs in the lab. Please clarify whether these are pre-made encapsulated mRNAs or prepared in the lab. If naked mRNAs will be handled in the lab, add them as a separate hazard in this section. Also, specify whether the mRNAs themselves will be purchased from a vendor or synthesized in the lab. There is a discrepancy between the description of NPs used for mRNA delivery. Please be consistent about the nature of nanoparticles used- are these lipid-polymer hybrids as described here or LNPs as described in the section below. This should be congruent with the linked HSC application.
    - **Section Staff Identification:** Please confirm that all personnel have completed required CITI training for IBC/HSC and any HMRI-specific training. Additionally, clarify the relevance of the statement regarding formaldehyde use for crosslinking protein complexes and immunoprecipitation, as its inclusion in the protocol is unclear.
    - **Section Exposure Management – Laboratory:** Please provide specific details on spill cleanup procedures. The current statement, *"Spill cleanup will include RNase deactivation and surface disinfection,"* should be revised to include the use of

bleach and/or alcohol as appropriate. Additionally, clarify why RNase deactivation is necessary.

- **Section Summary Of Proposed Research:** Please clarify whether mRNA and nanoparticle preparations will be performed in the laboratory or purchased from a vendor. If prepared in the lab, provide details of the procedure. Additionally, confirm whether the mRNA itself will be synthesized in the lab.
- **Exposure Management - Animal Areas** - There is no need to use double gloves, please update PPE accordingly.

- **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: 0
- Absent: 0

IBC00002530
Title: IBC for Use of Adenovirus, Lentivirus, and siRNA in Studying Regulation of Cardiac Electrophysiology
Principal Investigator: Francisco Altamirano

***Edward Graviss, Voting Member, left the meeting prior to discussion and voting on this protocol.*

Study Overview: The study investigates mechanisms of cardiac rhythm and contractile dysfunction in autosomal dominant polycystic kidney disease (ADPKD) and atrial fibrillation (AF). In ADPKD, PKD1 mutations eliminate polycystin-1, and prior work shows that loss of polycystin-1 in cardiac cells alone causes early electrical abnormalities and increased AF risk. Using mouse models and human stem-cell–derived cardiomyocytes, the team will examine how defective polycystins disrupt pathways controlling rhythm and contraction and explore related proteins as therapeutic targets. In parallel, the study will assess how autonomic nerve activity and neuropeptide release during apnea contribute to AF, using patient biopsies, canine models, and human iPSC-derived atrial cardiomyocytes. All work is in vitro; no agents are administered to live animals or humans. Methods include transient transfection of siRNA or CRISPR-Cas9 plasmids, lentiviral-mediated gene modulation, generation of replication-incompetent adenoviral vectors, calcium imaging with GCaMP6f, and processing of de-identified human specimens under IRB-approved protocols at BSL-2 containment. All work in this protocol is in vitro; no agents are administered to live animals or humans.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-D-1, 2

- **Containment Conditions to be implemented**: BSL2
- **Risk Assessment & Discussion**: Human sample exposure is minimal and handled under BSL-2 conditions using a biological safety cabinet; most specimens are formalin-fixed, and sharps are not used. Lentiviral particles pose a small infection risk, so only the PI and a research associate will handle small aliquots, and once stable cell lines are created, other personnel will work only with virus-free cells. Recombinant adenoviruses are replication-incompetent but require standard BSL-2 precautions to avoid direct contact. All cell lines come from approved vendors screened for common pathogens, and transfections use non-infectious mammalian expression vectors with cationic lipids.
- **Comments sent to the PI for clarification**:
    - **Exposure Management – Laboratory –** Please include a transport SOP for the transport of the deidentified human samples to the lab. A template has been provided.
- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approvable by designated member review

- Yes Votes: 12
- No Votes: 0
- Abstained: 0
- Recused: 0
- Absent: 1, Edward Graviss

IBC AMENDMENTS

IBCA00001425
Title: Hazard Amendment 3 for IBC for Oxidative stress and lung diseases
Principal Investigator: Rodney Folz

Amendment Overview: The amendment adds three components to the protocol: (1) inclusion of non-targeting control siRNA for use in human and mouse cells via Lipofectamine and passive transfection methods; (2) addition of lipid nanoparticle–encapsulated non-targeting control siRNA for use in human cells, mouse cells, and mice; and (3) addition of lipid nanoparticle–encapsulated siRNA targeting the Translationally Controlled Tumor Protein (TCTP) gene for use in human cells, mouse cells, and mice.

- **Training**: All staff members have completed and are current with their required training
- **Applicable NIH Guidelines**: Section III-F-1
- **Containment Conditions to be implemented**: BSL2, ABSL2
- **Risk Assessment & Discussion:** The lipid nanoparticle–encapsulated siRNA targeting TCTP and non-targeting controls contain no substances considered hazardous at the concentrations used. These formulations are investigational and will be handled under standard BSL-2 practices, including the use of a biological safety cabinet and appropriate

PPE.

- **Comments sent to PI for clarification:**
    - **Section Summary of Proposed Research** - The group should remove Lipofectamine transfection from the hazard summary where they are using nanoparticles encapsulated siRNA
- **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: 0
- Absent: 0

ADJOURNMENT

The meeting adjourned at 12:01 pm