IBC Meeting Minutes

11/6/2025

Voting Members Present
Biana Godin, PhD Chair
Chas Gray, RPh
Nagendran Tharmalingam, PhD
Edward Graviss, PhD
Jiangyong Shao, MS
Tanya Herzog, DVM
Wenhao Chen, PhD
Sasha Azar, PhD
Francesca Taraballi, PhD
Vicente Zuno, BSO
Dimitrios L. Wagner, PhD
Anjana Tiwari, PhD

Other Non-Voting Attendees:
Malissa Mayer-Diaz
Mary Brugger
Prince Agyapong
Shane M. Wilson
Perla J. Rodriguez
Joylise Mitchell
Enid M. Burns

Voting Members Absent:
Sachin Thakkar, PhD
Daniel Kiss, PhD
Joan Nichols, PhD
Jillian Chahal
Tamara Steele

Non-Voting Members Present:
Leon Brown, M.S
Brenda Hartman, B.S
Astrid Quiroga
Gretchen Gotlieb

Deviation from HMRI IBC Charter

Due to unforeseen circumstances, no local community members were able to attend the IBC meeting. While the charter recommends that at least one local community member participate, it is not a strict requirement. However, the charter does state that a community member must be present to conduct official business. The committee members present voted to proceed with the meeting in the absence of a community representative.

To ensure transparency, community members will receive the draft meeting minutes and a recording of the session in advance, allowing them the opportunity to review and raise any concerns.

Motion: Proceed with the IBC meeting without a community member present.

Vote Results:

- **Yes:** 12
- **No:** 0
- **Abstained:** 0

The motion to proceed with the IBC meeting without a community member present was seconded and passed.

Call to Order:

The Institutional Biosafety Committee convened a virtual meeting via Microsoft Teams on November 6, 2025. The meeting was called to order at 10:00 a.m. with 12 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 October 2, 2025, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.

- **Motion: Approved**
    - Yes votes: 12
    - No votes: 0
    - Abstained: 0

- The meeting minutes from October 9, 2025, were reviewed. A motion to approve was made and seconded, and the minutes were subsequently approved.
- **Motion: Approved**
    - Yes votes: 12
    - No votes: 0
    - Abstained: 0

AGENDA ITEMS

IBC NEW APPLICATIONS

IBC00002512
Title: Research using Gasdermin C plasmid to facilitate other plasmid transfection efficiency in various mouse and human immortalized cell lines.
Principal Investigator: Gong Yinan

Study Overview: The study aims to investigate whether a specific protein can target Rab7+ vesicles to modulate lipid-based immunoregulators and enhance type 2 anti-helminth immunity. Researchers will examine the molecular basis of vesicle targeting, focusing on lipid interactions, palmitoylation, and Rab7-associated protein binding. Additionally, the study will assess the potential to improve endosomal escape and nucleic acid delivery efficiency through in vitro transfection, establishing proof-of-concept for gene therapy applications.
The protocol is limited to in vitro work using purified recombinant proteins and mammalian cell cultures. Standard cell culture practices and plasmid transfection methods (e.g., lipofectamine-based delivery) will be employed. No animal work is planned at this stage; any future inclusion will require formal amendment and IBC review.

- **Applicable NIH Guidelines**: Section III-D-3, Section III-F
- **Containment Conditions to be implemented**: BSL2
- **Risk assessment and Discussion**: The study includes a variety of plasmids and genetically modified cell lines all handled appropriately at BSL2 containment. The principal investigator is the only individual listed in the protocol given that he is a new joining PI and will hire staff once on site. The hypothesis statement of the study

- **Comments sent to the PI for clarification**:
    - **Section: Summary of Proposed Research-** Regarding the stated hypothesis:
      "We hypothesize that a protein can target Rab7+ vesicles to alter lipid-based immunoregulators, thereby amplifying the anti-helminth type 2 immunity, and that this unique vesicle 'leakiness' can be exploited to enhance intracellular nucleic acid delivery." Please address the potential for gain-of-function effects due to immune system overactivation, which may lead to immune-related diseases. The protocol should include a description of how methods will be monitored and how any unanticipated immune signals will be reported. This is necessary to support additional risk assessments if needed.
    - **Section: Exposure Management- Laboratory Facilities-** The protocol currently lists biosafety cabinets in both R9-411 and R9-430. Please revise this to reflect that BSCs are only present in R9-411. R9-30 does not contain BSCs.
    - **Section: Animals** – While the protocol currently involves only in vitro work with cell lines, please note that any future inclusion of animal work will require formal amendment and subsequent review the IBC. At this time, the IBC cannot conduct a risk assessment for animal related procedures.
- **The motion to approve the study through designated member review was seconded and passed.**

Motion: Approve by Designated Member Review

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

IBC00002493
Title: Phase 1b Dose Expansion Study of NXC-201 for the Treatment of Patients with Relapsed or Refractory AL Amyloidosis
Principal Investigator: Yuen Carrie

Study Overview: This Phase 1b study evaluates the safety and efficacy of NXC-201 CAR T therapy in patients with relapsed or refractory AL amyloidosis. Subjects will undergo leukapheresis for CAR T cell manufacturing, followed by lymphodepletion with cyclophosphamide and fludarabine prior to infusion.

NXC-201 CAR T cells will be administered intravenously on Day 0 after lymphodepletion. The study includes:

- **Part A (Safety Lead-In):** Dose of 150 × 10^6 CAR T cells with 30-day safety

follow-up.
- **Part B (Dose Escalation/Expansion):** Dose of 450 × 10^6 CAR T cells, pending DSMB approval.

All work will be conducted using institutional cellular therapy facilities under standard biosafety and handling protocols.

- **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**: Proper containment and safety practices are in place for this study. NXC-201 CAR T cells are manufactured offsite by the sponsor using a replication-defective MSGV1-based gamma-retroviral vector to deliver a BCMA-specific CAR to patient T cells. The sponsor performs replication competence testing prior to release. Standard universal precautions during handling and administration are expected to mitigate potential exposure risks. It is noted that the cellular therapeutics facility onsite only performs work in biosafety cabinets class II, not glove boxes.

- **Comments sent to the PI for clarification**:
    - **Section: Exposure Management-Clinic/Hospital -** Engineering controls in cellular therapeutics facility include biosafety cabinets, not glove boxes. Update accordingly.
- **The motion to approve the study after administrative review was seconded and passed.**

Motion: Approvable by Administrative Review

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

IBC00002524
Title: Applied research into the engineering of RNA binding proteins and editors in plasmids, circular and linear mRNA towards the development of molecular medicines and treatment of cancer.
Principal Investigator: Brannan Kristopher

Study Overview: The research team is building on previous IBC-approved work to investigate RNA-binding protein (RBP) and RNA interactions both in vitro and in vivo. The laboratory has demonstrated that fusing APOBEC1, an RNA-editing enzyme, to an RBP

of interest enables identification of RNA edits at RBP-RNA binding sites using traditional RNA-Seq methods.

Triple-negative breast cancer (TNBC) and metaplastic breast cancer (MpBC) cell lines expressing RPL39-APOBEC fusion proteins have been established to analyze translational landscapes and gene expression. Additionally, patient-derived xenografts (PDXs) from TNBC and MpBC patients expressing RPS2-APOBEC have been developed, and single-cell RNA-Seq has been performed to characterize both translational and transcriptomic profiles in heterogeneous tumor samples. Genes identified as transcriptionally and translationally overexpressed in MpBC will be validated through functional assays.

ADAR1, another RNA-editing enzyme, is overexpressed in TNBC and MpBC. The team is designing and evaluating ADAR1-based RNA sensors using validated gene targets. This work aims to elucidate the molecular regulation of RPL39 in MpBC at both transcript and protein levels. Identified molecular targets may inform therapeutic strategies, including drug discovery or RNA sensor development.

The Lenti-X 293T cell line will be transfected with lentiviral vectors to produce high-titer lentivirus (>10^8 ifu/ml, as determined by flow cytometry).

TNBC accounts for approximately 20% of annual breast cancer diagnoses in the U.S. and lacks key druggable targets, limiting standard therapy options. The team will design RNA sensors that function inversely to site-directed RNA-editing systems. These sensors incorporate a premature termination codon (PTC) that inhibits translation of a downstream payload protein. Upon binding to a cellular target RNA, the PTC is edited, activating payload protein production. These sensors can be gated by tumor- and patient-specific RNA markers, which become abundant during TNBC chemoresistance. Delivery of apoptosis-inducing factors could enable highly specific elimination of resistant subpopulations.

Once mRNA constructs are developed, they will be tested in vitro using HEK-293T and TNBC cell lines (MDA-MB-231, BT549, HS578T) with lipofectamine and lipid nanoparticle (LNP) delivery systems. If successful, the team will proceed to in vivo mouse studies to assess safety, biodistribution, and functionality of mRNAs and/or therapeutic cargos for tumor reduction. Subsequent studies will evaluate combination therapies using chemotherapeutic agents and mRNAs to enhance TNBC treatment outcomes.

- **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**: Several concerns were noted in the protocol. The inclusion of Spike (B.1.617.2 Delta variant) pseudotyped lentivirus lacks a clear rationale within a study described as cancer-focused. Additionally, the DNA lentiviral expression vectors and RNAi vectors are presented under a single risk

assessment for knockdown and overexpression of more than 70 genes, making the specific risk exposure to staff unclear. Infectious agents and lentiviral vectors should not be handled in chemical fume hoods, as these hoods lack HEPA filtration and do not provide appropriate biological containment. The transport SOP does not adequately differentiate chemical and biological hazards during inter-facility transport; clarification is needed on the materials used (e.g., cardboard, styrofoam, iceboxes) and which are appropriate for chemicals versus infectious biological materials. Infectious materials must not be transported in cardboard or styrofoam, as these cannot be properly decontaminated. Under disposal methods, liposomes with therapeutic cargo and nanoparticle materials must be disposed of via the nanomaterial waste stream. For lipid nanoparticles encoding mRNAs, multiple disposal methods are listed; the protocol should clarify the correct method under "If other, please list," or remove any options that do not apply.

- **Comments sent to the PI for clarification**:
    - **General Protocol Formatting:** Throughout the protocol, several acronyms are used without definition. Please ensure all acronyms are clearly defined upon first use to maintain clarity and consistency.
    - **Section: Summary of Proposed Research-** The protocol is primarily framed as a cancer research study. Please provide a clear scientific rationale for the inclusion of the agent *Spike (B.1.617.2 Delta variant) pseudotyped lentivirus (SARS-CoV-2)* in this context.
    - **Sections: DNA Studies, Viral Studies, and Plasmid Studies-** The agent is listed as "DNA lentiviral expression and RNAi vectors," with a single risk assessment covering both gene knockdown and overexpression. To improve clarity and safety assessment, please categorize the listed genes into functional groups and treat each group as a separate agent. This will help the study team better understand potential risks in the event of accidental exposure.
    - **Section: Exposure Management – Laboratory Facility:** The use of a chemical fume hood for handling biological agents such as DNA lentiviral vectors and SARS-CoV-2 Delta spike pseudotyped lentivirus is inappropriate. Chemical fume hoods lack HEPA filtration and are not designed for biological containment. Please revise the protocol to specify appropriate biosafety cabinets for handling these agents.
    - **Exposure Management – Laboratory:** The transport SOP lacks detail on how chemical and biological hazards are differentiated during inter-facility transport. Please clarify the materials used for transport (e.g., cardboard, styrofoam, iceboxes), and specify which are appropriate for chemicals versus infectious biological materials. Note: Infectious materials must not be transported in cardboard or styrofoam, as these cannot be properly decontaminated. Under disposal methods, liposomes with therapeutic cargo and nanoparticle materials must be disposed of via the nanomaterial waste stream. For the agent *lipid nanoparticle encoding mRNAs*, multiple

disposal methods are listed. Please clarify the appropriate disposal method under “If other, please list,” or remove any options that do not apply.

- **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

IBC00002470
Title: SAGAN – Phase I Study of CD19-Directed CAR-T Cells (2nd/3rd Gen) for Advanced B-Cell Non-Hodgkin’s Lymphoma and Chronic Lymphocytic Leukemia
Principal Investigator: Carlos Ramos

Study Overview: Goal/Aim of the Study: Phase I dose escalation trial to assess the safety of treating relapsed/refractory aggressive or indolent NHL and CLL with autologous T lymphocytes genetically modified to target the CD19 antigen expressed by tumor cells. The study involves the use of CD19-directed CAR-T cell agents: CD19.CARCD28/CD137zeta and CD19.CARCD28zeta, initially tested at three dose levels, with later enrollment limited to the highest dose level. The patient population includes individuals with refractory or relapsed aggressive or indolent non-Hodgkin’s lymphoma (NHL) or chronic lymphocytic leukemia (CLL). This submission represents a three-year resubmission of the previous study. During this period, 23 patients completed treatment and initial follow-up, while three enrolled patients did not complete treatment—one died prior to the week 2 visit, another experienced disease progression and was transitioned to an alternative therapy, and the third died prior to the six-week evaluation. Of the 18 subjects who completed therapy, 12 died due to disease progression, two from other causes, and one was lost to follow-up. Eight patients remain in long-term follow-up. Reported adverse events included mild cytokine release syndrome in six patients and one case of dose-limiting toxicity at the highest dose level. The study is no longer enrolling new patients and is currently limited to follow-up visits. The maximum tolerated dose (MTD) was established as dose level three: 2 × 10^7 cells/m² for both CD19.CARCD28/CD137zeta and CD19.CARCD28zeta. **Target genes and packaging System**: The CD19.CAR-CD28zeta and CD19.CAR-CD28/CD137zeta constructs will be transferred into autologous T lymphocytes.

- **Training**: All staff members have completed and are current with their required training.
- **Applicable NIH Guidelines**: Section III-C-1, Section III-E
- **Containment Conditions to be implemented**: BSL2

- **Risk Assessment & Discussion**: This agent is no longer being administered to patients as the study is closed to enrollment. Retroviral risk is considered minimal, as replication-defective retrovirus is highly unlikely to be shed through urine, feces, saliva, mucus, tears, or other secretions. Any potential exposure would pose negligible hazard due to extremely low titers. All healthcare workers receive training on the safe handling and biological risks of the viral vector prior to working with patients.
- **The motion to approve the study seconded and passed. The IBC subsequently approved the protocol.**

Motion: Approve

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

IBC00002464
Title: Development of Nucleic Acid Delivery Platforms for Cancer Therapeutics and Gene-Modified Cell Analysis in Mai Lab 2025
Principal Investigator: Junhua Mai

Study Overview: The research team is conducting studies focused on three primary areas:

1. **Development of tumor-homing delivery systems:** Aptamers are being utilized as guiding molecules to bind unique targets on tumor cells or other cells within tumor tissues. This approach aims to enhance tumor-specific drug accumulation, improve therapeutic efficacy, and reduce systemic toxicity.

2. **Delivery of nucleic acids for cancer therapies and prophylactic vaccines:** mRNAs encoding reporter genes such as GFP or luciferase are used to assess biodistribution and uptake in cell and animal models. Additionally, mRNAs encoding cancer antigens are delivered to host immune cells to stimulate anti-cancer responses for treatment or prevention. Other strategies include delivering mRNAs encoding therapeutic proteins or using siRNAs, miRNAs, shRNAs, or sgRNAs to inhibit key proteins or pathways involved in tumor progression or metastasis.

3. **Understanding biological mechanisms during therapies using gene-manipulated cells:** Gene silencing tools such as siRNA, miRNA, shRNA, or sgRNA are employed to knock down or knock out critical genes in target cells. Replication-deficient lentiviral vectors are used for stable expression of reporter proteins or key proteins involved in biological processes. Reporter proteins like GFP or luciferase enable tracking of cancer progression in animal models, while

stable expression of proteins such as PHGDH or PINK1 helps elucidate their roles in cancer progression and therapeutic response.

- **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 primary risks associated with research using HIV-1–based lentiviral vectors include the potential for insertional mutagenesis following accidental exposure, the possibility of generating replication-competent lentivirus (RCL), and risks related to the nature of the transgene insert, particularly if it involves known or potential oncogenes or immunoregulatory genes. Additional considerations include vector titer, total amount of vector used, and biological containment of the animal host, if applicable. Negative RCL testing is required to confirm safety. There is also a theoretical risk for HIV-positive individuals, as native virus could recombine with or complement the vector. These risks can be mitigated by the safety features of the vector system and adherence to proper handling procedures. All work will be conducted in biosafety cabinets under BSL-2 containment, and staff will follow universal precautions when handling human cell lines to minimize exposure risk.

- **Comments sent to the PI for clarification**:
    - **Section Risk Assessment:** The only Risk Group 2 agent that belong in this section is the replication incompetent lentiviral vector. Please edit accordingly.
    - **Section Summary of Proposed Research**: It is not clear what "DNA" is being referred to in the discussion of the short hairpin RNA. Please be specific as to the expression of the shRNA.
    - **Section Funding Information**: Please provide the Research Plan as per IBC request.
    - **Section Staff Identification**: Reconsider the description of Xueying Ge's experience. "She graduated from Department of Chemistry, University of North Texas, where she was exposed to hazardous chemicals related to that work." Does that mean she suffered an exposure or gained experience?
    - **Section Human Cells, Tissue, and Fluids Used in the Laboratory**: List the commercial resources that are synthesizing the plasmids, aptamers, miRNA, siRNA and mRNA being used as per summary of proposed research.
- **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

IBC AMENDMENTS

IBCA00001392
Title: Hazard Amendment 3 for Preclinical development of CAR T Therapy for Metastatic Prostate Cancer using retroviral and lentiviral expression of various chimeric antigen receptors (CARs) in vitro and in vivo
Principal Investigator: Bin He

- **Amendment Overview**: This amendment adds mouse prostate cancer cell lines TRAMP-C1 and RM-2, which are approved under IACUC but were not previously linked to IBC protocol IBC00001985. These cell lines will now be included under the approved protocol IBC00001895. Lentiviral vectors carrying cDNA to express CAR or luciferase-GFP will be used to transduce mammalian cancer cells or T cells. For example, luciferase-GFP will be overexpressed in human prostate cancer cell lines (LNCaP, PC3, DU145) and mouse prostate cancer cell lines (TRAMP-C1, RM-2) using pLenti vectors. Transduction will involve centrifugation of cells with lentivirus for two hours at 780g and 32°C in the presence of polybrene, followed by incubation for six hours at 32°C and then 16 hours in complete media at 37°C. Successful transduction will be verified by flow cytometry or Western blot analysis. Cancer cells expressing luciferase will be detected in live mice using the IVIS imaging system.

- **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:** Established mouse cancer cell lines obtained from vendors or collaborators may carry a risk of unintentional contamination upon receipt or during routine experimentation. These cancerous cell lines pose an additional hazard, as they could cause localized tumors or, if malignant, present carcinogenic concerns in the event of exposure. Autologous blood samples (from the same individual) may also be altered during laboratory handling. If an individual is exposed to their own blood that has been contaminated with a laboratory pathogen, the immune response may be less effective compared to exposure to non-self (allogeneic) cells. Furthermore, if autologous blood samples are genetically engineered and accidentally reintroduced into the donor, the modified cells could evade immune rejection, unlike allogeneic cells. Adherence to BSL-2 containment practices will mitigate these potential exposure risks.
- **The motion to approve the amendment was seconded and passed. The IBC**

subsequently approved the amendment.

Motion: Approved

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

Adjournment:

- The meeting adjourned at 10:52 am.
