CHILDREN'S HOSPITAL BOSTON
Meeting of Boston Children's Hospital Institutional Biosafety Committee
AGENDA
12/18/2025 11 am to 12:30 pm
Karp 4 Conference Room or Zoom

Members Present: BS, MM, IJ, KK, DF, SG, EC, CH, HDL, PW, EG, SD, DC, AR, SVH, JM, TW

Members Absent:

RLSO: AL, DH

Guests: DG, CB, PS, SL

SD chaired the meeting.

1 IBC Meeting Minutes

Boston Children's Hospital Institutional Biosafety Committee meeting (11/20/2025)
IBC Meeting Minute was unanimously approved by the committee.

Committee Decision:
Motion: Approved
Majority (Approved): 17
Minority (Against): 0

2 Administrative Updates

- The annual BPHC inspection of the BSL-3 facility was conducted earlier this month, with no findings or violations identified.
- A poliovirus survey will be distributed the following week to determine whether fecal and/or oral samples collected during a specified period may have been contaminated with poliovirus.
- An IBC feedback survey will be distributed shortly after the meeting to gather input on areas for improvement or the need for additional expertise; results will be discussed at the January meeting.
- Beginning in 2026, Microsoft Teams will be used for virtual IBC meeting attendance.
- The 2026 IBC protocol submission deadlines have been posted on the E-bulletin board and will also be communicated at the Town Hall to ensure all labs are informed.

3 New submission – Clinical

IBC-P00002158 A Phase 1b, Multicenter, Open-Label, Dose Finding Study to Investigate the Safety and Tolerability of a Single Intravenous Dose of SGT-501 in Patients with Catecholaminergic Polymorphic Ventricular Tachycardia

PI: ED

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This is a Phase 1b, multicenter, open-label, dose finding study to

investigate the safety and tolerability of a single intravenous dose of SGT-501 in patients with catecholaminergic polymorphic ventricular tachycardia (CPVT). CPVT is a heart condition marked by an abnormally fast heartbeat which can be triggered by physical activity or emotional stress. These arrhythmias can cause unexplained fainting, seizures, cardiac arrest, and sudden death. SGT-501 is a recombinant, nonreplicating, AAV-based gene therapy designed to deliver a functional, full length, codon-optimized copy of the human cardiac calsequestrin (CASQ2) gene to heart muscle cells, restoring calcium regulation and reducing the risk of arrhythmias. The gene therapy product will be prepared and stored in BCH pharmacy and administered in the inpatient room via IV.

Regulations Applicable to this Protocol: NIH Guidelines III-C and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modification Requested:

- Clarify any precautions related to potential virus shedding at home.

IBC-P00002160 CC-97540 (BMS-986353) for Active SLE

PI: SP

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: This is a phase 2, multicenter, open-Label study of CC-97540 (BMS-986353), a CD19-Targeted NEX-T CAR T cells in participants with active SLE (including Lupus Nephritis) with inadequate response to glucocorticoids and at least 2 immunosuppressants. SLE develops when autoreactive B cells become activated and produce harmful autoantibodies that form immune complexes and drive tissue damage. CD19 is a relevant therapeutic target for autoimmune diseases because it is expressed ubiquitously on B cells and plasmablasts, which are known to have crucial roles in the pathogenesis of SLE. Treatment of SLE with CD19 CAR T cell therapy is expected to induce a deep depletion of the B cell compartment, including auto-reactive B cells and plasmablasts in peripheral blood, bone marrow, and tissues, followed by a repopulation with naive B cells of different repertoire, resulting in a reduction in autoantibodies and pro-inflammatory cytokines. The cell therapy product will be prepared and stored in DFCI Cell Manipulation Core Facility and transported to the inpatient room at BCH for administration via IV infusion.

Regulations Applicable to this Protocol: NIH Guidelines III-C and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Revise the summary in plain language so it is understandable to committee members without a scientific background. Spell out the abbreviations "SLE", "GC", "IS", and "NHL".
- Clarify where the product will be thawed, since it needs to be infused within 30 minutes of defrost. Will products be returned to the collaborating institution?
- Specify the tissues biopsied and describe how the tissues will be used in the Scientific Description.
- Include the specific biohazard risk of study product. The committee recommends removing the statement, "There is no risk of accidental release of study product as the study product is made for and can only be released to the patient the product was made for."
- Fludarabine and cyclophosphamide are mentioned. Include information about these drugs in the Scientific Description.
- Specify the biohazard risks of the study.
- Indicate bloodborne pathogens testing as this is an autologous cell product that will be tested. Specify the bloodborne pathogens tested and the method used.

4	**New submission – Laboratory**
IBC-P00002143	Numb and allograft transplantation
PI:	AC
Motion:	Modification Required for Approval – Return to IBC Analyst
Discussion:	**IBC Discussion**: The goal of this study is to evaluate whether overexpression of the protein NUMB in murine T cells enhances their immunosuppressive phenotype and improves transplant survival. Mouse T cells will be isolated in the PI's laboratory from spleen and lymph nodes using magnetic bead sorting, after which the cells will be transferred to a collaborator's lab for lentiviral transduction with either an empty lentiviral vector or a NUMB-expressing vector. Once NUMB expression is confirmed, the transduced T cells will be returned to the PI's lab for immediate adoptive transfer via intravenous administration into mice that have undergone cardiac and skin transplants. IV injection of murine lentiviral transduced T cells in mice will be done at ABSL-1.

Regulations Applicable to this Protocol: NIH Guidelines III-D.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Modify this section to address the main goals of the research and how it will be beneficial.
- Indicate the time interval between infection and return of cells to the lab and clarify whether the cells may still be shedding virus.
- Indicate the duration of study after T cell transfer in mice and the parameters examined.
- Clarify whether the analyses will focus on T cells or on transplanted tissues.
- Clarify that T cells overexpressing NUMB will be studied. It indicates that lentivirus will express NUMB shRNA which would constitute "knock-down" studies.
- Clarify that transduced primary cells will be used and not cell lines.
- Address any potential risk that might occur upon exposure to transduced primary T cells via needle puncture.
- Clarify what work is involved in “murine sample analysis” and specify if this includes isolation of T cells.
- Add room locations where work with biological agents will be performed.
- Clarify whether “murine transfected cell lines” refers to transduced primary T cells.
- Clarify what is expressed by the lentiviral vector.
- Clarify whether these cells will also be used in a skin transplant model as indicated in the Scientific Description.

5 Laboratory Amendments

IBC-A09-209-4 Amendment 4 : The Effect of Genetics and/or Angiogenic Modifiers on Angiogenesis in Mice

PI: RD

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The goal of this research is to understand how genetics and angiogenesis modifiers influence tumor growth using cellular and mouse models. In addition to ongoing studies involving human tumor xenografts, siRNA gene silencing, and CRISPR/Cas9-edited murine tumor cell lines, this amendment adds BCMA-targeted and non-targeted lipid nanoparticles encoding CRBN (cereblon) mRNA. CRBN is a substrate receptor of E3 ubiquitin ligase complex that regulates tumor cell survival and angiogenesis. These lipid nanoparticles, generated by a collaborator, will be delivered intravenously into mice in an effort to restore CRBN function. The amendment also adds human umbilical

vein endothelial cells (HUVECs). Work with lentivirus and human cell lines will be conducted at BSL-2. Injection of siRNA and BCMA-targeted or non-targeted lipid nanoparticles encoding CRBN mRNA will be performed at ABSL-1, while injection of human tumor cell lines into mice will be performed under ABSL-2 work practices and procedures.

Regulations Applicable to this Protocol: NIH Guidelines Section III-D, III-E, III-F and OSHA Bloodborne Pathogens Standard.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Specify the room locations where work with biological agents will be performed.
- Revise by stating the research goals in plain language. Define 'angiogenesis modifiers' clarify in lay terms these statements - 'We will also be knocking out genes using CRISPR/Cas9 in several mouse cell lines for analysis in vitro", 'These genes are identified though RNAseq of anti-VEGF treatment resistant tumor lines.
- Select ARCH Standard PPE.
- Update the BSL-2 entry to include transduction of murine cell lines with lentivirus.
- Include ultracentrifugation of viruses. Check off "70% ethanol" for surface inactivation of lentivirus.
- Select "10% bleach" for surface inactivation of siRNAs.
- Update the referenced 'eye shield' to safety glasses.
- Update the protocol to include needles used for mouse blood draws.
- Review the use of two types of needle gauges for cell collection and animal injection to prevent potential needle stick injuries. Clarify why a 30G needle cannot be used to draw up cells and inoculate mice.
- Update the protocol to include transport of lipid nanoparticles from the collaborating institution.

IBC-A08-287-10 Amendment 10 : RNA Discrimination by the Innate Immune System & mechanism of AIRE/Foxp3

PI: SH

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The amendment includes the use of patient sera or plasma samples for in-house MDA5 ELISAs to detect pathological immune complexes. Human cell lines, including iSLK2.19 and fibroblasts, will be utilized for studying infections of Herpes Simplex Virus-1 (HSV-1) and Kaposi Sarcoma Herpesvirus (KSHV). This aims to elucidate the mechanism by which Speckled-100 inhibits the replication of double-stranded DNA viruses. Kaposi Sarcoma is a cancer that develops from the cells that line lymph or blood

vessels and is caused by HHV-8, a member of the Herpesvirus family. HHV-8 is also primarily associated with Primary Effusion Lymphoma (PEL) and Multicentric Castleman Disease (MCD). Additionally, the lab will inject DT into mice to ablate DT receptor-expressing FoxP3+ regulatory T cells, aiming to study mechanisms of FoxP3-mediated regulation in vivo. Work involving HSV-1, KSHV, DT, antiviral research, patient plasma, and sera will be carried out at Biosafety Level 2 (BSL-2). Injection of DT into mice will be performed at Animal Biosafety Level 2 (ABSL-2), followed by ABSL-1 housing.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Describe the fibroblasts used for HSV-1 infection experiments.
- Clarify whether cells infected with HSV-1 or KSHV will be sorted and, if so, specify the associated biohazard risk to staff.
- Describe how the cellular and molecular consequences of FoxP3 ablation in mouse Tregs will be studied.
- Specify the amount of DT used for the mouse injections and the route of administration.
- Specify the form of DT the lab will receive (lyophilized powder or liquid stock). If provided as a powder, describe the reconstitution procedure.
- Include the risk of needlestick injuries to staff.
- Note that all staff members must complete a Tdap consultation prior to working with DT.
- A staff member is due for the Annual Research Safety Training.
- A reproductive health consult is recommended for staff working with HSV.
- Clarify that DT inoculations should be performed at ABSL-2 followed by ABSL-1housing.
- Clarify whether fibroblasts and SLK cells will be added to human or mouse tissues. If so, add descriptions of these procedures to the appropriate biosafety level.
- Include safety glasses or face shield for ABSL-2 inoculations of DT.
- Specify the room locations where work with biological agents will be performed.
- Include that the Tdap vaccine should be offered.
- Include needles used for mouse inoculations. Clarify what sharp instruments are used to extract lymphoid tissue following euthanasia.
- Clarify how KSHV is transported from the collaborator's institution to the lab at BCH.
- If the DT injection is prepared in the lab and then transported to ARCH, include how it will be transported to ARCH.

IBC-A00000509-9 Amendment 9 : Interneuron differentiation, noninvasive brain stimulation, and mechanisms of neuromodulation in neurological disease.

PI: AR

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab investigates how specific brain cell types regulate seizures and epilepsy, with the goal of developing new therapeutic approaches. This amendment proposes the addition of a new AAV vector, AAV-BI-hTRF1, in an already approved mouse model, as well as a new AAV construct for activity-dependent neuronal silencing responsive to seizures (AAV-ANSRS). All proposed work will be conducted at ABSL-1.

Regulations Applicable to this Protocol: NIH Guidelines Section III-E.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Clarify the payload/transgene that will be packaged into the AAV-BI-hTFR1 capsid.
- The protocol references both mice and nude rats; specify which species will receive IV administration of the AAV transgenes.
- Provide the dose and dosing frequency for IV administration of the AAV payload.
- Identify all tissues collected post-inoculation in ARCH in addition to brain tissue and indicate whether these tissues are collected fresh and/or fixed.
- Clarify whether downstream processing will occur in the laboratory or at the collaborating institution.
- Describe procedures for the safe handling of fresh human brain cortical tissue to minimize potential exposure to bloodborne pathogens before and during sectioning, including the laboratory space (open bench vs. BSC) and tools used.
- Clarify if electrophysiology recordings using unfixed brain tissue are performed on the open bench, describe measures to mitigate potential aerosol exposure and specify the method for disposal of solid tissue waste.
- Include a description of the specific risks associated with working with sharps, such as the increased potential for percutaneous exposure to lentivirus and bloodborne pathogens through punctures, cuts, or lacerations.
- Update the description to include risk of insertional mutagenesis when working with lentiviral vectors.
- Please ensure all personnel responsible for shipping have completed the shipping training.
- Specify the room locations where work with biological agents will be performed.
- Specify that cryostat will be decontaminated with 10% bleach followed by a 70% ethanol wipe. It currently reads 100% ethanol.

IBC-A09-102-6 Amendment 6 : Role of the Vasculature and the Complement Cascade in CNS Synapse Elimination During Development and Disease

PI: BS

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The goal of the study is to investigate the role of vasculature and complement-mediated synapse elimination in neurodegenerative diseases using human tissues, CSF samples, and primary cells. The previous work primarily isolated microglial from human brain tissues rather than direct manipulation of whole tissue. In this amendment, the lab aims to treat unfixed human brain tissues with drugs, dyes, or conjugated antibodies for live imaging and mass spectrophotometry. Work with human tissues and cell culture of microglia, vascular cells, neurons and macrophage cells will be done following BSL-2 work practices and procedures.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0
- Abstention: 0

Modifications Requested:

- Describe the drugs used to stimulate the brain cells, their associated hazards, and the type of vessels (plates or tubes) used during water-bath stimulation.
- Handling human brain tissue poses a potential risk for prion exposure. Describe how these risks are mitigated and specify the types of sharps used for tissue handling.
- Describe the risks associated with using a cryostat and the measures in place to mitigate those risks. Confirm that all personnel listed in the protocol have completed the required biosafety training.
- Include the experimental details of the RNA extraction procedure and downstream applications in the scientific description to allow assessment of the associated hazards.
- Include the room numbers where work with biological agents will be conducted.

IBC-RN07-164-5 Renewal 5 : Understanding molecular, cellular and organismal basis of childhood neurological diseases

PI: MS

Motion: Modification Required for Approval – Return to IBC Analyst

Discussion: **IBC Discussion**: The lab investigates neural function and connectivity to improve understanding of tuberous sclerosis complex (TSC). This renewal proposes using the Pcw107 third-generation backbone to generate both a control plasmid and a lentiviral transfer plasmid expressing the human SMO gene with a W535L point mutation, designed to study the role of cilia in TSC-deficient rat neurons. All work involving the SMO-expressing lentivirus will be conducted at BSL-2 work practices and procedures.

Regulations Applicable to this Protocol: NIH Guidelines Section III-D.

Motion: Modifications Required for Approval

- Majority (Approved): 17
- Minority (Against): 0

- Abstention: 0

Modifications Requested:

- The protocol states that "all chemicals and toxins will be disposed of following proper procedures." Clarify and revise this to specify that biological liquid waste containing toxins will be treated with bleach to a final concentration of 10% of the total waste volume prior to disposal down the sink.
- Clarify the quantities and storage locations of the neurotoxins picrotoxin, CNQX, and D-APV.
- Describe how the cryostat will be used.
- List and describe all animal experiments, including organoid generation.
- Note that a staff member is due for safety refresher training.
- Specify the bacterial plasmids handled at BSL-1.
- Remove descriptions of picrotoxin from the select agent entry.
- Specify the collaborating institution.
- Specify the room locations where work with biological agents will be performed.
- Specify the sharps used and for which procedures.

7	**Human Study Annual Reconfirmation**

IBC-P00001003 Gene Therapy for X-linked Retinitis Pigmentosa caused by RPGR mutations

PI:	**AF**
Motion:	Approved
Discussion:	The study is active and closed for enrollment.

8	**Administrative Reviews**

IBC-RN11-241-4 Renewal 4 : Mechanism of Immune Tolerance Breakdown

PI:	**TC**
Motion:	Administratively Approved
Discussion:	This is a three-year renewal with no changes to the risk assessment.

IBC-RN00001154-2 Renewal 2 : Elucidating the Biology of Inflammatory Bowel Disease

PI:	**WL**
Motion:	Administratively Approved
Discussion:	This is a three-year renewal with no changes to the risk assessment.

IBC-RN00000912-2 Renewal 2 : Performing functional assays using the MA900 Multi-Application Cell Sorter

PI: **PN**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no changes to the risk assessment.

IBC-RN11-016-4 Renewal 4 : Effect of Systemic Metabolic Status on Cancer Incidence and Progression

PI: **NK**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no changes or updates to the risk assessment.

IBC-RN00000719-3 Renewal 3 : Signal transduction in neutrophils-part 1

PI: **HL**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no changes or updates to the risk assessment.

IBC-RN00001066-2 Renewal 2 : The epithelial biology of Congenital Diarrheas and Enteropathies

PI: **JT**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no updates or changes to the risk assessment.

IBC-A00001908-3 Amendment 3 : Exploiting Antigen Presentation Pathways for Precision Immune Engineering

PI: **NP**

Motion: Administratively Approved

Discussion: The amendment adds pET32b(+) plasmid to the previously approved pET-series plasmids (pET16, pET30, pET28). This update does not change the risk assessment.

IBC-RN00000705-3 Renewal 3 : Signal transduction in neutrophils- part 2 (bacteria)

PI: **HL**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no changes to the risk assessment.

IBC-RN00001795-1 Renewal 1 : AAV vectors for use in mice

PI: **MF**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no changes to the risk assessment.

IBC-RN00000387-4 Renewal 4 : Immune signaling and inflammation

PI: **IZ**

Motion: Administratively Approved

Agenda Notes: This is a three-year renewal with no changes to the risk assessment.

IBC-RN00001801-1 Renewal 1 : Pseudoviruses and virus-like particles

PI: **MF**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no updates or changes to the risk assessment.

IBC-A00000100-2 Amendment 2 : Bioenhanced Repair

PI: **MM**

Motion: Administratively Approved

Discussion: This amendment is adding human, bovine and ovine primary cell lines of fibroblasts isolated from musculoskeletal (muscle, bone, tendon, ligament, cartilage etc.) and dermal tissues (such as skin, blood vessels, fat) to the already approved in vitro cell culture studies. All work involving human cells will be conducted at BSL-2 work practices, and bovine and ovine tissues will be handled at BSL-1.

IBC-RN00001800-1 Renewal 1 : Engineering B cells for in vitro and in vivo use

PI: **MF**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no updates or changes to the risk assessment.

IBC-RN06-283-5 Renewal 5 : Treatment of Perinatal Diseases with Mesenchymal Stem Cells

PI: **DF**

Motion: Administratively Approved

Discussion: This is a three-year renewal with no updates or changes to the risk assessment.

9 Laboratory Study Annual Reconfirmation

IBC-P00001490 Cell Identity Gene Dysregulation

PI: **LZ**

IBC-P00000180 Genetics of Human Hematopoiesis

PI: **VS**

05-147 Angiogenesis Inhibitors

PI: **MM**

IBC-P00001245 Challenges to the immune system due to infection, inflammation and vaccination

PI: **HS**

IBC-P00001953 Heart Donation after Circulatory Death for the Study of Pediatric Cardiac Surgery

PI: **SE**

08-287 RNA Discrimination by the Innate Immune System & mechanism of AIRE/Foxp3

PI: **SH**

91-153 GATA-binding Proteins and Hematopoiesis

PI: **SO**

IBC-P00001973 Screening the biocompatibility of synthetic biomaterials

PI: **YP**

IBC-P00000105 LNP- or GalNAc-siRNA injection

PI: **MF**

94-064 Role of Genes Important for the Immune System

PI: **RG**

IBC-P00001428 AAV Vector Administration to Mice

PI: **MR**

IBC-P00001037 Cfp1 Action

PI: **DC**

08-192 Isolation of platelet integrin and plasma proteins from blood products

PI: **TS**

IBC-P00000709 Human Immune Function Studies and The Genes Involved

PI: **TC**

IBC-P00002041 Molecular, Cellular and Animal Studies of Kidney Disease Genes, Proteins and Factors

PI: **AM**

02-204 Lentiviral Transduction of Endothelial Cells as a Tool to Determine Gene Function

PI: **JB**

IBC-P00000862 Targeting pediatric brain tumors with drug delivery

PI: **ES**

05-219 Virulence Gene Control in Francisella tularensis

PI: **SD**