IBC Meeting Minutes

September 18, 2025 (Thursday) at 11:00 A.M.
via Zoom Conference Bridge

IBC members present:

Tom Greenough (Chair)	X	Shaoguang Li		Carol Schrader	X	Edward Jaskolski (alt)	X
Lisa Cavacini	X	Philip Tai	X	Mohan Somasundaran		Timothy Kowalik (alt)	
Colleen Driskill	X	Robert Klugman	X	Richard Ellison III (alt)		Regino Mercado-Lubo (alt)	X
Kris Giaya*	X	Amelia Houghton	X	Sharone Green (alt)		Casey Moran (alt)	X
Hardy Kornfeld		Eric Rouse	X	Jennifer Wang (alt)			

Non-members present: Patrice Rando (IACUC/IBC Office)

KG* Left at 12:22

I. Introductory Remarks

1) The Chair brought to the attention of the Committee that on 09/09/2025 NIH announced their initiative to modernize and strengthen biosafety policies, practices and oversight. As part of this effort, hosting a virtual listening session to obtain input from across its stakeholder community including researchers, biosafety professionals, research institutions, policymakers, industry leaders, and members of the public. Possible meeting with Katheryn Harris and ABSA on 09/30/2025 at 2:00pm.
2) The Chair brought to the attention of the Committee the upcoming NEBSA meeting being held on 10/08/2025
3) The Chair brought to the attention of the Committee we are still awaiting guidance regarding DURC/ PEPP
4) The Chair brought to the attention of the Committee the meeting minutes from the previous IBC meeting. **Meeting Decision: Vote to approve August 21, 2025 Meeting Minutes**

II. Report on incidents/accidents from Employee Health Services (EHS)

Past Incidents

1) 07/08/2025- Needlestick in BSL-3 mice infected with MTb- Update provided
2) 07/21/2025- Needlestick (clean)- Update provided
3) 07/28/2025- Chemical Exposure- Tris-HCL- Update provided
4) 07/29/2025- Isoflurane exposure- Update provided

Recent Incidents

1) 09/15/2025- Needlestick potential exposure to human blood. Source tested negative for BBP.

III. Protocols Reviewed Administratively

1) Investigator: Leftwich, H (prev. Moore Simas)
Title: Protocols within the Division of Research, Obstetric/Gynecology Department
IBC Registration: 647-25, Renewal
Training Verification: Acceptable
Brief Summary: The objective of this project is to understand exposures and outcomes related to reproductive health—specifically focusing on the maternal-fetal dyad as well as gynecologic diseases in women. This includes the collection and utilization of biological specimens for research by basic science collaborators and for storage until transported to other authorized organizations.

BSL/ABSL: **BSL-2**
NIH Guidelines: N/A

2) Investigator: Mullen, A
Title: Collection and Preparation of Human Specimens, Blood, Urine, and Stool for Shipment to Central Laboratory as Designated by Sponsoring Pharmaceutical Company
IBC Registration: **635-25, Renewal**
Training Verification: Acceptable
Brief Summary: Goals for all clinical studies conducted by the GI/Hepatology Research Staff include collection and processing of Human specimens including blood, urine and stool. Samples may be clotted, spun, aliquoted and frozen or shipped immediately depending on the needs of the protocol. Samples are handled according to routine precautions for handling of human samples and there is no manipulation other than as described above.
All specimens are shipped ambient or on dry ice, packages are prepared by IATA certified personnel.

BSL/ABSL: **BSL-2**
NIH Guidelines: N/A

3) Investigator: Musch, G
Title: Department of Anesthesiology and Perioperative Medicine Clinical Research Laboratory
IBC Registration: **632-25, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The Department of Anesthesiology Clinical Research Laboratory is utilized for a number of clinical studies that require sample processing, storage and shipping.

BSL/ABSL: **BSL-2 (verify no animal work included as registered in 2021)**
NIH Guidelines: N/A

4) Investigator: Rothschild, A
Title: Processing of Human Samples from Clinical Trials Conducted by Center for Psychopharmacologic Research and Treatment
IBC Registration: **640-20, Renewal**
Training Verification: Acceptable
Brief Summary: The Center for Psychopharmacologic Research and Treatment (CPRT) is a research group in the Department of Psychiatry that conducts clinical research trials. Dr. Anthony Rothschild is the Director of CPRT.

BSL/ABSL: **BSL-2**
NIH Guidelines: N/A

IV. Protocols to Discuss

1) Investigator: Brown, R
Title: Targeting CCDC146 with Antisense Oligonucleotides in ALS Mice
IBC Registration: **552-23 Amendment**
Training Verification: Acceptable pending completion of PI training

Brief Summary: ALS is a neurodegenerative disease with no known cure and 100% fatal. Currently anti-sense oligos are being developed that target the genes associated with ALS pathology. The goal is to silence or suppress these genes in hopes of extending survival or delaying onset of symptoms.

The goal of this project is to examine how neuroinflammation contributes to Amyotrophic Lateral Sclerosis pathogenesis. To mimic neuroinflammation, we will use a widely established protocol in which we inject LPS IP into mice and examine how this neuroinflammatory challenge regulates Amyotrophic Lateral Sclerosis pathology. The ultimate goal of these studies is to develop new treatments for Amyotrophic Lateral Sclerosis.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overarching goal of this work is to understand molecular mechanisms involved in neurodegenerative and neuromuscular diseases and to develop and evaluate therapeutic interventions using preclinical cell and animal models. Amyotrophic lateral sclerosis (ALS) is a neurodegenerative condition with no known cure and a 100% fatality rate. Currently, antisense oligonucleotides (ASOs) are being developed to target genes associated with ALS pathology.

Specifically, the goal of this project (amendment) is to ASOs designed to silence or suppress ALS-associated genes with the aim of extending survival or delaying onset of symptoms. A mouse model will be used to examine the molecular mechanisms of neuro inflammation and to assess the therapeutic potential of ASOs treatments

Experimental Approach: To mimic neuroinflammation mice will be injected with LPS intraperitoneally. Briefly, a single dose of LPS (1-10mg/kg) or vehicle (PBS) will be injected IP using a 25G needle and sterile syringe using standard operating procedure. After the injection of LPS, the general condition of animals will be monitored for at least 1 hour and severely stressed animals will be sacrificed promptly. Once neuroinflammation is stablished, mice will receive ASOs via intracerebroventricular (ICV) injection, and then monitored for survival benefit as well as various behavior metrics that would show a change in phenotype. Animals will be euthanized at 1 hour to 24 hours post-injection of LPS and immununohistochemical and biochemical assays will be performed. LPS will be obtained from Escherichia coli 0111:B4 through commercial sources (Sigma). This is a standard procedure used by a great number of labs throughout the world, and poses minimal risk to all personnel.

IBC Discussion and Vote

Discussion: A committee member asked if ASO's require special precautions when used in animals. A separate committee member mentioned we typically do not require special precautions with ASO's. The chair went over the NIH guidelines and determined that, based on the guidelines, no Special Precautions are necessary, but animal addendum should be required.

Meeting Decision: Vote to approve upon completion of action items.

BSL/ABSL: **BSL-2; ABSL-1; Administration to animals using BSL-2 Precautions/ Sharps Safety**

NIH Guidelines: III-F

2) Investigator: Sirianni, R
Title: Pathway inhibition in vitro and in vivo
IBC Registration: **851-22, Amendment**
Training Verification: Acceptable pending completion of PI training

Brief Summary: Substance list: 1) LM02 siRNA- IV, 2)LMO2 knock-out cells- intracranial, 3) AG-016699- PARP inhibitor- IV, 4) siRNA anti SARM1- intracerebral and intrathecal, 5) RR10B peptide- intracerebral, 6) Nucleic acid (DNA/RNA) nanoparticles produced at another institution – intracerebral, intrathecal, intravenous

Substances will be used for both mechanistic (cells) and therapeutic (mice) work. Experimental approaches will include:

- Complexation of anti LMO2 or anti SARM1 siRNA with polymers or nanoparticles that may be composed of polymers and/or lipids.
- Attachment of the RR10B peptide to polymers or to the surface of nanoparticles
- Incubation of cells with siRNA or AG-016699
- Generation (using lentiviral approaches) of MDA-MB-231 cells lacking LMO2
- siRNA loaded / surface modified nanoparticles, free siRNA, and free peptide, will be studied in cell culture, which will involve use in a biosafety hood and standard sample assays (immunofluorescence on fixed specimens, collection of fresh cells, sonication, running gels, etc.). The cell culture experiments may run up to 96 hrs.

siRNA loaded / surface modified nanoparticles, free siRNA, and free peptide will be studied in vivo, in mice (either healthy or bearing tumors), which will involve substance preparation and administration, maintenance of the mouse in the animal facility, imaging of the mouse by IVIS or using our intravital confocal instrument, cardiac perfusion of mice, collection of tissues (both fixed and fresh) or biofluids, and analysis of tissues or biofluids by standard approaches (immunofluorescence, pathology, PCR, western blot, etc.)

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To investigate delivery, potency, and therapeutic efficacy of agents in vitro and in vivo. An amendment for an existing protocol describing use a mouse model to study potential treatments for pediatric metastatic medulloblastoma in humans. Human medulloblastoma tumor cells are injected into the cerebellum of immune deficient mice.

Experimental Approach: Substance list:

1. LM02 siRNA- IV
2. LMO2 knock-out cells- intracranial;
3. AG-016699- PARP inhibitor- IV
4. siRNA anti SARM1- intracerebral and intrathecal
5. RR10B peptide- intracerebral
6. Nucleic acid (DNA/RNA) nanoparticles produced at another institution – intracerebral, intrathecal, intravenous

Substances will be used for both mechanistic (cells) and therapeutic (mice) work. Experimental approaches will include:

- Complexation of anti LMO2 or anti SARM1 siRNA with polymers or nanoparticles that may be composed of polymers and/or lipids.
- Attachment of the RR10B peptide to polymers or to the surface of nanoparticles
- Incubation of cells with siRNA or AG-016699
- Generation (using lentiviral approaches) of MDA-MB-231 (human breast cancer) cells lacking LMO2
- siRNA loaded / surface modified nanoparticles, free siRNA, and free peptide, will be studied in cell culture, which will involve using standard sample assays (immunofluorescence on fixed specimens, collection of fresh cells, sonication, running gels, etc.).

- siRNA loaded / surface modified nanoparticles, free siRNA, and free peptide will be studied in vivo, in mice (either healthy or bearing tumors), which will involve substance preparation and administration, maintenance of the mouse in the animal facility, imaging of the mouse by IVIS or using a intravital confocal instrument, cardiac perfusion of mice, collection of tissues (both fixed and fresh) or biofluids, and analysis of tissues or biofluids by standard approaches (immunofluorescence, pathology, PCR, western blot, etc.)

Some mice will receive an intracranial infusion of MDA-MB-231 cells that have been genetically modified with lentivirus to knock out LMO2. The MDA-MB-231 cells also express a luciferase reporter (already approved; MDA-MB-231 [fenics BIO, firefly luciferase and GFP; plasmid transfections]), and we will conduct IVIS imaging on them to track the growth of tumor. These sessions are typically ~30 minutes of imaging in the A level vivarium.

Some mice will receive an intracranial infusion of non-transduced cells, and then they will receive treatments with siRNA, etc. Those mice will also be imaged with IVIS, typically ~30 minutes of imaging in the A level vivarium

IBC Discussion and Vote

Discussion:	Reviewer discussed that more clarification is required for some of the work they are adding specifically in regard to the lentivirus work. Action items were discussed. Animal addendum and flow sorting addendum are needed.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1 + BBP with Special Precautions; Administration to Animals using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-F

3) Investigator: Tang, Q (previously TABLED 8/21)
Title: Therapeutic Application of Chemically Modified Nucleic Acids
IBC Registration: **925-25, New**
Training Verification: Acceptable
Brief Summary: The overall goals of the lab are to develop RNA-based therapeutics for relevant disease indications. This is done by testing modified or formulated RNA oligonucleotides (or RNA/protein complexes) developed in the lab in in vitro experiments using mouse, human, NHP, cat and dog cell lines and primary cells followed by in vivo rodent and large animal models.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overall goals of the lab are to develop RNA-based therapeutics for relevant disease indications. This is done by testing modified or formulated RNA oligonucleotides (or RNA/protein complexes) developed in the lab in in vitro experiments using rodent and human cell lines and primary cells followed by in vivo rodent models.

Experimental Approach: Project 1: Screening modified RNAs in vitro: In vitro work involves testing modified RNA oligonucleotides in modified and primary cells of human and mouse origin. The oligonucleotides can either be naked, formulated (liposome, endosome, polymer, small molecule drugs). Also, we will use surgically discarded skin tissues from patients with and without the conditions of interest as a model to test the modified RNA oligonucleotides in a more relevant biological context.

Project 2: Screening modified siRNAs in vivo: Chemically modified oligonucleotides that were first screened and tested in vitro will be tested in animal models (naked, or formulated and/or administrated with a drug) for toxicity, tissue distribution, pharmacokinetic/pharmacodynamic (PK/PD) parameters, and efficacy. In addition, the specific oligonucleotide formulation, or whether the co-administration of a drug will enhance various in vivo parameters, will also be tested. In vivo experiments involve injection of mice by several routes (i.e, IV, SC, IP, transdermal, intradermal, topical, etc.).

Project 3: Cell type specific delivery of siRNA in mice and human cells: In this project we will inject mice and isolate specific organs to look at various cell populations to determine the amount of uptake of a fluorescently labeling siRNA. We will also use flow cytometry to determine knockdown in human and mouse cell lines. In addition, we will use FACS sorting of human cell lines and mouse tissues to quantitate uptake in specific cell types

IBC Discussion and Vote

Discussion:	The reviewer discussed that this protocol has been simplified significantly since the first initial submission, and they have removed all vectors. There are still some areas of the protocol that require more information for an appropriate risk assessment. ABSL-1 without special precautions is
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1**
NIH Guidelines:	III-F

V. Report on incidents/accidents/issues involving BSL-3 & ABSL-3 Facilities

1) CDC/USDA site visit Sept 3 and 24. Walk through of the renovated BSL-3 and ABSL-3 and inventory check.
2) Awaiting clarification from CDC/USDA about personal quarantine questions related to HPAIV and NDV and bird contact. NDV PI may register as storage only. SOP can be written to address nuances of degrees of "proximity to agent".
3) Site de-con after moving agents (done).

VI. Information from the field (Senior Biosafety Officer)

1) Animal bedding waste for compost – revived effort underway.
2) AAALAC preparation – Oct 27-29
3) Town of Shrewsbury rsNA permit renewal
4) Move process re-vamped; preparation, checklist, etc. Generally going very well but some questions about checklists/decon/etc for short distance moves (e.g. moving to nearby bench).

VII. Other Business

1) BSL-2+ sorting protocol for Pathology Dept Sorting Facility discussed briefly; appears adequate

Acknowledgement Items:

1) **D'Ambrosio 910-24** Update
   A Phase 1/2/3 Open-label Study to Evaluate the Safety, Tolerability, Efficacy, Pharmacodynamics, and Pharmacokinetics of Intravenous RGX-202 Gene Therapy in Males with Duchenne Muscular Dystrophy (DMD)

   RGX-202 is an AAV8 that contains a vector genome encoding a miniaturized dystrophin protein (microdystrophin).

   Administrative change dated 080125: Protocol Version 9.0 states that RGX-202 is manufactured at Brammer Bio, LLC, or Advanced Bioscience Laboratories, Inc. This change clarifies that RGX-202 is also manufactured at REGENXBIO Manufacturing Innovation Center (RMIC).

Adjourned at 12:37pm