IBC Meeting Minutes

January 15, 2026 (Thursday) at 11:00 A.M.
via Zoom Conference Bridge

IBC members present:

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

Non-members present: Patrice Rando (IACUC/IBC Office)
*RK left at 11:10 am
**RML joined at 11:15, left at 11:42
***LC joined at 11:21
****ER joined at 11:53

I. Introductory Remarks

1) The Chair brought to the attention of the Committee the meeting minutes from the previous IBC meeting. **Meeting Decision: Vote to approve December 18, 2025 Meeting Minutes**

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

Past incidents that remain open:

1) 070825: Needlestick in BSL-3. Potential TB exposure. 6 month follow-up
2) 112625: BSL-3. Wet sleeve noted; skin intact. Repeat IGRA screening planned
3) 120825: Cut noted after cleaning BSC. Low likelihood HIV exposure; PEP; 6 month serology planned

Recent incidents:

None new; NIH reports submitted and no further action needed

III. Protocols Reviewed Administratively

N/A

IV. Protocols to Discuss

1) Investigator: Bach, I
Title: Roles of LIM cofactor Rlim in mice
IBC Registration: I-277-25, Renewal
Training Verification: Acceptable pending completion of PI training
Brief Summary: The goals of this project are to identify functions, targets and molecular mechanisms of regulation by RLIM, applying methods used in biochemistry, cell biology and developmental biology. We will mainly concentrate on functions early during embryogenesis and in organs such as the nervous system, the extraembryonic trophoblast as well as reproductive tissues.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goals of this project are to identify functions, targets and molecular mechanisms of regulation by RLIM, a gene encoding the RING-H2 zinc finger protein shown to be an E3 ubiquitin ligase, crucial in cell signaling, transcriptional regulation, and development, known to target proteins like LDB1, and its dysregulation is linked to intellectual disability, and neurodevelopmental disorders.

RLIM targets and molecular mechanisms of regulation will be explored by applying methods used in biochemistry, cell biology and developmental biology. The study will primarily focus on RLIM functions during embryogenesis and in organs such as the nervous system, the extraembryonic trophoblast as well as reproductive tissues.

Experimental Approach: This project will employ mouse genetics in combination with biochemical, cell biological, and developmental biology approaches. The protein network surrounding Rlim will be expanded by identifying novel interaction partners using immunoprecipitation and GST pull-down assays. Functional analyses will be performed through transient transfection of Rlim and Rlim mutant constructs in cultured cells, including established cell lines and primary cell cultures. Ubiquitination assays, Western blotting, and cell proliferation and motility assays will also be employed. In addition, expression patterns in developing and adult mice will be examined using in situ hybridization and immunohistochemical approaches.

Mice with conditional knockout (cKO) of Rlim in specific tissues and cell types will be generated using established Cre-driver mouse lines or by stereotaxic delivery of adeno-associated virus (AAV) particles expressing Cre recombinase. AAV-Cre will be injected into defined brain regions of mice carrying a floxed Rlim allele to induce localized conditional Rlim deletion. Body weight and adipose tissue parameters will be monitored, and phenotypic analyses will be conducted for up to 24 weeks following cKO induction or AAV injection. All AAV vectors will be obtained from Addgene and directly injected into the mouse brain. AAV injections will be performed in collaboration with Andrew Tapper under approved IACUC protocol 202100216, using instrumentation in the LRB mouse facility. The effects of Rlim deletion on energy homeostasis will be assessed at the level of specific cell types, individual organs and tissues, and whole-body physiology.

IBC Discussion and Vote

Discussion:	The reviewer discussed that some clarification is required as to whether the lab is generating new transgenic animals or not. The submission was missing the animal addendum.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; ABSL-1 with Special Precautions; Administration to Animals using BL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-E, III-F

2) Investigator: D'Ambrosio, E

Title: A Phase 1, Multicenter, Open-label, Dose-Finding Study to Investigate the Safety and Pharmacodynamics of a Single Intrathecal Injection of INS1202 in Patients with Amyotrophic Lateral Sclerosis

IBC Registration: **I-932-25, New**

Training Verification: Acceptable

Brief Summary: INS1202 is an adeno-associated virus (AAV9) carrier to deliver a short hairpin RNA (shRNA) that targets and degrades the messenger RNA (mRNA) for SOD1, as a therapy for amyotrophic lateral sclerosis (ALS). Preclinical data in SOD1-ALS mice shows that a single dose of INS1202 can delay disease onset, improve motor function, and prolong survival by reducing toxic SOD1 protein. Patients will receive a single intrathecal dose of INS1202 followed by close monitoring for 1 year to determine safety and pharmacodynamics of INS1202.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: INS1202 is a non-replicating adeno-associated virus (AAV9) carrier to deliver a short hairpin RNA (shRNA) that targets and degrades the messenger RNA (mRNA) for SOD1, as a therapy for amyotrophic lateral sclerosis (ALS). Preclinical data in SOD1-ALS mice shows that a single dose of INS1202 can delay disease onset, improve motor function, and prolong survival by reducing toxic SOD1 protein.

This is a first in human trial; a Phase 1, open-label, dose-finding study that will evaluate the safety, tolerability and pharmacodynamics (PD) of a single IT injection of INS1202 gene therapy in participants ≥ 18 years of age with ALS who either carry SOD1 mutations or are negative for known ALS-related genetic mutations. Secondary objectives include: To identify the recommended Phase 2 dose (RP2D), and To evaluate viral vector shedding following the IT administration of INS1202

Experimental Approach: INS1202 is an engineered, self-complementary AAV9 vector that features ITRs and an H1 promoter driving expression of a 20-nucleotide shRNA targeted against the human SOD1 mRNA. A stuffer sequence has been added to optimize the packaging efficiency of the vector. The stuffer sequence was assembled primarily from the backbones of plasmids previously used in FDA-approved DNA vaccine trials (NCT00062907; NCT00536627; NCT01322802). The INS1202 vector has an 11-base pair deletion in the downstream ITR, which removes a target site that would otherwise be cleaved by the AAV endonuclease during capsid assembly and packaging. The consequence of this deletion is the formation of palindromic repeats of the viral genome, allowing it to fold into a double-stranded DNA hairpin structure referred to as a self-complementary genome. This self-complementary genome encodes for a shRNA that is processed into a single stranded siRNA, which binds to a specific target sequence on the human SOD1 mRNA, thus resulting in its inactivation and degradation resulting in a consequential decrease in SOD1 protein expression.
The product will be stored and prepared for infusion at the UMass Research Pharmacy. The research pharmacist who will be preparing the product for infusion will work in an ISO level 5 biocontainment hood. The clinical research center lab has a biosafety cabinet as well as sealed centrifuge containers for the processing of blood, CSF, and saliva.
Patients will be enrolled into the study after meeting protocol-specified eligibility criteria. They will receive a one-time treatment of the study drug (INS1202) via a fluoroscopically guided lumbar puncture and intrathecal infusion . Infusion of the product will occur within the neurointerventional radiology suite, University campus. ***
Blood and CSF will be collected to assess pharmacodynamics and safety. Blood will be drawn in-patient, but also in the clinical research center. Blood, urine, CSF, saliva, and feces will be processed and shipped to a central lab or stored temporarily in the -80C freezer within the clinical research center.
During the Screening period, disease characteristics, baseline health, medical history, and prior/concomitant therapies will be evaluated, and samples to assess pre-existing immunity to AAV9 and ALS gene-related mutation status will be collected. These tests will be used in confirming eligibility. Once eligibility is confirmed, a Baseline visit will be scheduled to take place within a 7-day window before the Treatment Day (Day 1). Participants will begin prophylactic treatment with corticosteroids on Day -1 (a day before administration of INS1202
On Treatment Day (Day 1), participants will be admitted to a clinical inpatient facility for an overnight stay (through Day 2). On Day 1, the participant will receive a single administration of INS1202 by IT injection (under fluoroscopic guidance unless contraindicated or otherwise unavailable to a participant) utilizing appropriate sedation and local anesthesia, per institutional standard of care and according to the needs of the individual participant, as assessed by the Investigator.
Following dose administration, participants will be monitored overnight as inpatients. Participants will be discharged on Day 2 after an assessment of well-being and review of local safety laboratory test results confirm participants are safe for discharge.
Study visits are every 1-2 wks for the first 8 wks.
Prophylactic corticosteroids, prescribed at 1mg/kg/day up to 60mg/day, must be initiated at Day -1 (Baseline).
Treatment will last 8 weeks and then participants will be tapered off through Week 12.

IBC Discussion and Vote

Discussion: Reviewer discussed that more information about how the viral vector is produced would help to do a proper risk evaluation. Reviewer discussed this has not yet been reviewed by the gene and cell therapy committee.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2**
NIH Guidelines: III-C, III-E

3) Investigator: McNally, D
Title: Plasmid Manufacturing
IBC Registration: **I-614-25, Renewal**
Training Verification: Acceptable
Brief Summary: MassBiologics intends to continue to manufacture recombinant Adeno-associated virus (rAAV) via transient transfection of mammalian cells.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: MassBiologics intends to continue to manufacture recombinant Adeno-associated virus (rAAV) via transient transfection of mammalian cells.

Experimental Approach: HEK293 cells will be grown in attachment and suspension mode in T-flasks, Cell stacks, shake flasks, spinner flasks, rocking motion bioreactors and stirred tank bioreactors in batch, fed batch and perfusion modes in volumes up to 1000 L. Small scale cell culture will take place in T-Flasks, Cell factories and shake flasks. Once sufficient cell mass has been achieved, cells will be inoculated undergo further culture in shakers, spinners, rocking motion or stirred tank bioreactors. To achieve high cell density in bioreactor culture an ATF or TFF based perfusion system may be used to remove spent media, with fresh media added directly to the bioreactor. Throughout the process samples will be taken to assess cell concentration and media biochemistry.
Adeno-associated virus (AAV) production will be induced via transient transfection.
The final AAV produced through cell culture will be further purified using centrifugation, filtration, chromatography and chemical methods. At each stage of the purification material will be assayed for titer and biochemical characteristics.
Ultracentrifugation may be used to ensure the production of a high-purity product. This will require the use of a needle to pierce the centrifuge tube. In order to mitigate the risk of a needle stick injury a jig will be used to hold the centrifuge tube, shield the operator from the needle and apply controlled force to ensure penetration of the tube. Additionally, MassBiologics' safety officer has performed an assessment of the proposed procedure and provided feedback in order to ensure worker safety.
Analytical techniques used will include, qPCR, ddPCR, ELISA, microscopy, flowcytometry, HPLC, capillary electrophoresis, gel electrophoresis, Dynamic Light Scattering, cell based infectivity and potency assays.
A TCID50 (50% Tissue Culture Infectious Dose)assay will be employed to measure infectivity, this assay utilizes a HelaRC32 cells and co-infection with an Ad5 helper virus.
The work will take place in two diferent locations, Mattapan and Fall River. Quality control and storage will take place in Mattapan and GMP manufacturing, analytical development and testing , process develoment and storagein in Fall River.

IBC Discussion and Vote

Discussion: Reviewer discussed that it seems like the lab will no longer be using adenovirus large scale but it's not entirely clear. The reviewer also discussed that it is unclear as to whether they will still be using NHP materials as well as the doggybone DNA.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; BSL-1 Large Scale**
NIH Guidelines: III-D, III-E, III-F

4) Investigator: Nandadasa, S
Title: ADAMTS metalloproteinase function in ciliogenesis and developmental birth defects
IBC Registration: **I-787-26, Renewal**
Training Verification: Acceptable
Brief Summary: The goal of this project is to investigate the role of ADAMTS metalloproteinases and their substrates in development and disease.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To investigate the role of ADAMTS metalloproteinases and their substrates in development and in disease

Experimental Approach: The experimental approaches utilized in this project involves the synthesis and expression of recombinant plasmid DNA constructs (non viral, non infectious) expressing various metalloproteinases related to ADAMTS family members and their substrates into mammalian cell cultures using in vitro transfection.
Also, siRNA and CRISPR/Cas9 plasmid transfections will be used in cells to knock down gene functions related to ADAMTS metalloproteinases. Transfected cells will be either fixed and used for immunostaining experiments, frozen for mRNA extraction or protein extraction.
Fixed tissues and embryos harvested from various mouse knockout models will be used to investigate the role of ADAMTS proteases.
Light microscopy will be used to visualize cultured human cell lines (RPE1, HEK293).
Flow sorting core will be used to sort live cells based on fluorescence signal intensity (BSL2-enhanced).
Electron Microscopy Core will be used to visualize primary cilia and ECM in fixed cell lines and mouse tissues. EM Core facility will handle tissue fixation through imaging utilizing SEM and TEM.
Proteomics core will be used to investigate the proteome of various related cell lines and mouse tissues generated from transgenic mouse models. Upon snap freezing of cells and tissues in liquid nitrogen, the Proteomics core facility will then handle tissue processing, labelling and mass spectrometry of samples.

IBC Discussion and Vote

Discussion: The reviewer discussed minor action items.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1**
NIH Guidelines: III-E, III-F

5) Investigator: Yemini, E

Title: MousePAL Color Barcoding of Retinal Neurons

IBC Registration: **I-933-26, New**

Training Verification: Acceptable pending completion of PI training

Brief Summary: This research will develop and use transgenic mice to identify how to target and express fluorescent-protein color barcodes in retinal neuron subtypes to determine how these neurons develop, the genes/proteins they express, and image neural activity in/ex vivo. We will also use brain tissue from euthanized mice to compare wild-type versus disease models.

- Goal 1: transgenic mice with fluorescent-protein color barcoded retinal cell subtypes.
- Goal 2: identification of retinal subtype functions (development, genetic/proteomic inventory, and neural activity) in wild-type versus disease models.
- Goal 3: spatial transcriptomics to identify and compare neuron subtypes in retina and brain tissue of wild-type versus disease models.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This research will develop and use transgenic mice to target and express fluorescent-protein color barcodes in retinal neuron subtypes to determine how these neurons develop, the genes/proteins they express, and image neural activity in/ex vivo. Three goals are listed:

- Goal 1: transgenic mice with fluorescent-protein color barcoded retinal cell subtypes.
- Goal 2: identification of retinal subtype functions (development, genetic/proteomic inventory, and neural activity) in wild-type versus disease models.
- Goal 3: spatial transcriptomics to identify and compare neuron subtypes in retina and brain tissue of wild-type versus disease models.

Experimental Approach: Cell culture: E. coli will be used to propagate plasmids and bacterial artificial chromosomes (BACs); and HEK239T will be used to prepare AAVs.

Cloning recombinant DNA: plasmids and BACs purchased from BACPAC and Twist Bioscience will be modified to add benign fluorescent proteins for color barcoding and elements that aid expression in retinal neurons. Mouse retinal neuron-specific enhancers, promoters, standard 3'UTRs, and fluorescent proteins will be cloned into plasmid vectors.

DNA Expression: Plasmids, BACs, and rAAVs will be injected intraocularly into mouse eyes for transgene expression in retinal neurons by and imaged by immunofluorescence. For plasmids and BACs, subretinal electroporation will be used. The Transgenic Core will be used to create a transgenic mouse line via pro-nuclear injection of fluorescent-protein tagged BACs.

AAV viral particles: replication incompetent AAVs will be prepared by transfection of HEK293T cells or through the Viral Vector Core. AAV vectors will be used to transduce mouse retinal neurons via intraocular injection.

Tissue harvesting: Mice will be will sacrificed and mouse tissues (e.g., retinas) expressing fluorescent color barcodes will be harvested. These will be used to image development and neural activity ex vivo using fluorescent-protein color barcodes to determine neuronal subtypes. Retinal and brain tissue gene/protein expression will be imaged using spatial transcriptomics, RNA probes, antibodies, and tissue stains (e.g. DAPI). Mouse models of human disease (FMR1, KMT2A, and KDM6b knockout strains) will be used for these experiments.

IBC Discussion and Vote

Discussion: The reviewer discussed that it was unclear what the appropriate BSL should be due to the human cell lines. Chair discussed it should be BSL-2 due to the chance of them being potentially infectious. The reviewer also discussed more information is required about vector shedding in the animal addendum.

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

BSL/ABSL: **BSL-2; ABSL-1 with Special Precautions**
NIH Guidelines: III-D, III-E, III-F

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

1) N/A

VI. Information from the field (Senior Biosafety Officer)

1) Worcester DPH Permitting on January 9, 2026, went well and has been completed.
2) Report from Decon of BT2 BSL-3 has been received and is completed

VII. Other Business

1) **CDC Inspection Response: ABSL-3 PPE**
Response to the CDC/USDA Inspection finding regarding PPE requirements in the ABSL-3. During the meeting it was agreed to use the existing ABSL-3 PPE Risk Assessment and further enhance to demonstrate that the level of PPE is appropriate for the tasks that are occurring, keeping in mind the engineering and administrative controls in place.

- **Observation:** The biosafety manual indicated that individuals only wear disposable PPE when performing select agent work in the ABSL-3 registered space, including a disposable Tyvek jump suit, water resistant gown, shoe covers, and two pairs of gloves. **However, entity researchers wear street clothes and not protective clothing (e.g. scrubs, uniforms) under this PPE. Although animal care staff wear scrubs, this protective clothing is not doffed for decontamination and laundering prior to exiting containment.** [
- BMBL:ABSL-3 C3]. (pg 91) Biosafety in Microbiological and Biomedical Laboratories—6th Edition
    - C. Safety Equipment (Primary Barriers and Personal Protective Equipment)
    - 3. Personnel within the animal facility wear protective clothing, such as uniforms or scrubs. a. Disposable PPE such as non-woven, olefin cover-all suits, or wrap[1]around or solid-front gowns are worn over this clothing before entering areas where infectious materials and/or animals are housed or manipulated. Front-button, laboratory coats are unsuitable. b. Reusable clothing is appropriately contained and decontaminated before being laundered. Animal facility and protective clothing is never taken home. c. Disposable PPE is removed when leaving the areas where infectious materials and/or animals are housed or manipulated. Scrubs and uniforms are removed before leaving the animal facility. d. Disposable PPE and other contaminated waste are appropriately contained and decontaminated prior to disposal.
- Corrective Action: Provide:
    - 1) the measures implemented to ensure dedicated protective clothing is worn when infectious materials and/or animals are housed or manipulated,
    - 2) an updated section of the biosafety plan that addresses protective clothing in donning and doffing procedures, and 3) evidence that relevant personnel have been trained on the updated PPE stance. Alternatively, provide a risk assessment describing how current practices are sufficient to mitigate against exposure to select agents.
- DISCUSSION: The concern is where there may be handling of contaminated or infected animals

outside of any containment and how this could affect the PPE Risk Assessment that is being prepared. For example, what about the use of the Glas-col machine? When this experiment is conducted don't the researchers take the mouse (mice) out of the cage(s) and place them in a basket which is then placed in the machine? The machine is a stand-alone piece of equipment that is not in a BSC.

  - Concerning the handling of infected animals outside of the BSC. Yes, Megan and Hardy noted that the MTb infected animals when they come out of the Glas Col machine, might have viable bacteria on their fur, and they are handled with gloved hands and placed into micro isolator cages. Hardy points out there is no threat of aerosolization of MTb, and it is known mice do not shed MTb.
  - For CoV2 and Megan confirms for Y.pestis infected animals, infected mice are not taken out of containment(BSC or cages).
  - With respect to Scrubs or Uniforms under the PPE, as Ed has pointed out, we wear the coveralls over our street clothes in addition to the BMBL recommendation of solid front fluid resistant gown.

- ABSL 3, Glas col and ABSL 2 risk assessment comments.docx
- Lab Vivarium PPE Assessment-Tool ABSL3 Mice and rats, entry and handling version 4 1.15.26.pdf
- Lab Vivarium PPE Assessment-Tool ABSL3 Glas Col Version 3 1.15.26.pdf

APPROVED

2) Biosafety Manual Update: 12/2025 version:

- 2025 Changes to Biosafety Manual.docx
- B-10 Biological Waste_120425v5.docx
- B-14 ABSL-2-3 Suite_09102024 (003)EJ .docx
- B-16 Registration Of Research Using Biological Agents_042825.doc

TO BE POSTED FOR ADMINISTRATIVE APPROVAL – ONE WEEK REVIEW PERIOD

- BSL3/ABSL3 Medical Surveillance Questionnaire Update: some out-of-date wording. The references to the BT-II BSL-3 lab have been removed in the BSL3 ABSL3 questionnaire.

Acknowledgement Items:

N/A

Adjourned at 1:08pm