IBC Meeting Minutes

February 12, 2026 (Thursday) at 11:00 A.M.

via Zoom Conference

Bridge

IBC members present:

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

*ER- Joined at 11:06

**EJ- Joined at 11:15

***SL- Left at 11:23

*ER- Left at 1:43

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

I. Introductory Remarks

1) The Chair brought to the attention of the Committee the action items completed since the previous meeting and those submissions still under review by IBC.
2) The Chair brought to the attention of the Committee the meeting minutes from the previous IBC meeting. **Meeting Decision: Vote to approve January 15, 2026 Meeting Minutes**

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

Past incidents that remain open:

1) 07/08/2025: Needlestick in BSL-3. Potential TB exposure. 6-month follow-up
2) 11/26/2025: BSL-3. Wet sleeve noted, skin intact. Repeat IGRA screening planned
3) 12/08/2025: Cut noted after cleaning BSC. Low likelihood HIV exposure; PEP; 6-month serology planned

Recent incidents:

1) 01/20/2026: Mouse bite. No rsNA. No infectious agent
2) 01/22/2026: Pipette scratch. Cord blood; CD34 + cells. Source testing negative for BBP, no rsNA.
3) 01/23/2026: Mouse bite. No rsNA and no infectious agent
4) 01/30/2026: Mouse bite. LNP with mRNA expressing GLP-1 receptor agonist similar to lixisenatide (a once-daily subcutaneous GLP-1 receptor agonist used to improve glycemic control in adults with type 2 diabetes). No infectious agent. Reports sent to NIH OSP and Worcester DPH.

III. Protocols Reviewed Administratively

N/A

IV. Protocols to Discuss

1) Investigator: Schärfen, L
Title: Large-Scale Characterization of RNA Structure Ensembles
IBC Registration: **I-935-26, New**
Training Verification: Acceptable
Brief Summary: RNA Structure formation, driven by base pairing, is a general feature of every coding or non-coding RNA. For most cellular RNAs, we lack an understanding of how RNA structure shapes its function.

- Map RNA structure ensembles of natural and synthetic sequence space
- Phenotypic characterization of designed RNA structure libraries
- Test the performance of predictive models in *E. coli* and *S. cerevisiae*

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of this study is to understand how a RNA forms its structure by base pairing using models in E. coli and S. cerevisiae, which involves both coding and non-coding RNA.

Experimental Approach: The experimental approach includes three areas:

1) To map RNA structure ensembles of natural and synthetic sequence space, in which fragmented natural genomes (phage lambda, E. coli, S. cerevisiae, M. musculus) will be cloned into expression vectors and transcribe the fragments into RNA in vitro, in E. coli, and in S. cerevisiae, and then use chemical RNA structure probing methods (DMS-MaPseq, SHAPE-MaP) to measure base pairing of these RNA libraries in vitro, in E. coli, and in S. cerevisiae.
2) To phenotypically characterize designed RNA structure libraries by taking the following experimental steps:
   a. RNAseq will be performed to measure stability of each cloned RNA in vitro, in E. coli, and in S. cerevisiae
   b. The genomic fragments will be attached to fluorescent reporter systems (translation, splicing, transcription)
   c. Fluorescence Activated Cell Sorting (FACS) will be conducted to separate sequences based on their performance in these reporter assays, followed by amplicon sequencing of the resulting cell population (Sort-seq)
3) To test the performance of predictive models in vivo by designing libraries of RNA sequence based on computational prediction of RNA structure, synthesizing and cloning the designed libraries into E. coli and S. cerevisiae, and then assessing performance of the designed libraries.

IBC Discussion and Vote

Discussion: Reviewer discussed that it isn't clear whether animal work is being done or not because there is conflicting information in the registration. Clarification is needed to verify no animal work is being done. The reviewer discussed that they provided a table of plasmids which was very useful. A discussion was raised regarding the lowest level of containment for the flow sorting is BSL-2 despite the items being sorted are all BSL-1.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-1; BSL-2 Flow Sorting**
NIH Guidelines: III-E, III-F

2) Investigator: Caricchio, R
Title: A PHASE I, MULTICENTER, OPEN-LABEL STUDY TO EVALUATE THE SAFETY, TOLERABILITY, CELLULAR KINETICS, PHARMACODYNAMICS, AND EFFICACY OF P-CD19CD20-ALLO1 IN PATIENTS WITH SEVERE, TREATMENT-REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS

IBC Registration: **I-934-26, New**
Training Verification: Acceptable pending completion of PI training
Brief Summary: To evaluate the safety and tolerability of P-CD19CD20-ALLO1

Brief Summary and Review by Primary Reviewer

Overview and Objectives: SLE is a B cell‐driven autoantibody-mediated disease in which B-cell depletion leads to clinical efficacy.
To evaluate the safety and tolerability of P-CD19CD20-ALLO1 in participants with highly active, severe, refractory systemic lupus erythematosus (SLE) with or without lupus nephritis (LN). P-CD19CD20-ALLO1 is a chimeric antigen receptor (CAR) T-cell treatment that targets both CD19 and CD20 antigens and is hypothesized to deplete autoreactive B cells and plasmablasts, thus limiting the production of autoantibodies in SLE and potentially providing sustained drug-free remission to patients with highly active, severe, and treatment-refractory disease. CAR T-cell products are being studied in this population. With a favorable nonclinical toxicity profile observed with P-CD19CD20-ALLO1, and risk mitigation measures, this IP is being studied as well.
P-CD19CD20-ALLO1 is comprised of allogeneic chimeric antigen receptor (CAR)-T cells that target both CD19 and CD20 and have been genetically modified using an electroporation-based, non-viral (DNA transposon) gene delivery system called the piggyBac® (PB) DNA modification system and the Cas-CLOVER™ (CC) gene editing system. Manufactured from PBMCs obtained by leukapheresis of healthy volunteer donors. Genes introduced using the PB transposon, include anti-CD19 and anti-CD20 targeting variable human heavy-chain domains (VH)-based CAR (VCAR) genes, a dihydrofolate reductase (DHFR) selection mutant protein (mutein) gene, and an inducible caspase-9 (iCasp9)-based safety switch gene, and the genes ablated using the CC gene editing system (the T cell receptor beta chain (TRBC) and beta-2-microglobulin (B2M) genes). After ex vivo cell expansion and purification to remove T cell receptor (TCR)-positive T cells, modified T cells are formulated and cryopreserved to yield the P-CD19CD20-ALLO1 drug product. Rimiducid (AP1903) is a small-molecule dimerizer used as a, "safety switch" to activate inducible Caspase-9 (iC9) in genetically engineered CAR T-cells, triggering rapid, selective apoptosis (>90% elimination). This system enhances safety in cell therapies by controlling adverse effects like graft-versus-host disease (GvHD) or cytokine release syndrome (CRS).
The PB DNA modification system efficiently moves DNA from a plasmid to a chromosome via a "cut and paste" mechanism. Compared to lentivirus or γ–retrovirus transduction, PB offers advantages, including a safer insertion profile, higher levels of transgene expression, significantly larger cargo capacity, more stable, longer duration transgene expression, and a preponderance of the highly favorable T-stem cell memory (TSCM) phenotype. The CC gene editing system approximates a hybrid between the clustered regularly interspaced short palindromic repeats (CRISPR) and transcription activator-like effector nuclease (TALEN) gene editing methods. CC uses the dCas9 protein to act as a DNA binding protein when combined with an appropriate guide RNA (gRNA) and guides dimerization of the components of a Clo51 endonuclease to specifically cut DNA at that site. Because CC cutting of a gene requires a dimeric binding event that is critically dependent on the specific binding of both a left and a right gRNA pair, there has been little to no off-target activity observed using the CC genome editing system as compared with conventional CRISPR. Additionally, CC can efficiently edit resting T cells, allowing for the maintenance of the TSCM composition in allogeneic CAR-T products.
P-CD19CD20-ALLO1 is designed in a way to reduce the chances of rejecting the modified T cells that have come from a donor. P-CD19CD20-ALLO1 also has another safety measure that allows for rapid killing of the modified T cells, if needed, through infusion of a study drug called rimiducid.

P-CD19CD20-ALLO1 is currently undergoing Phase I testing in patients with selected relapsed/refractory B-cell malignancies.
A key benefit of an off-the-shelf allogeneic cell therapy is the reduced burden on patients, eliminating the need for leukapheresis and shortening the time from medical decision to treatment administration.

Experimental Approach: Participants will receive a single dose of P-CD19CD20-ALLO1 (starting dose of 60 x 10^6 cells IV, with planned escalation to a dose of 160 x 10^6 cells). P-CD19CD20-ALLO1 cells are infused into the subject after a lymphodepleting chemotherapy (LDC) regimen.
CTU lab in the Ambulatory building (University Campus) is where the blood samples will be processed. Processing will take place in the CRC (is this same as CTU? what IBC registration applies?). Patients will be consented in the out-patient setting, they will be admitted to the BMTU on the 8th floor of UMass Memorial Medical Center, where they will receive the infusion and stay in-patient for about 24 hours after the infusion. Disposal/exposure/spills will follow the UMass Memorial Safety Hazard Policy and others related to cellular therapy.
Protocol states:"All participants will be hospitalized for the P-CD19CD20-ALLO1 cell infusion and remain hospitalized for observation for a minimum of 7 days after the day of infusion (Days 1-8; may be discharged on Day 8) in the dose-escalation stage. In the expansion stage, the minimum hospitalization requirement may be reduced based on the recommendation of a Safety Monitoring Committee (SMC) after review of the available safety and cellular kinetic (CK) data from the study…"
After discharge, required to stay within approximately a 1-hour travel time to the clinic for approximately 1 month. During this period, study visits occur every 1−3 days. Then, every 2 weeks until 2 months after the infusion. Then at 3 months after the infusion. Then every 3 months thereafter until 2 years. Then every 6 months thereafter until 5 years.

IBC Discussion and Vote

Discussion:	The reviewer discussed that the protocol is very interesting as they are working to develop an “off the shelf” reagent to be used for B-cell depletion in auto-immune diseases such as patients with lupus. The reviewer discussed that section A2 of the registration did not give a full description of the work being done for the experimental approach. This protocol also has not been reviewed yet by the Gene and Cell Therapy Advisory Committee.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2**
NIH Guidelines:	III-C, III-E

3) Investigator: Czech, M
Title: Characterization and treatment parameters for metabolic disease
IBC Registration: **I-350-23, Amendment**
Training Verification: Acceptable pending completion of PI training
Brief Summary: To see effects of genes on metabolism, we use tools to knock-out the genes or proteins or to overexpress the genes or proteins. The tools used are siRNA, sgRNA/CRISPR, mRNA, antibody oligonucleotide conjugates or viral vectors that overexpress the genes of interest etc.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This laboratory studies the metabolic syndrome, which is a complex set of physiological conditions resulting in obesity, insulin resistance, type II diabetes, heart disease, and nonalcoholic fatty liver disease. The goal of this study is to try and dissect out some of the important genes, proteins or metabolites that may lead to, or ameliorate, the metabolic syndrome. To see effects of genes on metabolism, they will knockout or overexpress the

genes or proteins. The tools used are siRNA, sgRNA/CRISPR, mRNA, antibody oligonucleotide conjugates or viral vectors that overexpress the genes of interest etc.

Experimental Approach: This amendment is to add the use of mRNA in vitro and in vivo - in cell culture systems, and in whole live animals (mice). They will be using some primary mouse, human and non-human primate cells and/or tissues with genes knocked out in metabolism or immune markers. They plan to deliver the mRNA, and/or these cells, to animals in vivo, in addition to using them in vitro.

IBC Discussion and Vote

Discussion: The reviewer discussed that the amendment was simple and straight forward, but more information is required on how the mRNA is going to be used in the study. It is also unclear whether mRNA is being used in a vector or not.
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

4) Investigator: Davis, R
Title: Signal Transduction in Metabolism and Growth
IBC Registration: **I-302-26, Renewal**
Training Verification: Acceptable
Brief Summary: We seek to understand the mechanism of stress responses mediated by the cJun NH2-terminal kinase (JNK) signaling pathway in the context of cancer, diabetes, ischemic disease, neurodegeneration, and memory formation. The overall goal of this research program is to design novel therapeutic strategies for the treatment of disease.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This project seeks to understand the mechanism of stress responses mediated by the cJun NH2-terminal kinase (JNK) signaling pathway in the context of cancer, diabetes, ischemic disease, neurodegeneration, and memory formation.

Experimental Approach: A combination of in vitro molecular biology and biochemical procedures will be employed. The in vitro procedures include reconstitution assays using purified components and tissue culture studies using cells with experimentally modified gene expression (plasmid and oligonucleotide transfection; virus transduction; homologous recombination; Cre/LoxP; Flp/Frt; CRISPR).
In vivo studies will be performed using mice with modified gene expression (e.g. oligonucleotide treatment; virus transduction; homologous recombination; Cre/LoxP; Flp/Frt; CRISPR).

IBC Discussion and Vote

Discussion: The reviewer discussed that it was a challenge to know how they are trying to use the added vectors because the experimental approach lacks pertinent information to make a proper risk assessment. The reviewer also discussed that the adenovirus vectors listed are not described and there is conflicting information on whether it is replication defective or not which could affect the Biosafety Level.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2, BSL-2 Enhanced Flow Sorting; ABSL-1 with Special Precautions; Administration to Animals using BSL-2 Precautions/ Sharps Safety**

NIH Guidelines: III-D, III-E, III-F

5) Investigator: Kang, J
Title: Costimulatory Regulation of T Cell Activation
IBC Registration: **I-287-26, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The goal of these experiments is to investigate how T lymphocyte development and activation is regulated. We will examine the integration of signals from the T cell receptor (TCR) and costimulatory/accessory molecules in order to understand the role of these molecules in self-tolerance induction. The results of these experiments have implications for understanding the etiology of human autoimmune disorders and for the design of novel therapeutic approaches to modify T cell responses during transplant and tumor rejection.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To investigate how T lymphocyte development and activation is regulated.
To examine the integration of signals from the T cell receptor (TCR) and costimulatory/accessory molecules in order to understand the role of these molecules in self-tolerance induction.
The results of these experiments have implications for understanding the etiology of human autoimmune disorders and for the design of novel therapeutic approaches to modify T cell responses during transplant and tumor rejection.

Experimental Approach: 1. Analyses of various transgenic and KO mouse models that have (or predicted to have) alterations in T cell activation/development. These mouse models are generated by UMASS Transgenic and Knockout Core Facility, or from a CRO (Jackson Laboratories). Mice will be infected with the listed pathogens (none above BSL2), iv, ip or sc. In case of Malassezia sp. (fungi) they are simply applied to ear skin in olive oil.
2. Analyses of mice reconstituted with syngeneic bone marrow or fetal liver cells (stem or progenitor cells) expressing exogenous immune modulators via replication-defective retrovirus-mediated gene transfer
Adenovirus and AAV5, 9 containing human ACE2 insert will be obtained from the vector core.
Phospho proteome analysis in human T cell line Jurkat.
Flow sorting by core

IBC Discussion and Vote

Discussion: The reviewer discussed that the description of the adenovirus vectors were lacking in the vector checklist. More information about what genes are missing and clarification is required about whether they are replication defective or not.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-2**
NIH Guidelines: III-D, III-E, III-F

6) Investigator: Lien, E
Title: Innate immune responses in health and disease
IBC Registration: **I-193-26, Renewal**
Training Verification: Acceptable
Brief Summary: Our goals are to identify receptor signaling pathways leading to immune activation induced by microbial components and define the immune-stimulating mechanisms following exposure of leukocytes to bacteria and viruses. Our studies focus on the role of Toll-like receptors (TLRs,

caspases, kinases and NOD -like receptors (NLRs) in host defense and the mechanisms developed by pathogens to avoid or minimize recognition by innate immune signaling.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Our goals are to identify receptor signaling pathways leading to immune activation induced by microbial components and define the immune-stimulating mechanisms following exposure of leukocytes to bacteria and viruses. Our studies focus on the role of Toll-like receptors (TLRs, caspases, kinases and NOD -like receptors (NLRs) in host defense and the mechanisms developed by pathogens to avoid or minimize recognition by innate immune signaling.

Experimental Approach: We propose to use combined approaches to identify mechanisms by which various microbes and microbial compounds activate mammalian cells. These include the use of whole live and killed bacteria and viruses, agents thereof (such as lipopolysaccharide) in combination with transfected cell lines, primary cells from humans and animals, immortalized cells from genetically deficient animals, and finally whole animals (innate in vivo animal responses and effects on certain molecules on in vivo susceptibility and pathogenesis). We will also collect plasma, isolate peripheral blood mononuclear cells (PBMCs) and monocytes from UMass Chan healthy subjects to assess their immune status. Read-outs include cytokine release (ELISA/western blots), activation of signal transduction molecules (typically western blots), transcription factor activation (western blots, reporter gene activity), cell death and disease severity (animal studies). We study microbes such as Yersinia pestis (exempt strains), Y. enterocolitica, Y. pseudotuberculosis, Salmonella typhimurium, and others. This project involves studies of microbial activation and evasion of central innate immunity signaling pathways, such as TLRs and NLRs. We propose to utilize both genetically deficient microbes, microbial agents, and cells/animals. We typically generate some of the bacterial compounds in the lab (LPS, lipid A).

IBC Discussion and Vote

Discussion:	The committee discussed that this protocol includes Citrobacter rodentium in some animals (RG1; not a human pathogen). Infected mice will be housed at ABSL-2 to protect vivarium (a recent change from previous practices where ABSL-3 was required). The reviewer discussed that the lab provided two SOP's for Employee Health but they were in the Lab SOP template not the standard Employee Health SOP template. The reviewer also discussed that it was unclear where the PBMC's are coming from and further information on this should be provided.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2+; BSL-2 Enhanced Flow Sorting; ABSL-2**
NIH Guidelines:	III-D, III-E, III-F

7) Investigator: Richter, J
Title: Translational control
IBC Registration: **I-229-26, Renewal**
Training Verification: Acceptable
Brief Summary: We study the detailed function of several proteins involved in mRNA translational control in neurons. We focus on the cytoplasmic polyadenylation CPEB protein and RNA-binding proteins such as FMRP. Our objective is to understand the molecular mechanisms underlying memory formation, synaptic plasticity and certain diseases of nervous system, including Fragile X Mental Retardation Syndrome and autism.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The objective is to understand the molecular mechanisms underlying memory formation, synaptic plasticity and certain diseases of nervous system, including Fragile X Mental Retardation Syndrome and autism. The lab studies function of several proteins involved in mRNA translational control in neurons. The lab focuses on the cytoplasmic polyadenylation CPEB protein and RNA-binding proteins such as fragile X messenger ribonucleoprotein (FMRP).

Experimental Approach: The lab employs different knockout mouse models for behavioral analysis, tissue harvesting and primary neuronal cell cultures. Tamoxifen is used to induce conditional gene deletion in mice. As an alternative, the lab strongly relies on mouse and human cell lines, performing experiments which often use plasmid DNA and AAV or lentiviral vectors. They plan to clone several genes into AAV vectors and produce the AAV using the Vector Core at Emory University. These AAV viruses will be used by collaborators for stereotactic injections to the mouse brain. The lab performs behavior analysis with the stereotacticly injected animals, and harvests brain tissue samples for further biochemical analysis. The lab uses LPS to induce inflammatory response in cell lines and mouse models.

IBC Discussion and Vote

Discussion:	The reviewer discussed that this was a difficult protocol to follow as the instructions were not well followed in the registration. There seemed to be some confusion by the lab about the retroviral and adenoviral vectors and whether they should be categorized as infectious agents or not. No major changes have been made since last approval.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1 with Special Precautions; Administration to Animals using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-E, III-F

8) Investigator: Rock, K
Title: Analysis of Immune Response
IBC Registration: **I-245-26, Renewal**
Training Verification: Acceptable
Brief Summary: The laboratory is studying the mechanisms through which the immune system detects pathogens or cancers and then mounts a T cell response. In one project we study how specialized cells in tissues recognize pathogens or cancerous cells allowing these cells to transport and report this information to T cells. In another project, we are studying how tissue specific proteases affect how T cells differentiate foreign proteins from self-proteins. We also study how dead cells and irritant particles, and their components, induce inflammation in vitro and in vivo.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The lab will study the mechanisms by which the immune system detects and mounts a T cell response against pathogens or cancers. In one project, they will study how specialized cells in tissues recognize pathogens or cancerous cells, allowing these cells to transport and report this information to T cells. In another project, they will study how tissue-specific proteases affect how T cells differentiate foreign proteins from self-proteins. They will also study how dead cells, irritant particles, and their components induce inflammation in vitro and in vivo.

Experimental Approach: The research procedures for these studies involve injecting mice with model antigens, viruses, and cells transfected with plasmids or rtandsuced with viral vectors. The viruses are also used in the laboratory to infect

cells that are then analyzed in cell culture. In some experiments, they will inject mice with toxics immunostimulators (LPS). Finally ,CRISPR technology will be used to study the effects of gene depletion in mouse cells and in mice. For in vivo studies, synthetic guide RNAs targeting a gene of interest will be co-injected with Cas9 nucleases in embyors by the Transgenic Core facility in order to achieve disruption of the targeted gene.

IBC Discussion and Vote

Discussion:	The reviewer discussed that the lab doesn't give details about what genes will be knocked down in the mice. The reviewer also discussed that two toxins will be used, LPS and saporin, but it is unclear how the saporin will be used in vitro. The lab plans to use eight out of eleven cores, and the lab provides details for some of the cores being used, but others have no description. A member of the committee noticed that an old version of the flow sorting form was used, and they should submit this on the new form.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-2**
NIH Guidelines:	III-D, III-E, III-F

9) Investigator: Vyas, J
Title: Innate Immune Responses to Fungi
IBC Registration: **I-923-25, Amendment**
Training Verification: Acceptable
Brief Summary: To make immortalized murine macrophages.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Amendment to add reagent to immortalize murine macrophages

Experimental Approach: Adding viral supernatants of CreJ2 cells from Golenbock lab.
To make immortalized murine macrophages viral supernatants of CreJ2 cells will be adde to cultures of murine bone marrow.

IBC Discussion and Vote

Discussion:	The reviewer discussed two action items. One action item was to confirm that replication defective virus in Cre-J2 supernatant is ecotropic.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2**
NIH Guidelines:	III-D

10) Investigator: Yamada, K
Title: Development of RNAi-based Therapeutics
IBC Registration: **I-927-25, New (prev. tabled)**
Training Verification: Acceptable
Brief Summary: The overall goals of the lab are to develop RNA-based therapeutics for several 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 and human cell lines. There are a variety of targets we work with including huntingtin, sFLT1, ApoE etc. RNA-based

therapeutics development includes overexpression and purification of recombinant Ago2 for use in *in vitro* experiments as well as study of the impact of siRNA gene modulation on ex vivo perfused organs.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To develop RNA-based therapeutics for several disease indications.
Testing modified or formulated RNA oligonucleotides (or RNA/protein complexes) developed in the lab in in vitro experiments using mouse, human, NHP cell lines and primary cells followed by in vivo rodent and large animal models. Targets include huntingtin, sFLT1, ApoE and others. RNA-based therapeutics development includes overexpression and purification of recombinant Ago2 for use in vitro as well as study of the impact of siRNA gene modulation on ex vivo perfused organs.

Experimental Approach: Chemically modified oligonucleotide test article description: Oligonucleotides can be administrated by themselves or combined with mRNA/ protein (CAS9 or similar) and virus to enhance distribution. All the compounds are being synthesized in house and are HPLC purified. Full length and identity are confirmed by mass spectrometry. Resulting compounds are considered to be "pharmaceutical grade". In addition, oligonucleotide might have a fluorescent dye for detection in distribution studies.
Project 1: Screening modified RNAs in vitro.
Testing modified RNA oligonucleotides in modified and primary cells of human and mouse origin. The oligonucleotides can either be naked, complexed with mRNA, protein or formulated (liposome, endosome, polymer, small drugs). Use peripheral blood (hPBMCs, serum, and whole blood), fibroblasts etc from patients with and without the conditions of interest (i.e Huntington's disease, ALS, etc.) to test the modified RNA oligonucleotides.
Project 2: Screening modified siRNAs in vivo.
Animal models will be used to test toxicity, tissue distribution, pharmacokinetic/pharmacodynamic (PK/PD) parameters, and efficacy of modified siRNAs. In some experiments co-administration of a drug (i.e guanabenz or dextran sodium sulfate (DSS, etc.) will be tested. In vivo experiments involve injection of mice by several routes (i.e IV, sc, ip, ICV etc.) with the in vitro tested oligonucleotides. Oligonucleotides can be naked, in liposomes, and/or injected with a drug.
Project 3: Cell type specific delivery of siRNA in mice and human cells
Mice will be treated with siRNA. Specific organs will be harvested to determine the amount of uptake of a fluorescently labeling siRNA in various cell types. Cytometry to determine knockdown in human cell lines and the mouse. Flow sorting of human cell lines and mouse tissues to quantitate uptake in specific cell types.
Project 4: Overexpression and purification of recombinant Ago2 for use in in vitro experiments.
Baculovirus containing the mouse Argonaute 2 (Ago2) transgene will be produced in Sf9 cells to overexpress and purify recombinant Ago2 from Sf9 or High Five cells. Baculovirus will be produced by transfecting Sf9 cells with a baculovirus genome containing the Ago2 transgene. Virus will be produced to a titer of ~1e8 pfu/mL in the culture supernatant. This virus-containing supernatant will then be used to infect either Sf9 or High Five cells to induce overexpression of Ago2.
Core use:
Flow sorting of unfixed human and mouse cells treated wth fluorophore conjugated oligonucleotides (ex. cy3 or cy5.5, etc.), Animal imaging; mice, Mouse metabolics, Ligtht microscopy, Morphology.

IBC Discussion and Vote

Discussion:	Reviewer discussed this protocol was previously tabled from August of 2025 but was very broad and has since been more targeted and streamlined in their experimental approach. A member of the committee pointed out that this involves flow sorting of human cells making this enhanced flow sorting. Reviewer discussed some 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-D, III-E, III-F

11) Investigator: Zhao, Q
Title: Protein and Antibody Generation and Evaluation
IBC Registration: **I-734-26, Renewal (From 2024- returning due to additional animal work)**
Training Verification: Acceptable pending completion of PI training
Brief Summary: Generate and evaluate proteins and antibodies for research and therapeutics purposes. Adding animal work.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Generate proteins and antibodies for research and therapeutics purposes and evaluate function.

Experimental Approach: Antigens are either purchased or produced by recombinant N/A. They are used to immunize alpaca after which RNA is extracted from single sorted cells for antibody sequencing. Mice will also be immunized for antibody production. Tumor xenografts and DMPK studies added.

IBC Discussion and Vote

Discussion: Reviewer discussed that the lab is using Drug Metabolism and Pharmacokinetics Studies it is unclear if the lab is making antibodies or proteins or something else. Clarification is required. The reviewer also mentioned that a lot of abbreviations are used and the lab should spell out their abbreviations to avoid misunderstandings.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1 + BBP; Administration to Animals using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines: III-F

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

1) Select agent observations addressed adequately except ABSL-3 PPE issue (pending further review)
2) New BSL-3 lab design/equipment meeting last week (Possible start date 7/2026)

VI. Information from the field (Senior Biosafety Officer)

1) Scientific council presentation next week

VII. Other Business

N/A

Acknowledgement Items:

N/A

Adjourned at 1:56pm