IBC Meeting Minutes

June 12, 2025 (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		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		Jennifer Wang (alt)			

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

I. Introductory Remarks

1) The Chair brought to the attention of the Committee that the IBC Minutes are now publicly posted as of 06/01/2025
2) The Chair brought to the attention of the Committee the meeting minutes from the previous IBC meeting. **Meeting Decision: Vote to approve May 22, 2025, Meeting Minutes**

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

1) 05/21/2025: BSL-3 PAPR malfunction. Blood testing was done and repeat testing to be done in 8-10 weeks. No rNA material involved.

Recent incidents: None relevant to IBC oversight

1) 05/26/2025: Dog bite during imaging. No rNA material involved.
2) 05/27/2025: Waste from an RNA isolation kit was mixed with bleach.

III. Re-visited discussion about SARS-CoV-2

Proposal to develop guidance similar to UW and posting guidance on IBC website. Other suggestions:

- Developing a BSL-2+ SOP Template for different spaces (LRB, Other procedure rooms)?
- Bring LRB BSL-2+ under BSL-3 Core management?
- Regular BSL-2+ lab users meetings?

Agreement to develop SOP; a base template to start

BSL-3 new space – consider designating some of this space for BSL-2+

IV. Protocols Reviewed Administratively

1) Investigator: Hafer, N
   Title: RADx Tech COVID-19 Test Us
   IBC Registration: 773-25, Renewal
   Training Verification: Acceptable
   Brief Summary: The RADx COVID-19 Test Us study was designed to rapidly test novel diagnostic tests for SARS-CoV-19. As part of these studies we created a large biobank of blood and oro-respiratory tract samples. All studies have ended but we still maintain these samples in storage.

2) Investigator: Luzuriaga, K
Title: Clinical Research Center Specimen Processing Lab
IBC Registration: 631-25, Renewal
Training Verification: Acceptable pending completion of PI training
Brief Summary: The CRC is a research core under the CCTS that provides clinical research resources to Umass investigators. Varied services include providing staff, space, and equipment. The laboratory within the CRC is CLIA-waived, Environmental Health and Safety inspected, with maintenance of equipment being provided through the Biomedical Engineering department of UMass Chan Medical School. Investigators' research staff can drop in and use centrifuges, dry ice, etc

V. Protocols to Discuss

1) Investigator: Ceol, C
Title: Identifying events and genetic regulators of melanoma progression
IBC Registration: 436-25, Renewal
Reviewer: Somasundaran
Training Verification: Acceptable
Brief Summary: The goal of this work is to identify oncogenes and tumor suppressor genes that may be useful as diagnostic and prognostic indicators of disease as well as therapeutic targets. For some targets we will test candidate therapies to inhibit them.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The objectives of this project are (1) to identify oncogenes and tumor suppressor genes that may be useful as diagnostic and prognostic indicators of disease, and (2) to identify and potentially use these disease-markers as therapeutic targets to inhibit and modify disease progression
(melanoma formation) with test candidate therapies.

Experimental Approach: To accomplish the objectives to investigate melanoma pathogenesis and treatment, PI will utilize 3 different model systems - zebrafish, in vitro cell culture, and rodent models
1. Experimental models will involve zebrafish transformed with melanoma-related genes, in vitro cell cultures transduced with signaling activity or other related transgene expression, and mice xenografted with various human/mouse melanoma cells.
a. Direct injection of Zebrafish embryos with genes ('naked' DNA) that are mutated or subject to copy number variation in melanomas
b. Retroviral-transfected or replication-defective lentiviral transduced genes to express transgenes or shRNA constructs to knockdown candidate cancer genes
2. Monitoring parameters –
a. Melanoma onset and other characteristics, such as degree of invasiveness
b. Effects on signaling activity will be measured using western blots with pathway-specific antibodies and colorimetric assays of biochemical intermediates
3. Xenografts of human cancer cell lines in nude/NSG immuno-compromised mice or mouse melanoma cell line into C57/BL6 mice will be performed via IP and Subcutaneous delivery
a. Xenografted mice will be treated to evaluate the effect of anti-GDF6 antibodies (anti-Growth differentiation factor 6), either alone or in combination with dabrafenib and trametinib (melanoma targeted therapy drugs) or with anti-PD1 therapy
b. Efficacy of the antibody and drug therapy will be assessed by measuring the tumor volume
4. Flow cytometry/sorting -
a. Transduced cells will be selected with drug, then selected cells will be subject to flow cytometry to measure cell death

initiation (AnnexinV positivity, using AnnexinV-specific cell surface antibody), or cell death execution (Caspase Glo assay, using
fluorometric caspase substrate), or DNA content (Hoechst)
b. Additionally, transduced cells will be subjected to FACS to select for GFP (or other fluorophore) positivity or to seed wells to make single-cell clones
PI will be following -
a. BSL-2 biosafety protocols during transfection, transduction and subsequent experiments
b. ABSL-1+BBP for in vivo (Mus musculus) xenograft experiments
c. BSL-2 enhanced flow sorting

IBC Discussion and Vote

Discussion:	The reviewer discussed that this was well written, and no action items were found. A member of the committee discussed the specific type of mouse being used has a defective DNA repair mechanism. The lab is targeting the braf protein using 2 different treatments that specific protein is important for DNA repair and the concern is that they could run into issues as the committee member ran into this issue previously. The chair found a single check box item as an action item.
Meeting Decision:	Vote to approve
BSL/ABSL:	**BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1+BBP; Administration to Animals Using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, II-E, III-F

2) Investigator: Corvera, S
Title: Adipose tissue development and metabolic disease
IBC Registration: 609-25, Renewal
Training Verification: Acceptable pending completion of PI training
Brief Summary: Objectives of this research are to understand how fat (adipose tissue) develops in humans, and how it is associated with diseases such as type 2 diabetes and its effects on liver and heart. We obtain progenitor cells from human and non-human primate adipose tissue, study them in culture, and introduce them into mice to determine how they form adipose tissue and their metabolic effects on other organs. We analyze how expression of certain genes affects cell function in culture or in mice. For this we use viral vectors and electroporated CRISPR-Cas9 systems to overexpress or knock out specific genes, or siRNA transfection to knockdown gene expression.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The objectives of the research are to understand how fat (adipose tissue) develops in humans and how it is associated with diseases, such as type 2 diabetes and its effects on liver and heart. Progenitor cells from human and non-human primate adipose tissue will be obtained and studied in culture and introduced into mice to determine how they form adipose tissue and their metabolic effects on other organs. The expression of certain genes and how they affect cell function in culture or in mice will be examined. The group will use viral vectors and electroporated CRISPR-Cas9 systems to overexpress or knock out specific genes. Transfection of siRNAs will be employed to knockdown gene expression.
Experimental Approach: Human adipose tissues will be obtained under IRB approved protocols (#14734) from patients undergoing surgery at UMass Memorial. Non-human primate adipose tissues will be obtained from external collaborators under established MTAs. Cells will be grown under sterile culture conditions for approximately 20 days.

The effects of cells will be studied by transplanting them into mice, typically NSG and Nude backgrounds, under approved IACUC protocol (A-2007). In selected experiments, cells (both in culture and after implantation in mice) are transduced with commercially sourced 3rd generation replication-defective viral vectors, or AAV vectors provided by the Umass Chan Vector Core. Cells are also transfected with RNA guides or siRNA using commercially sourced transfection reagents (e.g. Promega ViaFect™). Examples of genes targeted by siRNA for knockdown include FASN, NGF, and BDNF, all of which are normally expressed in adipocytes. In other experiments, cells are sorted and selected on the basis of cell surface markers or GFP fluorescence.

IBC Discussion and Vote

Discussion:	Reviewer asked to clarify 3rd generation replication defective viral vector if different from AAV vectors. A discussion around the BSL safety level due to the types of vectors being used. Reviewer also discussed that a medical alert card and B-virus kits are necessary as NHP materials are being used.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL- 2; BSL-2 Enhanced Sorting; ABSL-1 + BBP with Special Precautions; Administration to Animals Using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-E, III-F

3) Investigator: Futai, K
Title: AAV- and Lenti- based transgene delivery in ex vivo and in vivo samples
IBC Registration: 444-25, Renewal
Training Verification: Acceptable
Brief Summary: The overall aim of our research is to understand the molecular mechanisms that regulate communication between cells in the brain. These mechanisms are important for mediating many cognitive functions, such as learning and memory. Dysfunction of neuronal communication is likely to underlie many neuropsychiatric illnesses, including schizophrenia and autism. We aim to overexpress or knock down genes, as well as activate or inhibit neuronal circuits involved in circuit function, using adeno-associated virus (AAV) and lentiviral vectors. For the past five years, we have studied the role of synaptically localized proteins in the development and function of various inhibitory synapses. The next five years will focus on the role of synaptic proteins at serotonergic synapses. Additionally, we will induce inflammatory responses in our mouse models by the injection of lipopolysaccharide to understand how neuroinflammation protects and/or aggravates brain functions.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overall aim ofthis project is to understand the molecular mechanisms that regulate communication between cells in the brain. Genes will be overexpressed or knock down in order to activate or inhibit neuronal circuits involved in circuit function. Adeno-associated virus (AAV) and lentiviral vectors will be used. The past five years, were focused on the study of role of synaptically localized proteins in the development and function of various inhibitory synapses. The next five years will be focused on the role of synaptic proteins at serotonergic synapses. Additionally, inflammatory responses will be induced in mice by injecting lipopolysaccharide to understand how neuroinflammation protects and/or aggravates brain functions.
Experimental Approach: Genes for various synaptic molecules or kinases that contribute to synaptic function (cell adhesion, receptors, neurotransmitters) will be overexpressed or knocked down in cultured neurons and in the mouse brains (by stereotaxic injector) utilizing adeno-associated and lentiviral vectors. Additionally, a genetically encoded calcium indicator (GCaMP) and optogenetic tools (Channelrhodopsin, Cheriff and Halorhodopsin, eNpHR3.0) will be utilized to monitor or gain control of biological functions. The effect of gene manipulation will be evaluated by

measuring the synaptic response (by electrophysiological and cell biological techniques) or animal behavior. Pharmacological experiments using Tetrodotoxin (TTX: working concentration: 0.3-1 µM) will be performed in only ex-vivo preparations. Following gene manipulation with AAV viruses, the susceptibility of neurons against TTX will be measured. Additionally, to study the immune response in the mouse brain and how neuroinflammation protects and/or aggravates brain functions, inflammatory responses will be induced in mouse models by IP injection of lipopolysaccharide.

IBC Discussion and Vote

Discussion:	Reviewer discussed that the use of AAV would require special precautions. The chair brought to the attention of the committee that the SOP is out of date and needs to be updated. The reviewer also noted that the lab members appear to be rather new and there is highly toxic neurotoxin being used so there should be an emphasis on training. TTX inventory is needed.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; ABSL-1 with Special Precautions; Administration to Animals Using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-E, III-F

4) Investigator: Gao, F
Title: Understanding Pathogenic Mechanisms of ALS and Frontotemporal Dementia
Principal
IBC Registration: **435-25, Renewal**
Training Verification: Acceptable
Brief Summary: To use fruit flies, mouse models, and human cell lines to study the molecular pathogenic mechanisms of Frontotemporal Dementia and related disorders.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To use fruit flies, mouse models, and human cell lines to study the molecular pathogenic mechanisms of Frontotemporal Dementia and related disorders.

Experimental Approach: They use two experimental systems in the laboratory. (1) they make transgenic or loss of function mutant fly lines, and (2) they transfect human cell lines or postmitotic neurons from rodents or induced-pluripotent stem cells. In addition, the lab uses Cerebrospinal fluid (CSF) samples (~0.25 mL per person) from non-ALS/FTD individuals, non-C9ORF72 ALS/FTD patients, and C9ORF72 patients, obtained from Mayo Clinic Florida, Northeast ALS Consortium, Target ALS, and additional sources if necessary. Poly(GR) levels will be measured in these CSF samples for correlation with disease progression.

IBC Discussion and Vote

Discussion:	Reviewer discussed the few action items they found.
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**
NIH Guidelines:	III-D, III-E, III-F

5) Investigator: Harris, J
Title: Skin Diseases Research Core

IBC Registration: **772-25, Renewal**
Training Verification: Acceptable
Brief Summary: The mission of the Skin Diseases Research Core provides an efficient way to conduct preclinical mouse studies and translational research services to investigate skin diseases for UMMS faculty as well as investigators from external sources.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The mission of the Skin Diseases Research Core provides an efficient way to conduct preclinical mouse studies and translational research services to investigate skin diseases for UMMS faculty as well as investigators from external sources.

Experimental Approach: Section A2 states: Preclinical studies will include testing novel treatments in mouse models of skin disease for efficacy and mechanism of action, as well as exploring functional contributions of cells or proteins in the pathogenesis of skin diseases. Translational studies will include recruiting subjects with skin diseases and sampling their skin and blood for analysis of cells and proteins.
From other sections of the registration:
siRNA treatments are a potential test article for our client base; BSL2 and ABSL2. Mouse and/or human cells may be analyzed in the flow core based on contracted experiments (in vivo/in vitro).
Recombinant vaccinia virus (rVV) vectors, strain Western Reserve, expressing autoantigens (rVVhgp100, rVV-tyr, rVV-MART1, rVV-trp1)
We may use a mouse model of vitiligo that is based on transfer of transgenic CD8 T cells, followed by infection of the host with recombinant vaccinia virus. We may need to sort unfixed cells to isolate specific cells in blood or skin of the host mouse.
We may also be using discarded excess skin from unidentified patients undergoing panniculectomy surgery and may need to sort unfixed human cells to isolate specific cells in skin; cell sorting of primary human cells derived from blood and other bodily fluids (incl. PBMCs), and also human and non-human primate cell lines, fixed or unfixed.
Animals will receive Human material (cells/tissues/body fluid) by various routes of administration. ABSL-1+BBP in LRB is an option listed.
From past registrations:
We may use the following samples from unidentified human subjects: discarded excess skin from panniculectomy surgery; PBMC; tissues/skin; other bodily fluids (i.e. blister fluid from heat/pressure induced skin blister procedure, etc), and may need to sort fixed and/or unfixed human cells to isolate specific cells in these tissues. Limited detail on the experiments is included, although some relevant publications are cited. The investigator lists the following:
1. Recombinants using modified vaccinia virus (VV) vectors for autoantigens (hgp100, tyr, MART1, trp1) provided by a researcher at NIH for BSL2/ABSL2 and to be produced in HeLa cells
2. RNA oligos for injection to animals
3. Primary human samples (PBMC, blister fluid, blood, skin) for BSL2/ABSL2
4. Cells to be injected in mice (Vero, HeLa, B16-F10, human osteosarcoma) for ABSL2
5. Infectious agents: VV Western Reserve, Staph aureus, Candida albicans for BSL2/ABSL2
6. Toxins: resiniferatoxin, diphtheria, brefeldin A for BSL2/ABSL2
From I-465 responses: Disease in our model can be initiated one of two ways - one is using vaccinia virus (although that is not the primary way we initiate disease). The mice are injected once, and they clear the virus within 14 days. By the time we get to the flow cytometry part, vaccinia is not an issue.

IBC Discussion and Vote

Discussion: Reviewer discussed the use of Staphylococcus aureus and Candida albicans in the previously approved registration but noted it was not mentioned in this renewal. Some clarification is needed as to know if this is currently in storage or not.

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

BSL/ABSL: **BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-2; Administration to Animals using BSL-2 Precautions/ Sharps Safety**

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

6) Investigator: Hayward, L

Title: A Randomized, Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Intravenous AOC 1020 for the Treatment of Facioscapulohumeral Muscular Dystrophy (FSHD)

IBC Registration: **921-25, New**

Training Verification: Acceptable

Brief Summary: This is a phase 3 study of investigational drug AOC 1020 to treat patients with facioscapulohumeral muscular dystrophy (FSHD). FSHD is a progressive muscular dystrophy caused by aberrant expression of DUX4 in muscle cells. AOC 1020 is an antibody oligonucleotide conjugate composed of (1) a humanized immunoglobulin G1 antibody targeting transferrin receptor 1, (2) maleimidomethyl cyclohexane-1-carboxylate maleimide linker, and (3) a double-stranded siRNA oligonucleotide targeting DUX4 messenger RNA.

Objectives include:

- Evaluate efficacy of AOC 1020 of muscle strength
- Evaluate efficacy of AOC 1020 on mobility
- Evaluate effects of AOC 1020 on circulating biomarkers of FSHD

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This is a phase 3 study of investigational drug AOC 1020 to treat patients with facioscapulohumeral muscular dystrophy (FSHD). FSHD is a progressive muscular dystrophy caused by aberrant expression of DUX4 in muscle cells. AOC 1020 is an antibody oligonucleotide conjugate composed of (1) a humanized immunoglobulin G1 antibody targeting transferrin receptor 1, (2) maleimidomethyl cyclohexane-1-carboxylate maleimide linker, and (3) a double-stranded siRNA oligonucleotide targeting DUX4 messenger RNA.

Mechanism of action

AOC 1020 binds human and cynomolgus monkey TfR1 with high affinity and specificity to facilitate delivery of siDUX4.6 to muscle, without detectable interference with transferrin binding to TfR1; the humanized IgG1 antibody (AV01mAb) targeting TfR1 is engineered to be effector function null. The anti-TfR1 antibody component of AOC 1020 affords broad distribution to several tissue types.

After entering the cell through transferrin 1 receptor (TfR1)-mediated endocytosis, one of the strands of siDUX4.6 (guide strand) that complements the mRNA of DUX4 is loaded into the RISC, a protein complex that displays the strand to the intracellular milieu, including in the nucleus. Once a complementary sequence within the DUX4 mRNA molecule hybridizes with the guide strand, an enzyme that is part of RISC cleaves the DUX4 mRNA, leading to degradation of the DUX4 mRNA.

Objectives include:

- Evaluate efficacy of AOC 1020 of muscle strength
- Evaluate efficacy of AOC 1020 on mobility
- Evaluate effects of AOC 1020 on circulating biomarkers of FSHD

Experimental Approach: The anticipated study duration is approximately 21 months (6-week Screening/Baseline, 78-week Treatment Period, 6-week Post-treatment Follow-up [12 weeks from the last dose of Study Drug]).
Participants will be randomized (1:1 ratio) to receive an intravenous infusion of either AOC 1020 or placebo (saline) at the clinical study site every 6 weeks for a total of 13 doses. The final dose will occur at Week 72, followed by final assessments at Week 78.
Participants (n≈200) 16 to 70 years of age (inclusive), with a clinical diagnosis of FSHD and a confirmed genetic diagnosis of FSHD1 or FSHD2.
After meeting eligibility criteria, patients will be enrolled and subsequently administered AOC 1020 via an IV infusion every 6 weeks at a dose of 2 mg/kg. The study drug will be prepared and dispensed by investigational drug services (IDS) and the infusions will occur within the clinical research center (CRC). Labs will be collected for safety assessments and samples will also be shipped to the study sponsor for biomarker analyses and for future research assessments. Blood is screened for infectious agents (HIV, Hep B & C) at the patient's first visit and if positive, they are not eligible to participate in the study. Patients will perform physical activities and complete questionnaires, which will be used to evaluate the study objectives. Each patient will receive 13 doses of the study drug and be enrolled in the study for approximately 2 years. In total, we expect 5 people to participate at UMass Chan.
The product will be prepared for infusion in the UMass Investigational Drug Services (IDS) research pharmacy. Administration of the product will occur in the clinical research center. Processing of human samples will occur in the Clinical Research Center lab under IBC registration I-631-20 (Luzuriaga). Human samples will be processed and shipped to a central lab for testing. These samples may also be stored in the -80C freezer within the clinical research center.

IBC Discussion and Vote

Discussion: Reviewer discussed this is a minimal risk clinical trial.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2**
NIH Guidelines: III-C

7) Investigator: Lawson, N
Title: Cell Culture and Related Protocols
IBC Registration: **766-25, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The goal of these studies is to use cell lines to test molecular assays to identify cells that bear the c.548G>A mutation in GNAQ, which causes Sturge-Weber Syndrome. For this purpose, we will apply scATAC-seq coupled with a targeted amplicon genotyping or immunostaining using an antibody that recognizes the mutant protein on wild type and GNAQ mutant cell lines.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of this protocol is to conduct molecular assays in human cell lines to identify cells that bear the c.548G>A mutation in the GNAQ gene that causes Sturge-Weber Syndrome. To achieve this goal, the PI's group will carry out scATAC-seq coupled with a targeted amplicon genotyping or immunostaining using an antibody that recognizes the mutant protein on wild type and GNAQ mutant cell lines.

Experimental Approach: Two types of human cell lines will be grown in culture: 1) immortalized (telomerized) human aortic endothelial cells that have been modified by CRISPR gene to create one copy of GNAQ bearing c.548G>A, which results in expression of GNAQR183Q (teloHAEC-GNAQR183Q); and 2) CRISPR-modified same type of human cells with the comparable silent mutations at the same site in GNAQ, having the wild type amino acid sequence maintained (teloHAEC-GNAQWT). These wild type and mutant cells will be passaged, maintained, and flow-sorted for analysis of

individual cells with scATAC-seq and targeted amplicon genotyping on a 10x Chromium device. The GNAQR183Q mutantion will also be assayed using specific antibody by conducting immunostaining of the cells or by Western analysis of proteins from the cells.

IBC Discussion and Vote

Discussion: No need for flow sorting addendum with 10x Chromium sorting (low pressure, closed cassette).
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2**
NIH Guidelines: III-F

8) Investigator: Punzo, C
Title: Photoreceptor Metabolism in Ocular Diseases
IBC Registration: **453-25, Renewal**
Training Verification: Acceptable
Brief Summary: The goal of the project is to understand and prevent the progression of retinal diseases that lead to blindness and are characterized by a major loss of photoreceptors. We found that during the progression of retinal diseases photoreceptors are metabolically compromised. To understand how lower energy levels affect photoreceptors we will over-express or down-regulate genes that are involved or control cellular metabolism.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of the project is to understand and prevent the progression of retinal diseases that lead to blindness and are characterized by a major loss of photoreceptors. The lab found that during progression of retinal diseases photoreceptors are metabolically compromised. To understand how lower energy levels affect photoreceptors we will over-express or down-regulate genes that are involved or control cellular metabolism.

Experimental Approach: 1. Work in mouse and pig: Up- or down-regulation of genes done by either electroporating DNA plasmids directly into photoreceptors or genetic crosses, both of these will occur only in mouse, or by infecting photoreceptors with AAV that carries the gene/shRNA/microRNA of interest or by delivery of an siRNA (in mouse and pig). Delivery of plasmid DNA, rAAV or siRNA will be performed by intra-ocular injection. In addition, topical formulations of siRNA will be tested for use as eye drops to test penetration into the eye. Only mice might also be treated with streptozotocin, rapamycin or insulin to alter insulin signaling and the activity of mTOR in vivo. All three will be delivered by intraperitoneal injection or by addition of rapamycin to the drinking water.
2. Work with NHP and human: NHP and human work involves dissection of fresh eye globes. We will obtain tissue either pre-fixed in 4% formalin (4% paraformaldehyde) or as fresh tissue. Human eye globes are collected under the IRB protocol from Dr. Johanna Seddon (I-722). We are not involved in collecting the tissue, only dissecting it. Fixed tissue may be procured also from Dr. Seddon or from vendors such as the NDRI or from collaborators that have IRB approved protocols for tissue collection. All human tissue used is de-identified with exception of age, sex and retinal disease condition. We have obtained an exception from the IRB at UMASS for this work as only de-identified tissue is used. NHP eye globes may be obtained from our collaborators and will be either fixed upon arrival or in some instances fresh (unfixed). Tissue will be dissected and processed in the lab. Additionally, we may obtain blood samples from diseased and non-diseased patients with age-related macular degeneration. These blood samples were also collected under the IRB protocol of Dr. Seddon and will be used to identify auto-antibodies in diseased and non-diseased patients with age-related macular degeneration. NHPs used are generally healthy as they are kept in primate centers due to the work we do with our collaborators, where the effect of siRNA or viruses will be tested on eye health. Procedures in NHP will not

be done on our IACUC protocol but on the protocol of our collaborators. We only process the tissue. Human blood or eye donors are considered generally healthy. We will not process samples of individual who died from any infectious disease (not natural cause of death).

3. Work with cell lines: Work with cell lines of human, pig or mouse origine involves established cell lines that are commercially available. No primary cell line will be generated of human or pig origin. The most used cell lines in the lab include, Hek293, HTRET-RPE1 and ARPE-19. Cell line work may include rAAV vector production, standard transfection to test the effect of a gene in cell culture and confirm in vivo data or screening for efficient siRNA sequences. Finally, we also use a mouse hybridoma cell line that produces antibodies against a retinal protein.

IBC Discussion and Vote

Discussion:	Reviewer discussed whether the flow sorting should be held at BSL-2 or not because of the presence of AAV and lentivirus. A member of the committee brought up that there is no need for separate animal addenda for different species providing they are all receiving the same biohazards. B-virus SOP, medical alert cards and kit needed for NHP work.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	**BSL-2; BSL-2 Flow Sorting; ABSL-1 with Special Precautions; Administration to Animals using BSL-2 Precautions/ Sharps Safety**
NIH Guidelines:	III-D, III-E, III-F

9) Investigator: Ruscetti, M
Title: Senescence-Associated Secretory Phenotype (SASP) modulation of the tumor microenvironment as a therapeutic strategy for KRAS-driven tumors
IBC Registration: 769-25, Renewal
Reviewer: Giaya
Training Verification: Acceptable
Brief Summary: The goal of this research project is to identify the genetic mechanisms by which tumors evade the immune system in prostate and pancreatic cancers, and to target those mechanisms to make immunotherapy more effective.

- Determine the role of MYC in blocking the SASP and promoting pancreatic and prostate tumor suppression
- Test the impact of various genetic alterations on prostate cancer immune suppression
- Evaluate mRNA delivery of SASP cytokines as an immunotherapy in pancreatic cancer
- Evaluate LNP delivery of immune agonists as an immunotherapy in pancreatic cancer

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of this research project is to identify the genetic mechanisms by which tumors evade the immune system in prostate and pancreatic cancers, and to target those mechanisms to make immunotherapy more effective.

- Determine the role of MYC in blocking the SASP and promoting pancreatic and prostate tumor suppression
- Test the impact of various genetic alterations on prostate cancer immune suppression
- Evaluate mRNA delivery of SASP cytokines as an immunotherapy in pancreatic cancer
- Evaluate LNP delivery of immune agonists as an immunotherapy in pancreatic cancer

Experimental Approach: They propose to generate a number of mouse models of prostate and pancreatic cancer to test the impact of genetic and pharmacological interventions on immune and tumor responses. First, mouse prostate and pancreatic tumor cell and organoid lines that have been genetically modified in vitro to knockdown or express

oncogenes and fluorescent markers through transfection or transduction will be orthotopically transplanted into the prostate or pancreas of immunocompetent mouse strains. Second, mouse lung tumor cell lines that have been genetically modified in vitro to knockdown or express oncogenes and fluorescent markers through transfection or transduction will be transplanted intravenously into immunocompetent mouse strains. Third, genetically engineered mice will receive adeno-Cre administration intratracheally in order to induce lung tumor formation in KrasLSL-G12D/wt;Trp53flox/flox genetically engineered mice. Fourth, PT3 vectors containing oncogenes and PX330 vectors with CRISPR/Cas9 constructs targeting tumor suppressor genes will be electroporated into mouse prostates of adult mice to generate mouse prostate tumors de novo. Fifth, human pancreatic, lung, and prostate tumor cell lines will be transplanted orthotopically or by intravenous injection into immunodeficient Nude or NSG mice. Finally, patient-derived xenograft (PDX) pancreatic tumors will be orthotopically transplanted into NSG mice humanized with human PBMCs and NK cells to study tumor-immune interactions in the human setting.
Using these mouse models, we will test a number of novel immunotherapy agents for their ability to elicit anti-tumor immunity. First, prostate and pancreatic tumor-bearing mice will be administered lipid nanoparticles (LNPs) containing naturally occurring STING(Stimulator of Interferon Genes) and TLR4 agonists by intravenous injection to determine the effects on tumor growth, survival, and immune responses. Second, pancreatic tumor-bearing mice will be administered mRNAs encoding various cytokines or antigens as free mRNAs directly injected into the tumor or as LNP-encapsulated mRNAs administered by intravenous injection to determine the effects on tumor growth, survival, and immune responses. Finally, Diphtheria Toxin (DT) will be used to deplete regulatory T cells (Tregs) in FOXP3-DTR mice to understand the role of depleting Tregs in prostate tumor progression and response to therapy. IVIS, ultrasound, and micro-CT imaging will be performed on mice using machines available through the Animal Imaging Core to track changes in tumor growth. At the end of each experiment and following sacrifice, tumor and other tissues will be collected, and live cell flow sorting performed through the Flow Cytometry Core to isolate tumor and immune cells for downstream analysis.

IBC Discussion and Vote

Discussion:	The reviewer discussed that the protocol was well written, and experiments were well described. No major action items were noted only 1 single minor action item.
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

10) Investigator: Wang, Y
Title: Regulation of fatty acid and glucose metabolism by PPARs and co-regulators
IBC Registration: 217-25, Renewal
Reviewer: Wang
Training Verification: Acceptable
Brief Summary: Fatty acid and glucose metabolism must be properly regulated to maintain energy homeostasis. We have identified several genes that might play important roles in fatty acid and glucose metabolism. We plan to perform pharmacological and genetic studies to address the functions of these genes in cell culture and mice. We hope that our studies will help us to better understand the mechanism of fatty acid and glucose metabolism and the etiology of obesity and diabetes.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To study fatty acid and glucose metabolism by investigating specific genes that might play important roles. Perform pharmacological and genetic studies to address the functions of such genes in cell culture and mice.

Experimental Approach: Knockdown or overexpress genes 1) in cell culture using replication-defective retrovirus, lentivirus and adenovirus vectors, and 2) in mouse liver and adipose tissue using replication-defective adenovirus and adeno-associated virus. Target genes include Adissp, Pkn1, and Asra.

IBC Discussion and Vote

Discussion:	The reviewer discussed a single checkbox action item.
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

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

1) Upgrade attempt on Lenel system June 3 was unsuccessful.
2) Facilities update – HVAC and certification

VII. Information from the field (Senior Biosafety Officer)

1) Select Agent Inspection: In person inspection instead of remote. Emphasis on inspection of new/renovated facility on 9/21/2025
2) Currently working on relocating SAT

VIII. Other Business

Acknowledgement Items:

1) Ramanathan 908-24, **Expanded Access Protocol (EAP) for Subjects Receiving Idecabtagene Vicleucel that is Nonconforming for Commercial Release** Update BB2121-EAP-001
   ICF v4.0 and IB v11. Updated Names, Trials, Efficacy and PK data. No new safety data
2) Ramanathan 901-24, **Intermediate-Size Population Expanded Access Program (EAP) for Ciltacabtagene autoleucel (cilta-cel) Out-of-Specification (OOS) in patients with Multiple Myeloma United States EAP** Update Janssen on
   ICF v7.0 and IB v10. Updated Trials, Efficacy and PK data. New safety data describing adverse effects in greater detail (esp. CRS, now including IEC-HS as a separate entity; IEC-enterocolitis).

Section 1: Intro Shortened, **Section 4:** Updated overview of ongoing and completed clinical studies, pharmacokinetics, pharmacodynamics, efficacy, safety and immunogenicity data & post marketing cilta-cel exposure data, **Section 5:** Updated precautions and warning information, **Section 6:** Updated table

Adjourned at 2:04pm