IBC Meeting Minutes
May 21, 2026 (Thursday) at 11:00 A.M.
via Zoom Conference Bridge

IBC members present:

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

Non-members present: Patrice Rando (IACUC/IBC Office)
*RK- left at 11:53
**ER- left at 12:59
***CS- left at 12:47

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 April 16, 2026, Meeting Minutes**

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

Past incidents that remain open:

1) 12/08/2025: Cut noted after cleaning BSC. Low likelihood HIV exposure; PEP given; serology planned 060826.

Recent incidents:

1) N/A

III. Protocols Reviewed Administratively

1) Investigator: Grigorieff, N
Title: **Entry of rhesus rotavirus into mammalian cells**
IBC Registration: **I-808-26, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The goal of this project is to add high resolution details to Rhesus Rotavirus (Reoviridae Family) infection mechanism(s) in cellular context. Viral fusion, internalization and/or replication will be studied by in situ cryo-electron microscopy. Mammailian Cells (Cercopithecus aethiops (Green Monkey)) will be infected with virus, cryofixed or lysed and imaged at UMass Chan Cryo-EM Facility.

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

2) Investigator: Karlsson, E
Title: 1) Total nucleic acids extraction from ticks for the detection of tick-borne bacterial and other pathogens, 2) safe handling of biological specimens from wolf-dog hybrids, and 3) total nucleic acid extraction from domestic and wild canid and felid samples for sequencing and genetic analysis

IBC Registration: **I-637-26, Renewal**
Training Verification: Acceptable pending completion of PI training / Acceptable
Brief Summary: 1) Total nucleic acids extraction from ticks: Ticks are vectors for a wide range of bacterial, viral, and protozoan pathogens that impact human and animal health. Understanding the genetic diversity of both ticks and their associated pathogens is important for improving surveillance and epidemiological inference.

Goals/objectives:
•Characterize genetic diversity of ticks and associated pathogens
•Identify host–pathogen interactions and pathogen prevalence
•Use sequencing-based approaches to study pathogen evolution and transmission dynamics

2) Biological specimens from wolf-dog hybrids: Wolf-dog hybrids represent a unique population for studying the genetic basis of behavior and domestication due to their mixed ancestry and phenotypic diversity. These systems provide insight into genotype–phenotype relationships relevant to both animal and human biology.

Goals/objectives:
•Identify genetic variants associated with behavior and domestication traits
•Analyze genotype–phenotype relationships in hybrid populations
•Investigate population structure and evolutionary history

3) Genomic analysis of domestic and wild canid and felid specimens: Domestic animals (dogs and cats) and wild canids (e.g., wolves, coyotes, foxes, and related species) provide important systems for studying genetic variation underlying disease susceptibility, population structure, and evolutionary history. Biological specimens from these animals enable comparative genomic analyses across domesticated and wild populations.

Goals/objectives:
•Extract and sequence nucleic acids from blood, saliva, fur/hair, and tissue samples
•Characterize genetic variation across domestic and wild animal populations
•Support studies of disease susceptibility, population structure, and comparative genomics

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

IV. Protocols to Discuss

1) Investigator: Almeida, S
Title: Exploring molecular pathogenic pathways in Frontotemporal dementia
IBC Registration: **I-670-26, Renewal**
Training Verification: Acceptable
Brief Summary: To use human cell-based models to investigate the molecular mechanisms underlying Frontotemporal Dementia and related disorders.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To use human cell-based models to investigate the molecular mechanisms underlying Frontotemporal Dementia and related disorders.

Experimental Approach: They primarily use human cell lines, including induced pluripotent stem cells (iPSCs), which are differentiated into various brain cell types such as endothelial cells, astrocytes, pericytes, oligodendrocytes, and neurons. They perform a range of protein-, RNA-, and enzyme activity-based assays. Some experiments involve genetic manipulation through transfection or lentiviral transduction.

IBC Discussion and Vote

Discussion: The reviewer discussed that the protocol was missing information and the previous review wasn't available for further clarification. The reviewer highlighted the use of high-titer lentiviral particles and the proposed risk mitigation measures, including the BSL-2 containment and RCV testing. The mentioned minor action items, such as clarifying the use of PPE and the transport of biologicals. Another member of the IBC discussed that it is unclear how the induced pluripotent stem cells and lymphoblastoid cell lines were derived which requires clarification.

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

BSL/ABSL: **BSL-2**

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

2) Investigator: Donahue, K

Title: Virus-Mediated Gene Transfer to Porcine Hearts

IBC Registration: **I-556-24, Amendment**

Training Verification: Acceptable pending completion of PI training

Brief Summary: Our hypothesis posits that the genetic modification of cardiac electrical function through lentivirus, adenovirus, or adeno-associated virus-mediated gene transfer has the potential to eradicate cardiac arrhythmias. In the developed world, abnormal heart rhythm disorders claim more lives than any other cause. Existing therapies face limitations that extend beyond the scope of a brief explanation. Our aim is to pioneer gene therapy as an innovative approach to address and eliminate these rhythm disorders, ultimately enhancing the quality of life for individuals affected. The overall objective of this study is to assess efficacy of RNA interference of calcium/calmodulin-dependent protein kinase-II (CaMKII) for prevention of sustained atrial fibrillation (AF). To address this objective, we assess two questions: Does Alnylam's test article suppress atrial expression of CaMKII, and does this suppression prevent sustained AF? We test both questions in a porcine model of burst pacing induced AF.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overall aim of the registration is to pioneer gene therapy to modify cardiac electrical function for the treatment and eradication of cardiac arrhythmias. This amendment seeks to further assess efficacy of RNA interference of calcium/calmodulin-dependent protein kinase-II (CaMKII) for prevention of sustained atrial fibrillation (AF).

Experimental Approach: Gene transfer is being performed using Adenovirus, AAV, and lentiviral vectors in vivo in a pig model. This amendment is to add siRNA duplexes in vivo.

IBC Discussion and Vote

Discussion: The reviewer discussed that the Donahue lab is already approved for gene transfer using adenovirus, AAV, and lentiviral vectors for gene therapy in vivo, and this amendment is to add duplex siRNA against CaMKII in vivo. The reviewer identified the transgenic core will generate the transgenic mice, and the lab will handle the tissue harvesting. A separate Animal Addendum is needed for swine siRNA experiments.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; ABSL-1**
NIH Guidelines: N/A

3) Investigator: Emery, P
Title: Emery Lab Recombinant DNA Protocol
IBC Registration: **I-801-26, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: Studying circadian rhythms and sleep in Drosophila at the molecular level, using various molecular approaches

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Studying circadian rhythms and sleep in Drosophila at the molecular level, using various molecular approaches

Experimental Approach: Simple plasmids and oligos will be used for basic molecular approaches such as cloning, transfection in insect cells, quantitative PCR

IBC Discussion and Vote

Discussion: The reviewer discussed there was a lot of information missing from this renewal registration and compared the two protocols submitted in 2021. Information that was highlighted in the final edition in 2021 registration was missing from the submitted 2026 renewal. The reviewer mentioned that genetically modified Drosophila strains will be used to allow the lab to overexpress or down regulate circadian and sleep genes that manipulate the activity of circadian and sleep neurons. These strains are used to monitor circadian behaviors, such as locomotor activity and sleep, using behavior or molecular and imaging approaches, e.g. Luciferase report reporters and immunohistochemistry. A more in depth description of the experimental plan in section A2 was discussed.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-1**
NIH Guidelines: III-D, III-E, III-F

4) Investigator: Luzuriaga, K
Title: Studies of HIV treatment, Viral Immunity, and HIV pathogenesis
IBC Registration: **I-210-26, Renewal**
Training Verification: Acceptable
Brief Summary: The laboratory is directed by Dr. Katherine Luzuriaga. There are three broad areas of research: 1) HIV treatment, 2) viral immunity and 3) viral pathogenesis in humans. Research has

focused on Epstein Barr virus (EBV) and human immunodeficiency virus (HIV-1). In addition, past projects have included cytomegalovirus and SARS-CoV2. (No current work with SARS-CoV2.)

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Three broad areas of research: 1) HIV treatment, 2) viral immunity and 3) viral pathogenesis in humans. Research has focused on Epstein Barr virus (EBV) and human immunodeficiency virus (HIV-1). Past projects have included cytomegalovirus and SARS-CoV2. There is no current work with SARS-CoV2.

Experimental Approach: Previously CLIA certified for assays including lymphocyte phenotype analysis, quantitative HIV-1 RNA & qualitative DNA measurements, virus culture, and transport of infectious materials. The Laboratory still maintains all GCLP laboratory guidelines as previously outlined in CLIA SOP compliance.
Routine lab activities include: collection and processing of EBV- and HIV-infected and uninfected patient and donor samples for repository, flow cytometry (including unfixed, live cell sorting), HIV-1 stock preparation, qualitative and quantitative virology (EBV and HIV-1). The lab has an extensive repository of samples from past studies of EBV and HIV-1 infected individuals collected under a program project and as part of the UMMS Center for AIDS Research. The lab routinely processes samples known to contain high titers of HIV-1.
Project specific lab activities include:
Well-controlled HIV-1 replication in children: Virus-specific immune responses in children with well- controlled viral replication. Neutralizing antibodies are measured against panels of pseudotyped, Env- defective HIV-1. Cellular immunity is measured using flow cytometry assays to detect intracellular cytokine production. These experiments often make use of Staphylococcal enterotoxin B (SEB) (exempt quantities) as a positive control. Viral reservoirs are measured in some cases using assays that may involve culture of virus.
Maternal to child transmission: Cloning and sequencing of viruses that have been transmitted from mother to child. Tropism and virus entry are measured using pseudotyped viruses in studies of maternal to child transmission. Infectious molecular clones of HIV-1 are being generated to measure differences in a spreading infection. Standard molecular clones of HIV-1 (NL4-3; JR-CSF; JR-FL; ADA; etc) may be used for the "backbone" into which the env gene of mother and child viruses are substituted.
Epstein Barr Virus virology and immunology: Samples from UMass Amherst students were collected for sero-surveillance studies to detect and characterize new infections with EBV. Samples were also collected from students presenting with acute infectious mononucleosis (AIM) and then followed to convalescence. Virologic studies include EBV quantitation in blood and saliva, and full-length genome sequencing using "next generation" sequencing. Immunologic studies include characterization of neutralizing antibodies in AIM and convalescence. These studies make use of lab strains of EBV (Akata and B.958), including recombinant versions that express GFP (in a BAC). Cellular immunity to characterize CD8+ T cell responses by T cell receptor (TCR) usage and avidity, and gene and protein expression. In a number of these experiments, flow sorting of live, unfixed CD8+ T cell subsets and single cells is required. Studies will make use of lentiviral vectors to expressed cloned TCR to measure avidity and functionality in cell lines.
Using vaccinia vectors expressing viral proteins to measure virus-specific responses, and B-LCL as targets for CTL studies. Parental Vaccinia strains from which recombinants were derived are all attenuated vaccine strains (NYCBH, Wyeth, MVA). Aldrithiol-2 inactivated (non-infectious) HIV-1 particles have been used in some experiments to measure virus-specific responses. CMV immunovirology. Currently Vaccinia is in storage.
HIV-1 virology in collaboration with UMMS investigators working with humanized mice. Currently, there are no in vivo experiments.
Flow core analysis & sorting of fixed & unfixed, transduced Jurkat or human PBMCs to characterize CD4 T cells & macrophages and isolate cells that have stably integrated the TCR- containing lentivirial genome and express similar protein expression level of TCRs.

Flow core sorting of unfixed, untested human PBMC to isolate CD4 T cells; sorting at BSL-2 enhanced.

- Flow sorting of unfixed, human cells for analyses of EBV-specific CD8+ T cell responses (TCR avidity measurements, single-cell sequencing and cloning of TCR, and gene expression).
- Flow sorting of resting memory CD4+ T cells for studies of viral reservoirs in HIV-infected children.

IBC Discussion and Vote

Discussion: The reviewer discussed this is a 5-year renewal and was last approved in 2021 at BSL-2+; BSL-2 Enhanced Flow Sorting. The renewal contained highlighted text to clearly identify what is being newly added since the prior registration approval. The broad areas of research include studies in HIV treatment, viral immunity, and viral pathogenesis in humans. The lab measures cellular immunity by flow cytometry, looking at cytokine production and surface markers. Their work sometimes involves cloning and sequencing of viruses that are transmitted from mother to child, testing tropism in assays using pseudo typed virus vectors. The reviewer noted that the IBC discussed last meeting, the need to pay attention to the different strains of viruses, Vaccinia being one of those. The viral vectors that have been in storage are attenuated strains. The lab has modified Vaccinia Ankarra and some canarypox/fowlpox viruses that are being stored.

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

BSL/ABSL: **BSL-2+; BSL-2 Enhanced Flow Sorting**

NIH Guidelines: III-D; III-F

5) Investigator: Mao, J
Title: Hedgehog Signaling in organogenesis and tumorigenesis
IBC Registration: **I-370-23, Amendment**
Training Verification: Acceptable pending completion of PI training
Brief Summary: Lentiviral vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be transduced via replication deficient virus to human cancer cell lines, such as PANC1. Cells will be selected for transduction using puromycin or blasticidin, allowed to grow, and then subjected to viability assays. These stably selected cells will also be injected into immunocompromised mice to examine the role of these genes in xenograft tumor formation and growth, as well as molecular analysis of cell signaling pathway status. AAV vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be IP injected to infect the liver and asses the effect on organ growth. DNA plasmids expressing the components of Hedgehog and Hippo signaling will administrated through hydrodynamic tail vein injection to induce liver overgrowth, and antisense oligonucleotides will be administrated through IV or SC to assess their effect on cell growth. We will use Transgenic core to generate a transgenic mouse strain that allows conditional expression of TAZ, a transcriptional co-regulator of Hippo signaling.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: to study the roles of Hedgehog signaling pathways and its functional interactions with other pathways during organogenesis and tumorigenesis

Experimental Approach: Lentiviral vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be transduced via replication deficient virus to human cancer cell lines, such as PANC1. Cells will be selected for transduction using puromycin or blasticidin, allowed to grow, and then subjected to viability assays. These stably selected cells will also be injected into immunocompromised mice to examine the role of

these genes in xenograft tumor formation and growth, as well as molecular analysis of cell signaling pathway status. AAV vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be IP injected to infect the liver and asses the effect on organ growth. We will use Transgenic core to generate a transgenic mouse strain that allows conditional expression of TAZ, a transcriptional co-regulator of Hippo signaling.
Newly added: DNA plasmids expressing the components of Hedgehog and Hippo signaling will administrated through hydrodynamic tail vein injection to induce liver overgrowth, and antisense oligonucleotides will be administrated through IV or SC to assess their effect on cell growth.

IBC Discussion and Vote

Discussion: The reviewer discussed this is an amendment adding experiments that involve hydro and hydrodynamic tail vein injections of DNA plasmids expressing the components of hedgehog and hippo signaling, and the administration of antisense oligonucleotides, either IV or subcutaneous, to measure their effect on cell growth. The lab is working with human cancer cells, like pancreatic tumor cells and xenograft tumor formation in animals. The lab is also using viral vectors, including AAV vectors and lentivirus vectors. The antisense oligos the lab has listed in the registration are all short and none meet the criteria for IBC oversight.

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-F

6) Investigator: Moreno-Leon, L (Prev. Khanna)
Title: Pharmacology and mechanism of action of oligonucleotides-based therapies for retinal degeneration

IBC Registration: **I-449-25, Renewal**

Training Verification: Acceptable

Brief Summary: The project aims to investigate the pharmacokinetics of an ocular therapy administered via injection to the eye in rabbits, focusing on the absorption, distribution, metabolism, and excretion of the drug within the ocular tissues. By analyzing the drug's behavior over time, we seek to optimize its therapeutic efficacy and safety for potential clinical applications in treating ocular conditions.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: to study the roles of Hedgehog signaling pathways and its functional interactions with other pathways during organogenesis and tumorigenesis

Experimental Approach: Lentiviral vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be transduced via replication deficient virus to human cancer cell lines, such as PANC1. Cells will be selected for transduction using puromycin or blasticidin, allowed to grow, and then subjected to viability assays. These stably selected cells will also be injected into immunocompromised mice to examine the role of these genes in xenograft tumor formation and growth, as well as molecular analysis of cell signaling pathway status. AAV vectors which allow gene silencing or overexpression of the components of Hedgehog and Hippo signaling will be IP injected to infect the liver and asses the effect on organ growth. We will use Transgenic core to generate a transgenic mouse strain that allows conditional expression of TAZ, a transcriptional co-regulator of Hippo signaling.

Newly added: DNA plasmids expressing the components of Hedgehog and Hippo signaling will administrated through hydrodynamic tail vein injection to induce liver overgrowth, and antisense oligonucleotides will be administrated through IV or SC to assess their effect on cell growth.

IBC Discussion and Vote

Discussion: The reviewer discussed this registration was reviewed in December 2025 as a renewal registration; however, some action items prompted a revision. The submitted revision had additional information, new agents and a different title. The M2D2 project was previously submitted by Dr. Khanna who has now been replaced with Dr. Moreno-Leon as the new Principal Investigator. When addressing the original action items, the lab added ocular therapy with vascular progenitor cells as potential therapy for wet acute macular degeneration and now includes the use of vascular progenitor cells. The reviewer highlights the need for the lab to describe how the iPSC were derived and to describe how the AAV vector(s) are used to modify the MHC molecules.

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

BSL/ABSL: **BSL-2; ABSL-1 + BBP; Administration to Animals using BSL-2 Precautions/ Sharps Safety**

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

7) Investigator: Schrader, C
Title: Regulation of Antibody Diversity
IBC Registration: **I-671-26, Renewal**
Training Verification: Acceptable
Brief Summary: To understand the mechanism of action of DNA repair proteins during antibody class switch recombination (CSR) and somatic hypermutation (SHM). The enzyme initiating these processes is activation-induced cytidine deaminase (AID), and repair of AID lesions involves various mismatch repair and base excision repair proteins, including uracil DNA glycosylase (UNG) and AP endonucleases 1 and 2 (APE1 and APE2). Repair of DNA damage by AID is error-prone, causing DNA breaks and mutations that are necessary for CSR and SHM, but can also lead to lymphoma. Our goal is to understand the balance between accurate and error-prone DNA repair in B cells.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The lab seeks to understand the mechanisms of action for DNA repair proteins during antibody class switch recombination (CSR) and somatic hypermutation (SHM). The enzyme initiating these processes is activation-induced cytidine deaminase (AID). The repair of AID-mediated lesions involves various mismatch repair and base excision repair proteins, including uracil DNA glycosylase (UNG) and AP endonucleases 1 and 2 (APE1 and APE2). Repair of DNA damage caused by AID is error-prone, resulting in DNA breaks and mutations that are necessary for CSR and SHM, but can also lead to lymphoma. The lab's goal is to understand the balance between accurate and error-prone DNA repair in B cells.

Experimental Approach: Full-length or mutated forms of AID, APE1, and APE2 will be expressed in primary mouse B cells by retroviral vectors to study antibody isotype switching and somatic hypermutation using flow cytometry and DNA sequencing. Lipopolysaccharide (LPS) will be used to stimulate mouse primary B cells to divide, induce antibody class switching, and permit infection via retrovirus.
B cells will be obtained from previously generated knockout or transgenic mouse strains, or obtained from collaborators.

APE1-Tg mice are being created by the Transgenic Animal Core Facility. The model will express APE1 from the Rosa26 locus when crossed to other mouse lines expressing Cre recombinase. A synthetic DNA transgene containing mCherry and murine Apex1 exons, with loxP STOP cassette upstream of the exons to prevent expression in the absence of Cre, have been cloned into an AAV vector by the transgenic core. Founders were created and are in the final stages of testing in the transgenic core.
Modified antisense oligonucleotides (ASOs) may be used to knock-down APE1 in primary mouse B cells, in vitro.
Human cell lines are in storage and not currently being used, except for the Phoenix E packaging cell line.

IBC Discussion and Vote

Discussion: The reviewer noted this is a 5-year renewal and the submission is relatively straightforward. The reviewer highlighted if the lab is going to be housing transgenic animals and that the IBC should list this with the inclusion of ABSL-1 in the registration.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2; BSL-2 Flow Sorting; ABSL-1**
NIH Guidelines: III-E, III-F

8) Investigator: Shim, J
Title: Understanding key regulators in skeletal homeostasis and development
IBC Registration: **I-678-26, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: We focus on understanding molecular and genetic pathways controlling bone cells and immune cells in chronic inflammatory and skeletal disorders. This will advance towards harnessing the mechanisms that we studied for therapeutic benefit in humans, identify new genes and mechanisms controlling immune and skeleton cross-talk, and develop novel genetic medicine to treat these diseases using recombinant adeno-associated virus (rAAV) or short interfering RNA (siRNA).
1. Our goal is to develop novel therapeutics to treat prevalent skeletal diseases (osteoporosis, fracture, critical-sized bone defects, and trauma-induced heterotopic ossification (HO) using rAAV and/or siRNA.
2. Our goal is to develop novel therapeutics to treat rare skeletal diseases (Fibrodysplasia Ossificans Progressiva (FOP), Osteogenesis Imperfecta (OI) using rAAV and/or siRNA.
3. Our goal is to develop novel therapeutics to treat sepsis, osteoarthritis, spondylarthritis, rheumatoid arthritis, and autoinflammatory diseases using rAAV and/or siRNA.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The objective of this project is to understand the molecular and genetic pathways controlling bone physiology in chronic inflammatory and skeletal disorders. This will identify new genes and mechanisms that control immune–skeletal cross-talk, develop novel genetic medicines using recombinant adeno-associated virus (rAAV) or short interfering RNA (siRNA) to treat these diseases.

Experimental Approach: The studies are aimed at describing how specific genes regulate bone, cartilage, inflammatory, and skeletal disease processes using both cultured cells and genetically modified mice. In vitro, human and mouse stem cells, osteoblasts, osteoclasts, chondrocytes, and disease-specific induced pluripotent stem cells (including cells from patients with Fibrodysplasia Ossificans Progressiva) will be used to overexpress, silence, or edit genes through lentiviral vectors, recombinant adeno-associated viruses (rAAV), siRNA, and CRISPR/Cas9 systems, then assess cellular functions and protein interactions. In vivo, mouse models with tissue-specific or inducible gene deletions will be generated by rAAVs or siRNAs.

IBC Discussion and Vote

Discussion: The reviewer discussed that this submission is a 5-year renewal and the lab studies different skeletal diseases, including osteoporosis, fractures, critical size bone defects, trauma-induced heterotopic ossification as well as rare skeletal diseases, including FOP and osteogenesis imperfecta. The lab aims to address inflammatory skeletal issues, including sepsis, osteoarthritis, spondyloarthritis, rheumatoid arthritis, and auto-inflammatory diseases. The lab is also going to collaborate with the Alterman Laboratory in which that'll provide siRNAs targeting mouse and/or human bone cell regulators, inflammatory regulators, and cartilage regulators. The reviewer highlighted the lab will use flow cytometry of cells transduced with siRNA or AAV vectors, and sorting of unfixed cells isolated from skeletal muscle, femoral tissues following siRNA or AAV treatments using the flow core facilities.

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**

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

9) Investigator: Watts, J

Title: Development of Oligonucleotide Therapeutics

IBC Registration: **I-656-26, Renewal**

Training Verification: Acceptable

Brief Summary: Our lab's work centers around the use of chemically modified oligonucleotides for gene silencing, gene activation, and gene editing:

- We seek to use modified oligonucleotides to silence and activate gene expression in cells through the antisense and RNA interference pathways.
- We are developing modified guides and HDR donors to improve the efficacy and precision of CRISPR-based genome editing in cells and in animals.
- We need to use viral vectors both to deliver effectors of genome editing in vivo, and to induce trans differentiation into different cell types (for example, fibroblasts into neurons) to create systems to test our agents.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The lab work centers around the use of chemically modified oligonucleotides for gene silencing, gene activation, and gene editing.

Experimental Approach: (1) use modified oligonucleotides to silence and activate gene expression in cells through the antisense and RNA interference pathways (2) developing modified guides and HDR donors to improve the efficacy and precision of CRISPR-based genome editing in cells and in animals; (3) use viral vectors both to deliver effectors of genome editing in vivo, and to induce transdifferentiation into different cell types (for example, fibroblasts into neurons) to create systems to test agents.

IBC Discussion and Vote

Discussion: The reviewer discussed this is a 5-year renewal and the registration is straightforward. The reviewer highlighted the registration describing drug delivery into mice and/or rats however, the animal addendum is only written for mice specifically making it unclear if rat work is still being done. Clarification is required as there is no mention of what drugs being delivered are.

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-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) N/A

VII. Other Business

Acknowledgement Items:

1) **Caricchio 878-23: A Phase 1 Open-Label, Multicenter Study of KYV-101, an Autologous Fully-Human Anti-CD19 Chimeric Antigen Receptor T-Cell (CD19 CAR T) Therapy, in Subjects with Refractory Lupus Nephritis**
   Kyverna KYV101-001 IB v9.0 for SLE
   There is no change to the KYV-101 product or to the procedures used to administer the product. Only changes made to the Investigator's Brochure.
2) **Caricchio 888-24: Kyverna NKX019-102 (Ntrust-1) A Phase 1/2 Study of NKX019, a CD19 Chimeric Antigen Receptor Natural Killer (CAR NK) Cell Therapy, in Subjects with Autoimmune Disease**. Amendment 5.0 (September, 2025). Lower doses may be used (optimization); Re-treatment may be offered; increased enrollment;

Adjourned at 1:10pm