

IBC Meeting Minutes
June 18, 2026 (Thursday) at 11:00 A.M.
via Zoom Conference Bridge

IBC members present:

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

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

*RML- left at 11:40

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 May 21, 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:

- 2) 06/10/2026: Pipette laceration. MDA-MB-231 (human breast cancer) cells expressing a recombinant IRS2 gene that is stably integrated into the genome; introduced by transduction with replication defective lentivirus vector

III. Protocols Reviewed Administratively

- 1) Investigator: Caricchio, R
Title: CLN-978-SL-101: A Phase 1b, Open-Label, Pilot Study Of CLN-978 For The Treatment Of Moderate To Severe Systemic Lupus Erythematosus (SLE)
IBC Registration: I- 941-26, New
Training Verification: **Acceptable**
Brief Summary: This is an exploratory, Phase 1b, open-label study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and effect on disease activity of subcutaneously (SC) administered CLN-978 for the treatment of active Systemic Lupus Erythematosus (SLE). Primary Objective: To evaluate the safety and tolerability of CLN-978 in patients with SLE
Secondary Objectives: To evaluate pharmacokinetics (PK) of CLN-978 in patients with SLE, To evaluate the immunogenicity of CLN-978 in patients with SLE, and To evaluate PD-related biomarkers following CLN-978 in patients with SLE
BSL/ABSL: BSL-2
NIH Guidelines: N/A

- 2) Investigator: Kelliher, M
 Title: The role of Rip1 in TNF transduction and Mechanism(s) of Tal1/scl mediated Leukemogenesis
IBC Registration: I-267-25, Amendment
 Training Verification: Acceptable
 Brief Summary: U2AF1 mutation S34F is commonly detected in patients with MDS which leads to bone marrow failure (BMF). We will elucidate the role of U2AF1 mutation in triggering programmed cell death by using MLL-AF9 leukemia cells carrying U2AF1 S34F mutation. MLL-AF9 cell lines require in vivo implantation for line maintenance and expansion therefore we will implant these cells into mice intravenously or retroorbitally to propagate the lines and use for ex vivo analyses of programmed cell death pathways. These proposed experiments pose low risk to research personnel
BSL/ABSL: BSL-2; ABSL-1+BBP
NIH Guidelines: N/A
- 3) Investigator: Miller, S
 Title: Improvement of Bioluminescence Imaging
IBC Registration: I-591-24, Amendment
 Training Verification: Acceptable
 Brief Summary: Adding animal work back into registration that was previously removed during renewal.
BSL/ABSL: BSL-2; BSL-2 Flow Sorting; ABSL-1 with Special Precautions
NIH Guidelines: III-D, III-E, III-F
- 4) Investigator: Singh, J
 Title: FLOW CYTOMETRY OF EX-VIVO DRUG TREATED WHOLE BLOOD TO STUDY INHIBITION OF T-CELL SIGNALING
IBC Registration: I-798-26, Renewal
 Training Verification: Acceptable pending completion of PI training
 Brief Summary: STUDY THE EFFECTIVENESS OF A JAK3 SMALL MOLECULE KINASE INHIBITOR TO BLOCK T-CELL SIGNALING EX-VIVO IN HUMAN BLOOD
BSL/ABSL: BSL-2
NIH Guidelines: N/A

IV. Protocols to Discuss

- 1) Investigator: Levitz, S
 Title: The Immune Response to Fungi
IBC Registration: I-314-26, Renewal
 Training Verification: Acceptable
 Brief Summary: The Levitz Lab studies host-pathogen interactions in fungal infection. Our goals: 1. To better understand how the immune system responds to fungal infections and the virulence factors that fungi employ to evade immune responses. 2. To develop preventive vaccines and effective therapies for medical mycoses.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The primary goal of this registration is to study host–pathogen interactions during fungal infections. The project aims to improve the understanding of how the immune system responds to fungal pathogens and to identify the virulence factors that fungi use to evade or manipulate host immune defenses. These findings will contribute to the development of preventive vaccines and more effective therapeutic strategies for treating medical mycoses

Experimental Approach: The fungal species *Cryptococcus*, *Aspergillus*, and *Candida* species (including *C. auris*) are proposed for study. Depending upon the experiment, a single fungal colony or bulk harvesting will be performed. The fungi will be cultured on fungal culture medium such as Sabouraud dextrose agar or yeast nitrogen broth. Following adjustment to desired, concentration. Fungi will be used to infect mammalian cells or mice. In vitro work is performed at BSL-2 with live fungi. Animal work with live fungi is performed exclusively in the A-level animal facility. Flow cytometry experiments will use only fixed (1% paraformaldehyde) organisms.

Bacterial species: Standard laboratory strains of *E. coli* are grown and transformed. Work includes use of plasmids and recombinant proteins. Other potential infectious sources: Human blood samples, not known to be infected with pathogens but handled using universal precautions under BSL-2 conditions.

Flow sorting of unfixed, live mouse cells from infected animals (done at BSL-2 enhanced). Some experiments involve sorting of fixed cells from infected animals (done at BSL-2).

IBC Discussion and Vote

Discussion:	The reviewer mentions this is a 5-year renewal focusing on the study of host-pathogen interactions during fungal infections. The reviewer highlighted the need for clarification on whether the fungi are mutated and how human blood is used. The reviewer also discussed the need for medical alert cards for <i>Candida auris</i> and the risk group classification for <i>Aspergillus</i> .
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

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|--------------------------|--|
| 2) Investigator: | Rogaev, E |
| Title: | Molecular genetic mechanisms of neuropsychiatric diseases |
| IBC Registration: | I-286-26, Renewal |
| Training Verification: | Acceptable pending completion of PI training |
| Brief Summary: | The goal of the project is to uncover the key neuronal-adaptive immune-genomic axes that drive pathogenesis of human psychiatric diseases. We will identify disease-associated T-cell subtypes and their unique TCR clonotype signatures by integrating transcriptomics and TCR repertoire profiling in Alzheimer's disease (AD) transgenic mouse tissues, as well as in a large cohort of human AD brain specimens. Furthermore, we will elucidate the neuroimmune epigenetic and genetic landscapes in the brain, with a particular focus on MHC gene regulation, the impact of individual HLA haplotypes, and how B-cell and T-cell depletion shapes the neuronal epigenome in the context of AD. We will study genetic variations, chromatin modifications and gene/protein expression profiles in mouse cells lines, mouse tissues, human tissues and human blood samples. No agents will be introduced into live animals |

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of the project is to uncover the key neuronal-adaptive immune-genomic axes that drive pathogenesis of human psychiatric diseases. The researchers seek to identify disease-associated T-cell subtypes and their unique TCR clonotype signatures. Furthermore, they will elucidate the neuroimmune epigenetic and genetic landscapes in the brain, with a particular focus on MHC gene regulation.

Experimental Approach: Experimental approach includes:

- Transfection of mammalian cell cultures with plasmid constructs.

- Extraction of nuclei, DNA, RNA, and proteins from mouse cell cultures, transgenic and wild-type mouse tissues, human tissues, and blood. Nuclei isolated from brain tissues will be sorted using the Fluorescence-Activated Cell Sorting (FACS) Facility at UMass Chan Medical School. Methods will include PCR, real-time PCR, genomic DNA sequencing (gDNA-seq), ChIP-seq, RNA-seq, ATAC-seq, deep-sequencing library preparation, protein assays, and Western blotting.
- Fixation of mouse tissues and cells with paraformaldehyde (PFA) for immunohistochemistry and in situ hybridization analyses. Immunohistochemical staining and quantification of amyloid- β (A β) plaques and immune cells will be performed.

IBC Discussion and Vote

Discussion: The reviewer discussed that this is a 5-year renewal and highlighted the focus on identifying disease-associated T cell subtypes and their unique TCR clonotype signatures. Reviewer identified the need for clarification on the in vivo containment level and the use of human blood and blood products.

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

BSL/ABSL: **BSL-2; BSL-2 Enhanced Flow Sorting; ABSL-1**

NIH Guidelines: III-E, III-F

3) **Investigator:** Bazzone, L (Prev. Kurt-Jones)
Title: Characterizing the innate immune responses to pathogens
IBC Registration: **I-304-26, Renewal**
Training Verification: **Acceptable**
Brief Summary: The goal of the study is to characterize and define the innate immune response to viral pathogens.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of the study is to characterize and define the innate immune response to viral pathogens.

Experimental Approach: In vivo experiments will be performed in wild-type and knockout mice to characterize the role of key innate immune genes in the response to pathogens

IBC Discussion and Vote

Discussion: The reviewer discussed this is a 5-year renewal and PI transfer. The reviewer highlighted the use of infectious agents, toxins like lipopolysaccharides and various viruses in the study. The reviewer identified the need for clarification on the use of human cells, blood, and blood products and additional experimental detail. Additional information is needed regarding stewardship and use of previously listed infectious agents.

Meeting Decision: Vote to approve upon completion of action items. A discussion for the need for accurate descriptions of the infectious agents and their attenuation.

BSL/ABSL: **BSL-2; ABSL-2**

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

4) **Investigator:** Bindal, P
Title: A Phase 3, Randomized, Open-Label, Multicenter Study Evaluating the Efficacy of KITE-753 Versus Axicabtagene Ciloleucel in Participants with Relapsed or Refractory Large B-Cell Lymphoma After First-Line Therapy

IBC Registration: I-940-26, New

Training Verification: Acceptable pending completion of PI training

Brief Summary: Primarily, this study will seek to evaluate the efficacy of KITE-753 versus axicabtagene ciloleucel (axi-cel) pertaining to “event-free survival” (EFS) and 6-month complete response rate (6-month CRR). EFS is the time from randomization until the earliest occurrence of death (for any reason), disease progression, or initiation of any non-protocol specified anti-lymphoma therapy for the treatment of residual disease (including stable disease and partial response). 6-month CRR is the proportion of patients who have achieved a complete response at Month 6.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To evaluate the efficacy of KITE-753 versus axicabtagene ciloleucel (axi-cel) pertaining to “event-free survival” (EFS) and 6-month complete response rate (6-month CRR) in the treatment of relapsed or refractory Large B-Cell Lymphoma.

Experimental Approach: KITE-753 is an investigational, autologous chimeric antigen receptor (CAR) T-cell therapy designed for the treatment of B cell malignancies. The product consists of a patient’s own T cells that are genetically modified ex vivo using a third generation, self-inactivating (SIN) lentiviral vector (LVV) to express a bicistronic CAR targeting CD19 and CD20, antigens commonly expressed on malignant B cells. Extensive clinical experience with SIN lentiviral vectors in CAR-T products supports the safety of this vector system.

Axicabtagene ciloleucel (Axi-cel) is a chimeric antigen receptor (CAR) T-cell therapy directed against the B-cell specific cell surface marker CD19 and is commercially approved for the treatment of adult patients with relapsed/refractory (r/r) LBCL. Axi-cel is produced by genetically modifying a patient’s own T cells ex vivo using a retroviral vector (RVV) to introduce a gene encoding a CD19-specific chimeric antigen receptor. Expression of the CAR enables engineered T cell to recognize and eliminate CD19-positive malignant B cells. Extensive clinical and commercial experience with RVV in CAR-T products supports the safety of this vector system. RVV is not handled at the UMass clinical site.

Vectors used (manufacturing intermediates; not handled at UMass clinical site):

- Kite-753: KITE-CD19/20(pCDL8499)-LVV: Key mutations design features include the self-inactivating (SIN) motif (enhancer regions in U3 LTR region are removed), removal of accessory genes (Δ Env, Δ tat, Δ vpr, Δ vpu, Δ nef, Δ vif). Gag and Pol are expressed in trans from separate plasmids. LVV is pseudotyped with the glycoprotein derived from the vesicular stomatitis virus. Encodes the FMC63-28z/scFv14- BBz transgene.
- Axi-cel:MSGV1(murine stem cell virus-based splice-gag vector)-derived retroviral vector (PG13-CD19-H3), produced from a qualified PG13-derived stable producer cell line. The PG13 CD19 H3 retroviral vector lacks coding sequences for retroviral Gag, Pol, and Env. These functions are provided by the PG13 derived stable producer cell line, preventing the formation of replication competent virus. The vector encodes the FMC63 CD28 ζ CAR transgene.

Inserted Genes

- Kite-753 (FMC63-28z/scFv14- BBz): Encodes two chimeric antigen receptors (CARs) separated by a T2A self-cleaving peptide motif derived from *Thomomys* asigma virus. The first CAR, FMC63-28z, encodes a recognition domain that enables binding to the CD19 receptor. The CAR further encodes a truncated extracellular domain, transmembrane domain and intracellular signaling domain derived from human CD28. Lastly, the CAR encodes a CD3 ζ co-stimulatory domain. This CD19 CAR is analogous to the axi-cel CAR. The second CAR, scFv14-BBz, encodes a recognition domain enabling binding to the CD20 receptor. The CAR further encodes a truncated extracellular domain, and transmembrane domain derived from CD8. Lastly, the CAR encodes a 4-1BB costimulatory and CD3 ζ stimulatory domain.
- Axi-cel (FMC63-CD28 ζ -CAR): This transgene encodes a chimeric antigen receptor (CAR) that consists of a recognition domain enabling binding to the CD19 receptor. The chimeric antigen receptor further encodes a truncated extracellular domain, transmembrane domain and intracellular signaling domain derived from human CD28. Lastly, the CAR encodes a CD3 ζ stimulatory domain.

RCL/RCR monitoring: PBMCs for RCL/RCR testing will be collected at baseline (before leukapheresis) and during follow-up at Months 3, 6, and 12; after Month 12, additional testing will be performed if clinically suspected or if a prior sample is positive, with annual follow-up as applicable.

IBC Discussion and Vote

Discussion: The reviewer discussed this is a new protocol on evaluating the efficacy of an investigational agent for treating relapsed or refractory large B cell lymphomas. The reviewer explained the use of autologous chimeric antigen receptor T cells and the safety of the lentiviral vector system. The careful dose escalation and monitoring of patients in the study was highlighted.

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

BSL/ABSL: **BSL-2**

NIH Guidelines: III-C, III-D

- 5) Investigator: Bosco, D
Title: Investigating the Effect of Mutant ALS-Linked Proteins on Neuronal Function to Determine Biological Causes of Amyotrophic Lateral Sclerosis (ALS)
- IBC Registration:** **I-466-22, Amendment**
- Training Verification: **Acceptable pending completion of PI training / Acceptable**
- Brief Summary: *To identify neuron loss after TBI (traumatic brain injury), we will express a neuron-specific AAV with a green fluorescent protein reporter (AAV.PHP.eB::hSyn1-Cre-NLS-GFP) to mark neurons throughout the brain. This reporter will allow us to identify and quantify neuron loss after TBI. To perform a genetic screen and to identify genes that protect against TBI, AAV.PHP.eB::hSyn1-Cre-NLS-GFP (above) will be co-injected with pAP215 (PHP.eB::pAP215). pAP215 is an AAV vector for single-guide RNA (sgRNA) expression that will be used for a genetic screen in vivo. pAP215 contains an mU6-driven sgRNA sequence followed by a Lox71/Lox66-flanked 175 bp 'handle' cassette that undergoes predominantly unidirectional16 inversion in cells expressing Cre recombinase. The construct expresses a nuclear-localized blue fluorescent protein (NLS-mTagBFP2) for visualization.*
- To identify neurons exhibiting TDP-43 loss of function, SynAdeno-associated virus (PHP.eB)-human Synapsin 1-TAR DNA-binding protein 43 (TDP)-Regulated (REG)-version 2(v2)-(mScarlet-FLAG)#9 [or TDP-REGv2(mScarlet-FLAG)#9] will be delivered to mice. This reporter will mark cells with mScarlet fluorescence due to TDP-43 loss-of-function with respect to RNA splicing.*
- To elucidate the role of FUS on mouse motor function and CNS health, including the integrity of the nucleocytoplasmic transport pathway, we will deliver ASOs targeting FUS compared to non-targeting ASO.*

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overall goal of the objectives is to understand how some mutant proteins contribute to amyotrophic lateral sclerosis (ALS) pathogenesis using ALS mouse models. The proteins to be tested will be expressed in vivo by AAV vectors or will be suppressed by anti-sense oligonucleotides (ASO), and neuron loss after TBI (traumatic brain injury) will be evaluated for the effects of these proteins. The proteins of interest include TDP-43, Ataxin-2, PFN1, FUS, etc.

Experimental Approach: Intracranial and intrathecal injection of 5uL of AAV-Syn1-GFP, AAV-Syn1-GFP-G3BP1 or AAV-Syn1-GFP-TIA1 will be carried out to express proteins of interest, and ASO will be injected to inhibit protein expression. Animals will then be treated with a chemical stressor (Sodium Arsenite), a mechanical stressor (TBI or sham surgery),

with no stress as control. The animals will be imaged through a cranial window with 2-Photon microscopy or sacrificed for histological analysis.

Human samples will also be used for analysis of protein expression.

IBC Discussion and Vote

Discussion: The reviewer discussed that this submission is an amendment. The lab is looking to see whether the proteins play a role in either delaying or accelerating brain injuries. The reviewer highlighted that the description was not brief and the information that was given was not laid out in a clear, concise way. The reviewer also discussed that there wasn't a lot of background information to give the amendment context.

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

- 6) Investigator: Garber, M
Title: Comparative Analysis of Human Skin in Health and Inflammatory Disease
IBC Registration: **I-732-26, Renewal**
Training Verification: **Acceptable pending completion of PI training**
Brief Summary: We study the molecular mechanisms that regulate gene expression and immune cell function in health and disease, with a particular focus on inflammatory and autoimmune skin diseases. We will use CRISPR-based technologies, including CRISPR nucleases (e.g., Cas9, Cpf1) and CRISPR effectors (e.g., CRISPRi and CRISPRa), to screen, modify, perturb, or enhance the function of regulatory DNA elements and genes in cultured human and mouse cells. We will also process and analyze human clinical samples and tissues to investigate pathways involved in immune-mediated diseases. These studies will integrate genomic, transcriptomic, and functional approaches to identify mechanisms of disease pathogenesis and potential therapeutic targets. The work may involve primary cells, established cell lines, and ex vivo analyses of human and animal-derived samples.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Studying molecular mechanisms that regulate gene expression and immune cell function in health and disease, with a particular focus on inflammatory and autoimmune skin diseases. They will use CRISPR-based technologies, including CRISPR nucleases, to screen, modify, perturb, or enhance the function of regulatory DNA elements and genes in cultured human and mouse cells.

They will also process and analyze human clinical samples and tissues to investigate pathways involved in immune-mediated diseases. These studies will integrate genomic, transcriptomic, and functional approaches to identify mechanisms of disease pathogenesis and potential therapeutic targets. The work may involve primary cells, established cell lines, and ex vivo analyses of human and animal-derived samples.

Experimental Approach: To use established molecular, cellular, genomic, transcriptomic, proteomic, and spatial biology approaches to investigate gene regulation and immune cell function in human and mouse systems. The lab will use commercially available cell lines, primary mouse immune cells derived from bone marrow obtained under approved IACUC protocols (PROTO202000018), human clinical samples and tissues, including skin biopsies, and primary human skin cells derived from de-identified foreskin tissue obtained under an approved IRB protocol. Techniques may include cell culture, gene expression analysis, CRISPR-based genome editing and gene regulation (e.g., Cas9, Cpf1, CRISPRi, and CRISPRa), lentiviral transduction, flow cytometry, nucleic acid and protein isolation, next-generation sequencing,

transcriptomic profiling, proteomic analyses, single-cell genomics, and other standard molecular and cellular biology methods. Single-cell studies may be performed using microfluidics-based platforms, including commercially available 10x Genomics technologies for single-cell RNA sequencing, single-cell multiomic analyses, and related applications. Spatial transcriptomic analyses may be performed on human and mouse tissue sections, including skin biopsies and histological specimens, using commercially available platforms such as 10x Genomics Visium, Xenium, and related technologies to characterize cellular organization, gene expression, and tissue microenvironments in health and disease. We will perform functional genetic screens and targeted perturbation experiments to assess the roles of genes, enhancers, promoters, and other regulatory elements in immune-mediated and autoimmune diseases, following established approaches described in the scientific literature.

As part of this work, we will generate second-generation, replication-deficient lentiviral vectors using standard packaging systems (including pMD2.G and psPAX2) for gene delivery into cultured human and mouse cells, including established cell lines and primary mouse bone marrow-derived immune cells. Lentiviral vectors will be handled under appropriate biosafety practices and will be used exclusively for in vitro and ex vivo studies. No replication-competent lentivirus will be generated, and no recombinant or synthetic nucleic acids or lentiviral vectors will be administered to live animals as part of this protocol.

IBC Discussion and Vote

Discussion:	The reviewer highlighted that the description was not brief and although there was too much information in some areas, there was too little information in other areas of the protocol. The reviewer mentioned the lab was previously approved for the use of human and mouse cell sorting, that may be transduced with replication deficient lentiviral vectors. The reviewer went over the 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

- 7) Investigator: Koupenova, M
 Title: Role of Innate Immunity in Pathogen-Induced Inflammation
 IBC Registration: **I-474-26, Renewal**
 Training Verification: **Acceptable**
 Brief Summary: This research program focuses on defining the mechanisms that regulate immunothrombosis and contribute to acute coronary syndromes, with particular emphasis on the role of platelets as mediators of thromboinflammatory responses. Using complementary in vitro and in vivo approaches, these studies will investigate how platelet interactions with vascular and immune cells influence innate immunity, thrombosis, and cardiovascular disease during viral infections.

Goals/Objectives

- Define platelet-dependent pathways that regulate immunothrombotic responses and contribute to acute coronary syndromes.
- Determine how interactions between platelets, endothelial cells and leukocytes in addition to megakaryocytes influence thromboinflammation in vitro and in vivo.
- Characterize the effects of viral infection on platelet function and innate immune signaling.
- Define changes in platelet and plasma inflammatory profiles during infection with RNA viruses
- Identify mechanisms by which infection-induced alterations in platelets promote thrombosis, vascular inflammation and cardiovascular complications.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This research program focuses on defining the mechanisms that regulate immunothrombosis and contribute to acute coronary syndromes, with particular emphasis on the role of platelets as mediators of thromboinflammatory responses. Using complementary in vitro and in vivo approaches, these studies will investigate how platelet interactions with vascular and immune cells influence innate immunity, thrombosis, and cardiovascular disease during viral infections.

Goals/Objectives

- Define platelet-dependent pathways that regulate immunothrombotic responses and contribute to acute coronary syndromes.
- Determine how interactions between platelets, endothelial cells and leukocytes in addition to megakaryocytes influence thromboinflammation in vitro and in vivo.
- Characterize the effects of viral infection on platelet function and innate immune signaling.
- Define changes in platelet and plasma inflammatory profiles during infection with RNA viruses
- Identify mechanisms by which infection-induced alterations in platelets promote thrombosis, vascular inflammation and cardiovascular complications.

Experimental Approach: • Human blood (50mL) and mouse blood (~1mL/mouse) will be used for isolating various blood cells, plasma, and serum. These isolates will be used to determine the level of inflammatory and thrombotic markers by enzyme-linked immunosorbent assay. The markers of platelet activation and inflammation will be measured through an aggregometer, adhesion assay, flow cytometry, and microscopy. White blood cells, red blood cells, and endothelial cells will also be assessed for their interaction with and influence on platelets. Additionally, mRNA and miRNA levels will be assessed in both human and mouse cells, with phenotypic changes verified by western blot.

- Mouse bone marrow will be isolated from tibia and femurs of various mouse models, according to IACUC protocols, and cultured to characterize the effects of inflammation and thrombosis on megakaryocyte gene and protein levels, maturation, and platelet-producing abilities. Additionally, human megakaryocyte cell lines will also be used to assess these effects.
- To test the function of miRNAs in blood cells, miRNA inhibitors, miRNA precursors, miRNA mimics, hairpin-RNAs, and siRNA, all commercially available and synthetic, will be incubated with human and mouse platelets and ex vivo functional changes will be assessed using an aggregometer, adhesion assay, flow cytometry, and microscopy. These commercially available and synthetic RNAs will be used with and without transfection reagents (i.e. lipofectamine, incubation, and nucleofection). These RNAs may also be fluorescently labeled for visualization. Transfection efficiency will be determined through qRT-PCR and protein assays.
- Commercially available BrUTP, and GFP-labeled protein/genes (available from Life Technologies, Sigma, BD Biosciences, and Lonza) will be transfected into primary (mouse) and immortalized megakaryocyte cell lines (human), monocytes (human and mouse), neutrophils (human and mouse), and endothelial cells (human), to assess the maturation, interactions with platelets, and inflammatory and thrombotic phenotype. These cells will be transfected using lipofectamine, nucleofection, or through cellular uptake.
- Mice will be infected in biocontainment room of the animal facility (UMass Chan). Mouse blood and organs post infection with Encephalomyocarditis virus (strain-EMCV; provided by Dr. Kurt-Jones group, UMMS) or Influenza (PR-8; provided by Dr. Kurt-Jones group UMMS), will be collected and used for the following experiments: blood cell counts as determined by Coulter Series Analyzer, cytokine measurements will be done through enzyme-linked immunosorbent assay on platelets and plasma, platelets function studies using an aggregometer, adhesion assay, flow cytometer, and microscopy, platelet RNA and protein levels will be assessed by commercially available methods. Organs will be homogenized with detergents and tested for protein levels or fixed and stained with antibodies.
- 5'-ethynyl uridine will be used to label newly synthesized RNA in cells, which can be tracked through microscopy, flow cytometry, or qRT-PCR methods. This will allow us to analyze the movement of RNA in the cell and between cells. Commercially available 5'-ethynyl uridine (Click-IT EU; available from Life Technologies) will be incubated with primary

(mouse) and megakaryocyte cell lines (human), monocytes (human and mouse), neutrophils (human and mouse), and endothelial cells (human), to assess the maturation, interactions with platelets, and inflammatory and thrombotic phenotype. This reagent will incorporate into the cells through cellular uptake. No need for the use of transfection reagents.

- Agents: Pollens; InflueInfluenza A virus; Herpes Simplex Virus 1; Epstein-Barr virus (EBV); Cytomegalovirus (CMV)-human and mouse; Vaccinia Virus. All viruses will be provided by Dr. Evelyn Kurt-Jones. Mice will be infected in biocontainment room of the animal facility (UMMS). Organs and blood will be collected in the animal room. Organs will be fixed in 4%PFA before being brought to designated lab spaces. Plasma will be isolated in biocontainment, blood cells will be isolated in the biosafety cabinet located in the alcove of designated lab spaces. Plasma and blood cells will be stored at -80C in double containers. All further analysis will that do not involve fixation will be done in the hood. Except, platelets isolated from infected mice will be redissolved in buffer and incubated at 37C for 10 to 120 min in the lab, spun down and saved analyzed in the hood. All equipment used will be cleaned with 70% ethanol.
- LPS (from E. coli) from comercial source will be used to infect mice intraperitoneally. Blood will be collected, plasma and blood cells will be stored at -80C.
- Isolation of blood components from patients with SARS-CoV2 or influenza: 1. Blood will be collected from patients in yellow top ACD tube and transported to the lab in double bag and non-transparent container. ACD-tube will be taken from bags in biosafety cabinet sprayed with 70% EtOH, 1 mL will be transferred to a test tune, the rest will be capped back, sprayed with 70% EtOH, and covered with parafilm (all around the top). Blood will be centrifuged at 150 g for 17 min. Tube will be opened in the biosafety cabinet and platelet-rich plasma (PRP) will be transferred to 50 mL-screw top conical tube. PRP will be spun down at 800 g for 17 min. Platelets will be collected in screw-top tubes. Some of the platelets will be fixed for electron microscopy inside of the biosafety hood. The 1 mL of blood from the second step: Plasma will be isolated by double-spin method first at 500g followed by 2000g and frozen. Left-over blood fraction from step 3 will be lysed with RBC-lysis buffer, tube will closed, sprayed with 70% EtOH, covered with parafilm and spun down 300g, 10 min. Pellet will be frozen in screw top tubes.
- Proteomics: Plasma from influenza or COIVD19 patients will be tested by ELISA, as all procedures will be done in a biosafety cabinet. Levels of proteins in platelets will be evaluated by Western Blot as the step or lysis of the cells will be conducted in the biosafety cabinets.

IBC Discussion and Vote

Discussion:	The reviewer discussed this is a 5-year renewal and the protocol is focused on platelet-dependent pathways and the use of human and mouse blood for isolating various blood cells. The reviewer noted the use of infectious agents like influenza A virus, herpes simplex virus, and LPS. The reviewer identified the need for clarification on the use of flow cytometry and microscopy in the study. The reviewer also mentioned the need for clarification on the use of human tissues and the completion of lab compliance training. A detailed description of the infectious agents and their attenuation was also highlighted.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	BSL-2; ABSL-2
NIH Guidelines:	III-D

- 8) Investigator: Kowalik, T
Title: Genomic Variability of Cytomegalovirus in a Clinical Setting
IBC Registration: **I-573-26, Renewal**
Training Verification: **Acceptable pending completion of PI training**
Brief Summary: Human Cytomegalovirus (HCMV) is a ubiquitous pathogenic herpesvirus that rarely causes disease in healthy adults. However, in neonates, AIDS and cancer patients, and transplant

recipients, a CMV infection or reactivation can cause a range of symptoms, from few overt signs to death. Goals of this project are to understand the molecular biology, genetics and virology of CMV using laboratory and patient samples containing virus.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goals of the project are to understand the molecular biology, genetics, and virology of human cytomegalovirus (HCMV) using laboratory and patient samples containing virus. Human CMV is a ubiquitous pathogenic herpesvirus that rarely causes disease in healthy adults. However, in neonates, AIDS and cancer patients, and transplant recipients, a CMV infection or reactivation can cause a range of symptoms, from few overt signs to death. This registration covers studies on HCMV, a risk group 2 agent; and mouse cytomegalovirus (MCMV), an risk group 1 virus.

Experimental Approach: *Virus stocks: Production of HCMV occurs through infecting monolayers of HFF or ARPE19 cells. Cells will be monitored for extensive cytopathic effect (CPE). Supernatants will be harvested, debris pelleted, and supernatant aliquoted. Viruses will be titered on the same cell types that they will be cultured in via plaque assay. MCMV will be propagated and titered in a similar manner using mouse NIH 3T3 cells

*Virus-cell interactions: Infection experiments occur will be performed using cultured cells at different MOIs. HCMV replicates slowly, so time courses will run <1 week to 3 weeks. Supernatants and cells will be harvested and samples will be processed for standard molecular and biochemical assays, immunofluorescence, and viral genomic sequencing.

*Viral genomic sequencing of laboratory and clinical samples: Targeted, subgenomic, and genome-wide deep sequencing of HCMV in inactivated samples are performed via Sanger and Illumina deep sequencing.

*Replication assays: Virus replication in experiments will be determined by standard viral plaque assays or by a modification of the “shell assay” used in clinical laboratories. The modified shell assay measures the number of infectious viruses in samples by incubating aliquots on target cells and subsequently staining for HCMV proteins.

*Recovery of BAC-viruses: Infectious virus will be recovered from BAC clones by cotransfection of the viral genome containing BAC with a plasmid expressing HCMV pp71, an essential factor for viral gene expression. No infectious virus will be rescued without pp71 transcomplementation.

*Genetic manipulations: (NONE of the genetic manipulations will target oncogenes) HCMV genes will be mutated or deleted in genomic BAC clones using standard recombineering developed at UMass Chan. Mutations will NOT enhance infectivity. Rather, mutations will be made to moderate infectivity to uncover mechanism of virus entry and replication. siRNA approaches will be used to knockdown the expression of host genes to study their role in viral entry and replication. Some experiments will complement the knockdown by expressing mutant versions of host proteins to understand their function.

IBC Discussion and Vote

Discussion:	The reviewer discussed this is a 5-year renewal protocol on the genomic variability of cytomegalovirus in a clinical setting. The reviewer highlighted the use of bacterial artificial chromosomes and chromosome expression vectors to produce HCMV and MCMV in cell culture experiments and noted the use of lab and patient-derived strains of HCMV and MCMV. The reviewer identified the need for clarification on the use of human and/or mouse cell lines in the study.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	BSL-2
NIH Guidelines:	III-D, III-E, III-F

- 9) Investigator: Magnani, D
 Title: Lentivirus-Mediated Protein Expression
IBC Registration: I-797-26, Renewal
 Training Verification: **Acceptable**
 Brief Summary: Our goal is to generate stable cell lines which express a desired protein on their surface. The cell lines would be used to immunize mice and would be used to discover binding antibodies by flow cytometry.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The goal of the research is to generate stable cell lines that express desired proteins on their surface. The cell lines will be used to immunize mice and will be used to discover binding antibodies by flow cytometry.

Experimental Approach: The research team will use lentivirus vectors obtained from a vendor (Genscript) to transduce CHO cells and HEK293T cells to express recombinant proteins. Lentivirus vectors will be generated using a second generation (or third generation) expression system. The vectors will be tested for replication competent viruses by p24 ELISAs. Transduced cells will then be grown under a selection agent. Transduced cells will be detected and sorted a BD FACSMelody housed in a biosafety cabinet with aerosol containment in a BSL-2+ facility. Stably transduced cells will be used for mouse immunizations, as well as in flow cytometry experiments to test for antibodies that bind to the recombinant proteins.

IBC Discussion and Vote

Discussion: The reviewer discussed this is a 5-year renewal and discussed action items.
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-D

- 10) Investigator: Song, J
 Title: **Synthetic matrices for guiding tissue regeneration**
IBC Registration: I-308-26, Renewal
 Training Verification: **Acceptable**
 Brief Summary: Regenerative repair of volumetric bone loss or joint injuries due to trauma, aging and metabolic diseases or infection presents a significant scientific and clinical challenge. We are developing synthetic tissue grafts to guide the regeneration of bony or cartilage tissue with or without biotherapeutics. We are also modifying orthopedic implants to improve their performance (e.g. enhancing bone integration and reducing periprosthetic infections). Finally, we are developing novel antibiotic conjugates and testing their in vitro and in vivo efficacy against common strains of Gram-positive and Gram negative bacteria.
 Adding a few commercial strains of E. coli to the protocol. We would like to test whether our novel anti-infective therapeutics is effective against multiple commercial E coli strains (KPC-producing strain ATCC BAA-2340, NDM-producing strain ATCC BAA-2469, NDM-1 producer ATCC BAA-2471, resistant to imipenem and ertapenem).

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The studies are designed to improve the regenerative repair of volumetric bone loss or joint injuries due to trauma, aging and metabolic diseases or infection.

Experimental Approach: The group is developing synthetic tissue grafts to guide the regeneration of bony or cartilage tissue with or without biotherapeutics; modifying orthopedic implants to improve their performance (e.g. enhancing bone integration and reducing periprosthetic infections); and developing novel antibiotic conjugates and testing their in vitro and in vivo efficacy against common strains of Gram-positive and Gram negative bacteria.

IBC Discussion and Vote

Discussion:	The reviewer discussed that this is a 5-year renewal for improving volumetric bone loss following joint injuries. The renewal involves developing synthetic tissue grafts and testing them in vitro and in vivo. The reviewer highlighted the need to include all bacteria in the animal addendum and clarify potential exposure to animal medicine personnel.
Meeting Decision:	Vote to approve upon completion of action items.
BSL/ABSL:	BSL-2; ABSL-2
NIH Guidelines:	N/A

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

- 1) 06/06/2026 5:30 am- False fire alarm in BSL-3 lab. FDP responded. Ethylene glycol on smoke detector (leak in hot water line above ceiling; minor opening in floor above). 061726 follow-up meeting to review issues identified: action items identified. Drill scenario.
- 2) Campus emergency number changing: 5-5-5

VI. Information from the field (Senior Biosafety Officer)

N/A

VII. Other Business

Acknowledgement Items:

- 1) Ramanathan 901-24: Janssen _ 68284528MMY4006- for SLE ICF v8 & IB v11 (041626): **Intermediate-Size Population Expanded Access Program (EAP) for Ciltacabtagene autoleucel (cilta-cel) Out-of-Specification (OOS) in patients with Multiple Myeloma United States EAP.** Updated overview of ongoing and completed clinical studies. Updated efficacy and safety data for Study 68284528MMY2003. Added overview summary for Study 68284528MMY2012. Updated PK and pharmacodynamic analyses for Study 68284528MMY2002. Added PK, efficacy, and safety summaries for Study 68284528MMY4002.
- 2) Hafer I-443-24. & CRC I-864-23: IBC pre-review: New trial: VPX PCORI. **A Randomized Controlled Trial Comparing Renal Effects of Vancomycin Combined With Either Piperacillin/tazobactam or Meropenem: VPT Patient Safety (VPS) Study** | PI: Jennifer Wang
- 3) Bradley I-770-25: New trial: HelixBind. **Assessment Of Automated Assay For Identification And Characterization Of Bloodstream Infections From Whole Blood** | PI: Jennifer Wang

Adjourned at 1:43pm