Meeting Minutes

Date: 07/28/2025
Start Time: 2:00 PM
End Time: 3:05 PM
Location: Zoom Meeting

Meeting Chair: Joseph Elkhoury, MD;
Administrative Chair: Ryan Schlimgen, Ph.D;
Members Present: J. Healey; A. Sallee; T. Kwan; H. Widlund; K. Holthaus; T. Spitzer; D. Lingwood; Y. Xie; H. Wakimoto; S. Walsh; T. Jakobs; T. Scott; K. Joseph; M. Marketon; C. Sanchez Cano; S. Subburaju; R. Sandlin; X. Li; A. Gottlieb; M. Bergeron; J. Lemieux; M. Hogan; J. Morris; C. Moretti;

I. Welcome and Introductions

II. Review of the Minutes: Minutes can be found on the Other Business tab of this meeting

III. Review of Submissions

Phase I, open label dose-escalation and dose-expansion study to evaluate the safety, expansion, persistence and clinical activity of UCART22 (allogeneic engineered T-cells expressing anti-CD22 Chimeric Antigen Receptor) in patients with relapsed or refractory CD22+ B-cell Acute Lymphoblastic Leukemia (B-ALL) 2020B000231	
Participating Site(s): BWH	**Sponsor:**
rDNA: No	
Process Type: Clinical Amendment	**Animal Study:** No
Clinical Amendment Summary This clinical amendment covers the clinical trials response to a serious safety event involving a Grade 5 case of Disseminated Intravascular Coagulation (DIC) in a study participant. As a result, the risk of DIC is now addressed in the informed consent, study protocol, and investigator's brochure. The trial is a Phase I, open-label, dose-escalation and dose-expansion study evaluating the safety, expansion, persistence, and clinical activity of UCART22 (allogeneic engineered T-cells expressing anti-CD22 chimeric antigen receptor) in patients with relapsed or refractory CD22+ B-cell Acute Lymphoblastic Leukemia (B-ALL). The amendment also introduces a Phase 1 sub-study with a lower alemtuzumab dosing regimen, updates eligibility criteria, and increases the planned enrollment. **Meeting Discussion** The reviewer presented a detailed overview of the clinical amendment and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions. **NIH Citation**	

This clinical amendment falls under *NIH Guidelines* Section III-C-1.
Vote: (Approved) For: (21), Against: (0), Abstained: (0)

Human Models of Inherited Retinal Dystrophies Using Human-Induced Pluripotent Stem Cells 2025B000085	
Participating Site(s): MEE	**Sponsor:**
rDNA: Yes	
Process Type: Laboratory Initial Application	**Animal Study:** Yes

Initial Laboratory Registration Summary

The goal of this research is to model inherited retinal degenerations (IRDs) using human induced pluripotent stem cells (hiPSCs). These hiPSCs are derived from blood or urine samples of affected individuals or engineered to carry IRD-associated mutations. The cells are differentiated into retinal organoids and retinal pigment epithelium (RPE) to study disease mechanisms and evaluate gene-based therapies. The registration includes the use of replication-deficient AAV, CAV2, lentiviral, and Sendai viral vectors for gene delivery and genome editing (CRISPR/Cas9, base editing, prime editing). No viral vectors are constructed in-house. Sendai virus is used exclusively for reprogramming epithelial cells into hiPSCs and is the only vector in this protocol encoding oncogenes.

Meeting Discussion

The reviewer presented a detailed summary of the proposed laboratory registration and requested the Lab specify the use of viral vectors for gene delivery, specifically utilizing AAV and CAV-2 backbones with inserted cDNAs, as well as the lentiviral vector backbone. In addition, the use of rDNA requires a dedicated section for each viral vector system being used, with a clear listing of the specific genes incorporated into each system. Provided the Lab addresses the reviewer's requests, the reviewer recommended approval. The committee did not have any questions and voted unanimously to approve with the condition the Lab will resolve the reviewer's requests.

Containment

Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic *Escherichia coli* for plasmid amplifications, and for the use and handling of adeno-associated viral vectors and Canine Adenoviral vectors. BL2 containment and laboratory practices and procedures are required for the use and handling of replication incompetent lentiviral vectors and Sendai Viral vectors, and for the culture, use, and handling of human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation

This initial laboratory registration falls under *NIH Guidelines* Sections III-D-3, III-E-1, and III-E.

Vote: (Require BSO Review) For: (22), Against: (0), Abstained: (0)

Ex vivo delivery of therapeutics to transplantable organs using machine perfusion 2025B000087	
Participating Site(s): MGH	**Sponsor:**
rDNA: Yes	
Process Type: Laboratory Initial Application	**Animal Study:** Yes

Initial Laboratory Registration Summary

The goal of this research is to evaluate the use of ex vivo perfusion systems to deliver therapeutics to transplantable rat organs. The laboratory will use replication-deficient lentiviral vectors to express a surface receptor fused tom Cherry for tracking transduction, and LNPs containing mRNA encoding GFP or nano luciferase to assess transfection efficiency, expression kinetics, and tissue distribution. Organs are perfused with these agents while connected to a machine perfusion system, and outcomes are measured via flow cytometry and staining. All viral vectors are received ready-to-use from collaborators, and LNPs are formulated in-house using microfluidic encapsulation.

Meeting Discussion
The IBC Director presented a detailed summary of the proposed laboratory registration on behalf of the reviewer who was absent. The reviewer did not have any biosafety concerns and recommended approval. The committee did not have any questions and voted unanimously to approve without conditions.

Containment Level
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of naïve and lipid nano particle transfected rat organs. BL2 containment and laboratory practices and procedures are required for the use and handling of replication incompetent lentiviral vectors and the cells they transduce.

NIH Citation
This initial Laboratory registration falls under *NIH Guidelines* Sections III-E-1 and III-E.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Development of cell encapsulation matrices 2025B000088	
Participating Site(s): BWH	**Sponsor:**
rDNA: Yes	
Process Type: Laboratory Initial Application	**Animal Study:** Yes

Initial Laboratory Registration Summary
The goal of this research is to develop hydrogel-based matrices for cell encapsulation to support long-term survival and function of therapeutic cells. The encapsulated cells, including beta cells, B cells, fibroblasts, and ARPE-19 cells, will be evaluated for viability and secretory function under stress conditions such as hypoxia. The registration includes the use of commercially obtained or collaborator-engineered human and rodent cells, including MIN-6 and INS-1insulinoma lines. All engineered cells are received pre-modified; no genetic modification is performed in-house. Experimental procedures include cell expansion, viability assays, ELISA, mass spectrometry, immunohistochemistry, and flow cytometry to assess marker expression and function.

Meeting Discussion
The reviewer presented a detailed summary of the proposed laboratory registration and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment Level
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of rodent cell lines. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This initial Laboratory registration falls under *NIH Guidelines* Section III-E.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Development of Biomaterials for Diseases Theranostics 2023B000048	
Participating Site(s): BWH	**Sponsor:**
rDNA: Yes	
Process Type: Laboratory Amendment	**Animal Study:** Yes

Laboratory Amendment Summary
The goal of this research is to develop and evaluate novel biomaterials for cancer imaging and therapy. The research focuses on improving the pharmacokinetics, biodistribution, and therapeutic efficacy of biomaterials in treating advanced, drug-resistant, and metastatic cancers. This amendment adds a new scientific aim

involving the non-viral transfection of HEK293T cells with a plasmid encoding a mitochondrial-targeted antioxidant protein (mitoSOD2). Following expression, the protein localizes to the mitochondrial matrix, and mitochondria are isolated from the transfected cells. These engineered mitochondria, which carry the therapeutic protein internally, are then used as delivery vehicles in arthritic mice.

Meeting Discussion
The reviewer presented a detailed summary of the proposed scientific amendment and did not have any biosafety concerns. While this amendment does not alter the overall biosafety risk, the committee requested the Lab confirm that they will perform cell squeezing exclusively for cell transfection, given the rarity of this method. Additionally, the Lab should administratively update the Use of rDNA Form to reflect the changes in this amendment for consistency across the protocol. Provided the Lab addresses these requests, the committee voted unanimously to approve with conditions.

Containment
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic *Escherichia coli* for plasmid amplifications. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This scientific amendment falls under *NIH Guidelines* Section III-E.

Vote: (Require BSO Review) For: (22), Against: (0), Abstained: (0)

Bioprinting of 3D Organoid and Tissue 2020B000180	
Participating Site(s): BWH	**Sponsor:**
rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Five-Year Resubmission Summary
The goal of this research is to develop bioprinting techniques for constructing 3D organoid and tissue structures using hydrogel scaffolds and mammalian cells. The research focuses on optimizing dispensing parameters, characterizing hydrogel fidelity, and evaluating cell viability and growth in printed constructs. The lab also uses human ovarian cancer cell lines (including luciferase-expressing variants) for in vitro 3D culture and in vivo xenograft models to study tumor growth and therapeutic interventions such as ultrasound and chemotherapy.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns, noting that the use of non-safety sharps is justified. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 2 (BL2) containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials. Animal Biosafety Level 2 (BL2-N) containment and husbandry practices and procedures are required for mice administered human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Sections III-D-4.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

The role of chromatin modifying protein complexes in stem and blood cancer cells 2020B000139	
Participating Site(s): MGH	**Sponsor:** SUNDRY, Fox Chase Cancer Center

rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Five-Year Resubmission Summary
The goal of this research is to investigate the roles of Polycomb Repressive Complexes PRC1 andPRC2 in the development and maintenance of blood cancers such as leukemia and lymphoma. The laboratory focuses on identifying and validating gene drivers and biomarkers of leukemic aggressiveness using lentiviral-mediated gene modulationin human and murine hematopoietic cells. The research also explores the cell-type specificity of these gene effects using mouse embryonic stem cells, including knockout lines for PRC1 components Ring1b and Kdm2b. Lentiviral vectors are used to deliver doxycycline-inducible constructs for gene overexpression or knockdown, and molecular profiling is performed using RT-qPCR, RNA-seq, ChIP-seq, CUT&RUN, ATAC-seq, and Repli-seq.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic Escherichia coli for plasmid amplifications. BL2 containment and laboratory practices and procedures are required for the use and handling of replication incompetent lentiviral vectors, and for the culture, use, and handling of human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Section III-E-1.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Immune mechanisms in pulmonary and critical illness. 2020B000172	
Participating Site(s): BWH	**Sponsor:** American Heart Association, Inc., National Scleroderma Foundation, Inc., American Lung Association, American Heart Association, Inc., NIH-National Institutes of Health, St. Jude Children's Research Hospital
rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Five-Year Resubmission Summary
The goal of this research is to investigate the dysregulated immune responses in pulmonary and critical illness, including sepsis, cardiac arrest, and lung fibrosis. The research focuses on innate immunity and stromal cell interactions, particularly involving monocytes, T cells, and fibroblasts, to identify upstream immune regulators that contribute to disease progression and uncover potential therapeutic targets. The laboratory uses CRISPR/Cas9 to delete LIFR in primary human fibroblasts, siRNA delivery via lipid nanoparticles, and infectious models involving Candida albicans and influenza A virus in mice.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 1(BL1) containment and laboratory practices and procedures are required for the use and handling of lipid nanoparticles (LNPs) with siRNA. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials, Candida albicans, and influenza A virus. Animal Biosafety Level 1 (BL1-N) containment and husbandry practices and procedures are required for mice administered LNPs. BL2-N containment and husbandry practices and procedures are required for mice

administered Candida albicans or influenza A virus. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Section III-E.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Mechanisms of somatosensation in rodents **2020B000155**	
Participating Site(s): BWH	**Sponsor:** NIH-National Institutes of Health, Gordon E and Betty I Moore Foundation, NIH-National Institutes of Health, One Mind Institute, President and Fellows of Harvard College, Brigham and Women's Hospital - Internal Funds, McKnight Foundation, The, NIH-National Institutes of Health, NIH-National Institutes of Health
rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Laboratory Five-Year Resubmission Summary
The goal of this research is to characterize the cell types, circuits, and genes involved in pain processing and nerve repair. The study aims to uncover molecular mechanisms of somatosensation and develop novel pain therapeutics by manipulating gene expression in rodent models and analyzing human nervous system tissues. The laboratory uses adeno-associated viral vectors and rabies delta G virus for gene delivery and circuit tracing, CRISPR-Cas9 and dCas9systems for gene editing and regulation, and tetrodotoxin for neuronal silencing. Human iPSCs are used to model nervous system cell types, and transgenic mice are generated using gRNA and targeting vectors.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and requested the Lab update the Detailed Research Plan to describe the procedures utilized for CRISPR delivery by virus and to clearly state whether virus will be produced in the Lab; if it is, the Lab should detail this in the Use of Viral Vectors Form. Additionally, the Lab should identify the envelope plasmid and plasmid backbones wherein cDNAs are cloned. With the condition the Lab will address these requests, the committee voted unanimously to approve.

Containment
Biosafety Level 1(BL1) containment and laboratory practices and procedures are required for the use and handling of adeno-associated viral vectors that do not express or induce expression of oncogenes nor reduce expression of tumor suppressor genes. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials, and for the use and handling of delta G rabies viral vectors and adeno-associated viral vectors that expressor induce expression of oncogenes or reduce expression of tumor suppressor genes. Animal Biosafety Level 1 (BL1-N) containment and husbandry practices and procedures are required for mice administered adeno-associated viral vectors that do not express or induce expression of oncogenes nor reduce expression of tumor suppressor genes. BL2-N containment and husbandry practices and procedures are required for mice administered delta G rabies viral vectors or adeno-associated viral vectors that express or induce expression of oncogenes or reduce expression of tumor suppressor genes. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five year resubmission falls under *NIH Guidelines* Sections III-D-1, III-D-4, and III-E.

Vote: (Require BSO Review) For: (22), Against: (0), Abstained: (0)

Neutrophil-pathogen interactions in health and disease **2015B000010**

Participating Site(s): MGH	**Sponsor:** NIH-NIGMS National Institute of General Medical Sciences, Forsyth Institute, The, American Psychiatric Association (APA)
rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Laboratory Five-Year Resubmission Summary

The goal of this research is to study neutrophil-pathogen interactions using microfluidic devices and time-lapse imaging to visualize real-time responses of human neutrophils to bacteria, fungi, and parasites. Neutrophils are isolated from human blood or differentiated from HL-60 cells. Pathogens are provided by collaborators and include bacteria (e.g., *Pseudomonas aeruginosa, Staphylococcus aureus*), fungi (e.g., *Candida albicans, Aspergillus fumigatus*), and parasites (e.g., *Plasmodium falciparum*). The lab uses fluorescently labeled pathogens to monitor interactions in sealed microfluidic devices. No culturing or long-term storage of pathogens occurs in the lab. This resubmission includes a shift in focus toward neutrophil-fungal interactions, particularly with *Candida albicans*, and emphasizes the use of small sample volumes and strict biosafety practices.

Meeting Discussion

The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The committee did not have any questions and voted to approve without conditions.

Containment

Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic *Escherichia coli, Corynebacterium matruchotii,* and *Streptococcus cristatus*. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials, *Pseudomonas aeruginosa, Staphylococcus aureus, Actinomyces graevenitzii, Borrelia burgdorferi, Actinomyces neaslundii, Fusobacterium nucleatum, Candida albicans, Aspergillus fumigatus,* and *Plasmodium falciparum.* Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation

This five-year resubmission falls under *NIH Guidelines* Section III-D-1.

Vote: (Approved) For: (21), Against: (0), Abstained: (0)

Adeno Associated Viral-mediated Gene Transfer to Investigate APP and Presenilin Function in the Mouse Brain
2015B000031

Participating Site(s): BWH	**Sponsor:** NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH, NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH-National Institutes of Health, Beth Israel Deaconess Medical Center, NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH-NINDS National Institute of Neurological Disorders and Stroke, NIH-NINDS National Institute of Neurological Disorders and Stroke
rDNA: Yes	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes

Five-Year Resubmission Summary

The goal of this research is to investigate the molecular pathogenesis of Alzheimer's disease, focusing on the roles of presenilin genes (PS1 and PS2) and APP family proteins. Using adeno-associated viral vectors, the laboratory inactivates or restores gene expression in specific brain regions of mice to assess effects on synaptic and neuronal function. AAV vectors encoding Cre recombinase or GFP are handled at BL1, while those

encoding Presenilin 1 are handled at BL2. All vectors are administered via stereotaxic injection, and brain tissues are collected for electrophysiological and protein expression analysis.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic *Escherichia coli* for plasmid amplifications, and for the use and handling of adeno-associated viral vectors carrying GFP and CRE transgenes. BL2 containment and laboratory practices and procedures are required for the use and handling of adeno-associated viral vectors carrying Presenilin 1 transgenes, and for the culture, use, and handling of human source materials. Animal Biosafety Level 1 (BL1-N) containment and husbandry practices and procedures are required for mice administered adeno-associated viral vectors. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Sections III-D-4 and III-E.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Mechanisms of microtubule organization in cell division and cell signaling 2015B000042	
Participating Site(s): MGH	**Sponsor:** SUNDRY, NIH, Health Resources in Action, Pew Scholars Program in the Biomedical Sciences, American Cancer Society, NIH-National Institutes of Health, Johnson & Johnson, Inc., President and Fellows of Harvard College, NIH-National Institutes of Health, NIH-National Institutes of Health, NIH-National Institutes of Health, American Heart Association, Inc., NIH-National Institutes of Health, MGH Fund for Medical Discovery, NIH-National Institutes of Health, Charles A King Trust, NIH-National Institutes of Health, NIH-National Institutes of Health, NIH-National Institutes of Health, NIH-National Institutes of Health, American Cancer Society, NIH-National Institutes of Health, NIH-National Institutes of Health, Regents of the University of Colorado, Jane Coffin Childs Memorial Fund For Medical Research, MGH Fund for Medical Discovery, Alex's Lemonade Stand Foundation, Regents of the University of Colorado, a body corporate, for and on behalf of the University of Colorado Boulder, The, Regents of the University of Colorado, a body corporate, for and on behalf of the University of Colorado Boulder, The, NIH-National Institutes of Health, Regents of the University of Colorado, a body corporate, for and on behalf of the University of Colorado Boulder, The, NIH-National Institutes of Health, American Cancer Society, National Science Foundation, NIH-National Institutes of Health, NIH-National Institutes of Health, Boston University School of Medicine, National Science Foundation

rDNA: Yes

Process Type: Laboratory Five Year Resubmission | **Animal Study:** Yes

Five-Year Resubmission Summary
The goal of this research is to investigate the molecular mechanisms that govern the formation and function of microtubule-based architectures in eukaryotic cells. The lab reconstitutes these structures from individual components and analyzes their behavior using structural, biochemical, and live-cell imaging techniques. Proteins such as Kif7, Gli, and Sufu are expressed in *E. coli,* insect cells, and mammalian cells. Lentiviral vectors are used to transduce mouse cells for expression of tagged proteins or gene editing, and CRISPR is used to knock in fluorescent tags. Human and NHP cell lines are transfected for transient expression. The purified proteins and modified cells are used in TIRF and confocal microscopy to study protein localization and dynamics.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic *Escherichia coli*, baculoviral vectors, insect cells, and mouse cells. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human and non-human primate source materials, and for the use and handling of replication incompetent lentiviral vectors and for the culture, use, and handling of the cells they transduce. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Sections III-D-3 and III-E.

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Genetic analysis of Klebsiella pathogenesis
2015B000040

Participating Site(s): MGH | **Sponsor:** SUNDRY, The Broad Institute, Inc., The Broad Institute, Inc., The Broad Institute, Inc., NIH-National Institutes of Health

rDNA: Yes

Process Type: Laboratory Five Year Resubmission | **Animal Study:** Yes

Five-Year Resubmission Summary
This goal of this research is to study the genetic basis of *Klebsiellapneumoniae* pathogenesis, antibiotic resistance, and host immune response using recombinant zebrafish, mice, and human cell models. *K. pneumoniae* strains will be genetically manipulated via plasmid-based overexpression, allelic exchange, CRISPRi knockdown, and transposon mutagenesis, while *K. oxytoca* will be used in wild-type form only. Resulting mutants will be assessed for antibiotic susceptibility, biofilm formation, and capsule production. Lentiviral vectors will be used to modify human cell lines for host-pathogen interaction studies, and small molecules will be tested for their ability to modulate immune responses. Recombinant or wild-type KPN strains are co-cultured with recombinant human cells for microscopic observation of host response to infection. No new antibiotic resistance traits beyond natural profiles are expected.

Meeting Discussion
The reviewer presented a detailed summary of the five-year resubmission and requested the Lab confirm that additional special attention for potentially hypervirulent organisms is not required for study staff. The committee voted unanimously to approve provided the Lab addresses the reviewer's request on the Occupational Health Form of the protocol.

Containment

Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of non-pathogenic Escherichia coli for plasmid amplifications. BL2 containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials, Klebsiella pneumoniae, and *Klebsiella oxytoca,* and for the use and handling of replication incompetent lentiviral vectors. Animal Biosafety Level 2 (BL2-N) containment and husbandry practices and procedures are required for mice or zebrafish administered human source materials. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.

NIH Citation
This five-year resubmission falls under *NIH Guidelines* Sections III-D-1, III-D-2, III-D-3, III-D-4, III-E-1, and III-E.

Vote: (Admin Review) For: (22), Against: (0), Abstained: (0)

Mechanisms of Immunomodulation mediated by pathogens 2025B000074	
Participating Site(s): BWH	**Sponsor:**
rDNA: No	
Process Type: Laboratory Initial Application	**Animal Study:** Yes

Initial Laboratory Registration Summary
The goal of this research is to characterization of signaling pathways that control the activity of the immune system, with the ultimate goal of identifying novel therapeutic targets and biomarkers for immune-mediated disorders. Intestinal and/or respiratory pathogens are used to evaluate the role of specific molecular mechanisms previously identified as critical in neuroimmune and autoimmune disorders in the context of in vivo infection. Intestinal and respiratory pathogens (*C. rodentium, K. pneumoniae, Salmonella, S. aureus*, influenza, LCMV, and VSV) will be purchased from the ATCC. LCMV and VSV will be received ready to use, while the rest will be cultured or propagated. Infected animals will be sacrificed for tissue collection and flow cytometry analysis, and in vivo photo conversion will be used to track immune cells.

Meeting Discussion
The reviewer presented a detailed summary of the proposed laboratory registration and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.

Containment
Biosafety Level 1 (BL1) containment and laboratory practices and procedures are required for the culture, use, and handling of *Citrobacter rodentium*, Biosafety Level 2 (BL2) containment and laboratory practices and procedures are required for the culture, use, and handling of *Klebsiella pneumoniae, Salmonella enterica, Staphylococcus aureus*, Influenza Avirus (H1N1), Vesicular stomatitis virus (VSV), and Lymphocytic choriomeningitis virus (LCMV). Animal Biosafety Level 2 (BL2-N) containment and husbandry practices and procedures are required for mice administered *Citrobacter rodentium, Klebsiella pneumoniae, Salmonella enterica serovar Typhimurium, Staphylococcus aureus,* Influenza A virus (H1N1), Lymphocytic choriomeningitis virus (Armstrong), and/or Vesicular stomatitis Virus (VSV).

Vote: (Approved) For: (22), Against: (0), Abstained: (0)

Diagnosis and characterization of tick-borne, pathogens, respiratory pathogens, and sexually transmitted infections 2021B000068	
Participating Site(s): MGH	**Sponsor:** President and Fellows of Harvard College, President and Fellows of Harvard College, NIH-National Institutes of Health, NIH-National Institutes of Health, Centers for Disease Control and Prevention, The Broad Institute, Inc., NIH-National Institutes of Health, President and Fellows of Harvard College, Brigham and Women's Hospital, Inc., NIH-National

	Institutes of Health, NIH-NIAID National Institute of Allergy and Infectious Diseases, Centers for Disease Control and Prevention, Charles A King Trust, Board of Regents of the University of Wisconsin System, The, Board of Regents of the University of Wisconsin System, The, NIH-National Institutes of Health, President and Fellows of Harvard College, Sherlock Biosciences, NIH-NIAID National Institute of Allergy and Infectious Diseases, Centers for Disease Control and Prevention, Tufts University, Centers for Disease Control and Prevention, President and Fellows of Harvard College, President and Fellows of Harvard College, Texas A&M University, Gordon E and Betty I Moore Foundation, Tufts University, NIH-NIAID National Institute of Allergy and Infectious Diseases, Tufts University, President and Fellows of Harvard College, NIH-NIAID National Institute of Allergy and Infectious Diseases, NIH-National Institutes of Health, Trustees of Tufts College, Trustees of Tufts College, NIH-National Institutes of Health, Helen Hay Whitney Foundation, The, Regents of the University of Michigan, President and Fellows of Harvard College, NIH-OD Office of the Director
rDNA: Yes	
Process Type: Laboratory Amendment	**Animal Study:** Yes
Laboratory Amendment Summary The goal of this scientific amendment is to add a culture method for *Babesia microti*, using malaria culture techniques and media. Blood from subjects with acute babesiosis will be inoculated into malaria cell culture media overlaid on human red blood cells, with *Plasmodium falciparum* used as a positive control. The work involves handling human samples potentially infected with *B. microti*, as well as isolated *B. miyamotoi* and *P. falciparum*. **Meeting Discussion** The reviewer presented a detailed summary of the proposed scientific amendment and requested the Lab update the Occupational Health Form of the protocol to include a post-exposure prophylaxis for work with *Plasmodium*. The committee did not have any questions and voted to approve provided the Lab addresses the reviewer's request. **Containment** Biosafety Level 2 (BL2) containment and laboratory practices and procedures are required for the culture, use, and handling of human source materials, *Babesia microti* and *Borrelia miyamotoi*, culturing *Plasmodium falciparum*. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.	
Vote: (Admin Review) For: (21), Against: (0), Abstained: (0)	

Brush cell mediated sensing of allergens 2020B000101	
Participating Site(s): BWH	**Sponsor:** NIH-NIAID National Institute of Allergy and Infectious Diseases, American Academy of Allergy, Asthma and Immunology, NIH-NIAID National Institute of Allergy and Infectious Diseases, NIH-NIAID National Institute of Allergy and Infectious Diseases, NIH-NIDCD National Institute on Deafness and Other Communication Disorders

rDNA: No	
Process Type: Laboratory Five Year Resubmission	**Animal Study:** Yes
Five-Year Resubmission Summary The goal of this research is to investigate how allergens and epithelial damage interfere with airway mucosal repair and contribute to chronic inflammation and olfactory dysfunction. The study focuses on brush and tuft cells and their role in generating cysteinyl leukotrienes (CysLTs) in response to allergens and viral infections. Mouse models are used to study viral inflammation through intranasal inoculation with Influenza A/PR8 and Sendai virus, and allergic skin inflammation through epicutaneous sensitization with dust mite extract and SEB. Human samples, including nasal epithelial fluid and mucosal scrapings frompatients with chronic rhinosinusitis or COVID-19-related olfactory dysfunction, are used to validate findings. This resubmission includes expanded human sampling protocols and adds cell sorting procedures. **Meeting Discussion** The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns, noting that use of non-safety sharps is justified. The committee did not have any questions and voted unanimously to approve without conditions. **Containment** Biosafety Level 2(BL2) containment and laboratory practices and procedures are required for the culture, use, and handling of Influenza A virus (H1N1), Sendai virus, Staphylococcal enterotoxin B, and human source materials. Animal Biosafety Level 2 (BL2-N) containment and husbandry practices and procedures are required for mice administered Influenza A virus (H1N1), Sendai virus, and/or Staphylococcal enterotoxin B. Strict adherence to the OSHA Bloodborne Pathogen Standard is required since human source materials are being manipulated.	
Vote: (Approved) For: (22), Against: (0), Abstained: (0)	

IV. Other Business

Admin Approved report can be found on the Other Business tab of this meeting

Administratively Approved	July 2025 MGB Administrative Actions
Administratively Approved	July 2025 MGB Administrative Approvals
Meeting Minutes	June 28, 2025 MGB IBC Meeting Minutes
Incidents	Incident Discussion
General	FDA Requests Sarepta Therapeutics Suspend Distribution of Elevidys and Places Clinical Trials on Hold for Multiple Gene Therapy Products Following 3 Deaths
https://www.fda.gov/news-events/press-announcements/fda-requests-sarepta-therapeutics-suspend-distribution-elevidys-and-places-clinical-trials-hold Elevidys is an adeno-associated virus vector-based gene therapy using Sarepta Therapeutics, Inc.'s AAVrh74 Platform Technology for the treatment of Duchenne muscular dystrophy (DMD). It is designed to deliver into the body a gene that leads to production of Elevidys micro-dystrophin, a shortened protein (138 kDa, compared to the 427 kDa dystrophin protein of normal muscle cells) that contains selected domains of the dystrophin protein present in normal muscle cells. The product is administered as a single intravenous dose.	
General	Closed - non-recombinant General Business Session