Mass General Brigham

Meeting Minutes

Date: 06/30/2025
Start Time: 2:01 PM
End Time: 3:40 PM
Location: Zoom Meeting

Meeting Chair: Joseph Elkhoury, MD;
Administrative Chair: Ryan Schlimgen, Ph.D;
Members Present: K. Sonntag; J. Healey; T. Kwan; H. Widlund; C. Nascimento; K. Holthaus; T. Spitzer; Y. Xie; H. Wakimoto; S. Walsh; T. Jakobs; K. Joseph; M. Marketon; C. Sanchez Cano; S. Subburaju; A. Gottlieb; M. Bergeron; J. Lemieux; A. Giersch; S. Bromley; M. Hogan; J. Levine; 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

A multicenter Phase 1 double-blind, randomized, sham-controlled dose escalation study to determine safety and tolerability of single dose intrathecal ST-503 gene therapy for refractory pain due to idiopathic small fiber neuropathy (iSFN) **2025B000086**
Participating Site(s): MGH
Process Type: Clinical Trial Initial Application
Biological Agent: ST-503 (AAV9 vector encoding ZFP-TF targeting SCN9A**)**
Summary: This is a Phase 1, first-in-human, double-blind, randomized, sham-controlled, multicenter clinical trial (ST-503¬101) designed to evaluate the safety and tolerability of a single intrathecal dose of ST-503 gene therapy for refractory pain due to idiopathic small fiber neuropathy (iSFN). ST-503 is a replication-defective recombinant AAV9 vector carrying a zinc finger protein-transcription factor (ZFP-TF) designed to repress the SCN9A gene, which encodes the Nav1.7 sodium channel involved in pain signal transmission. The biological agent is administered via lumbar puncture and is expected to reduce neuropathic pain by decreasing Nav1.7 expression in sensory neurons. The study will enroll approximately 27 participants across 10–12 U.S. sites, with 1 subject expected at Massachusetts General Hospital (MGH). The trial includes extensive safety monitoring, vector DNA shedding analysis, and assessments of pain, quality of life, and immune response. The biological agent is manufactured by the sponsor and is prepared and administered by trained staff.
Meeting Discussion: The reviewer presented a detailed summary of the proposed clinical registration and did not have any biosafety concerns. The committee did not have any questions and voted unanimously to approve without conditions.
NIH Citation: III-C
Vote: (Require BSO Review) For: (20), Against: (0), Abstained: (0)
A phase 1 clinical trial to evaluate the safety and immunogenicity of the V3-region directed immunogens DV700P-RNA (prime) followed by DV701B1.1-RNA (boost) in adult participants without HIV (HVTN 321) **2025B000083**
Participating Site(s): BWH

Process Type: Clinical Trial Initial Application

Biological Agent: DV700P-RNA (prime), DV701B1.1-RNA (boost)

Summary:
This is a Phase 1, first-in-human, open-label, multicenter clinical trial (HVTN 321) designed to evaluate the safety and immunogenicity of two investigational mRNA-based HIV vaccines: DV700P-RNA (prime) and DV701B1.1-RNA (boost). These vaccines encode modified HIV-1 gp150 Env trimers and are delivered via lipid nanoparticle (LNP) formulations. The gp150 design reduces binding of non-neutralizing base-binding antibodies that occur with gp140 SOSIP trimers. This design is very similar to the gp160-encoded RNAs in trial HVTN 312, but the encoded gp150 protein lacks the cytoplasmic tail portion of the Env sequence that is included in the gp160 sequence. The gp150 design has enhanced cell surface expression relative to gp160. Each dose is administered as a bilateral split dose in each deltoid. There are three different dose levels with a pause in enrollment after the first five participants at each dose. The study will enroll 45 healthy, HIV-negative adults aged 18–55 across multiple U.S. sites, including Brigham and Women's Hospital (BWH). Participants will receive three doses of DV700P-RNA followed by one dose of DV701B1.1-RNA over a 10-month period with follow-up extending to 16 months. The trial includes extensive safety monitoring, leukapheresis, and lymph node fine needle aspiration to assess immune responses. The biological agent is manufactured by Evonik Canada Inc. and provided by Duke Human Vaccine Institute. The vaccine will be stored and prepared by the Investigational Drug Service. It will be administered by trained and licensed study staff clinicians in the Clinical Trials Center. The study hopes to enroll 15 participants at BWH.

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

NIH Citation: III-C

Vote: (Require BSO Review) For: (20), Against: (0), Abstained: (0)

PAH and vascular remodeling
2024B000018

Participating Site(s): BWH

Process Type: Laboratory Initial Application

Human Source Materials: Plasma, Primary Cells, Cell Lines

Viral Vectors: Adenoviral vectors, Adeno-associated viral vectors

rDNA: c-terminal src-kinase, GFP

Animals: Rodents – AAV1, siRNA (BWH IACUC - 2019N000236, 2016N000401, 2025N000057)

Containment Level: BL1, BL2, BL1-N

Summary:
The goal of this research is to understand the molecular mechanisms underlying pulmonary arterial hypertension (PAH), particularly the role of C-terminal Src kinase (Csk) dysfunction and its impact on vascular remodeling. The study involves in vitro work using purchased human pulmonary artery endothelial cells (PAECs), smooth muscle fibroblasts, and HEK 293 cells, as well as plasma samples and fixed tissues from PAH patients. These materials will be manipulated using adenoviral and adeno-associated viral (AAV) vectors encoding human or rat Csk and GFP controls. In vivo studies include the administration of siRNA and AAV vectors to rats and genetically modified mice (Col22A1 knockout and floxed strains) to model early PAH. Procedures include intratracheal instillation, cardiac catheterization, and tissue harvesting. All work involving viral vectors and human materials will be conducted under BSL-2 conditions with appropriate PPE and engineering controls.

Meeting Discussion:
The reviewer presented a detailed summary of the proposed laboratory registration and requested the Lab review and revise the Detailed Research Plan so that the study goals, technical procedures, and materials are succinctly described. After a brief discussion, the committee voted unanimously to approve with the condition the Lab will address the reviewer's requests.

NIH Citation: III-D, III-E

Vote: (Require BSO Review) For: (20), Against: (0), Abstained: (0)

Epidermal Organoid Generation
2025B000073

Participating Site(s): MGH

Process Type: Laboratory Initial Application

Human Source Materials: Cell Lines

Viral Vectors: Lentiviral vectors

rDNA: GFP

Animals: Mice – rodent and human cells (MGH IACUC)

Containment Level: BL1, BL2, BL1-N, BL2-N

Summary:
The goal of this research is to model and understand how epidermal cells differentiate and how cell–cell interactions influence skin development using both human and animal cell lines. The study employs a variety of established cell lines. Lentiviral vectors will be used to introduce fluorescent reporters (e.g., EGFP) for lineage tracking, and CRISPR/Cas9 will be used to knock out the p63 gene in selected cell lines to study its role in epidermal differentiation. Co-culture experiments will be conducted to observe differentiation dynamics, and modified cells will be introduced into mouse embryos to generate chimeric animals for in vivo analysis.

Meeting Discussion:
The reviewer presented a detailed summary of the proposed laboratory registration and requested the Lab provide the exact clone names and sources of the hESC and hiPSC lines. Additionally, the reviewer requested that the Lab review the protocol to ensure consistency, specifically when referencing the use of Addgene, pKK-TEV-EGFP. Following a brief discussion, the committee voted unanimously to approve with the condition the Lab will address the reviewer's requests.

NIH Citation: III-D, III-E

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

Develop of novel therapies against bladder cancer
2025B000075

Participating Site(s): BWH

Process Type: Laboratory Initial Application

Human Source Materials: Cell lines

Infectious Agents: *Salmonella enterica* serovar *Typhimurium*

rDNA: GFP, luciferase

Whole Animals: Mice – infectious agents, human cells (BWH IACUC)

Containment Level: BL1, BL2, BL1-N, BL2-N

Summary:
The goal of this research is to develop a bladder cancer-specific attenuated Salmonella platform (SPRINT) that integrates photodynamic diagnosis (PDD), photodynamic therapy (PDT), microbiotherapy, and local immunotherapy. The SPRINT strain expresses a bladder cancer-targeting peptide (PLZ4), a red fluorescent protein (KillerRed), and an immunotherapy protein, and is dependent on arabinose, rhamnose, and mannose for survival—nutrients absent in mammalian tissues. The study involves culturing and administering various Salmonella strains, including controls, to murine models via bladder instillation, oral gavage, or intravenous injection. Human and murine bladder cancer cell lines, including genetically modified lines expressing GFP and luciferase, will be used to establish tumor models. Transgenic mice expressing SV40T and K-Ras will also be used.

Meeting Discussion:
The reviewer presented a detailed summary of the proposed laboratory registration and requested the corresponding animal protocol and animal facility where mice will be housed be linked. Additionally, the reviewer requested that the Lab list Salmonella as BL2 for both routes of administration and to separate murine cells (approved at BL1/BL1-N) from human cells (approved at BL2/BL2-N). Following a brief discussion, the committee voted unanimously to approve with the condition that the Lab will address the reviewer's requests and update the protocol accordingly.

NIH Citation: III-D

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

Targeted mitochondria transplantation to human monocytes
2025B000082

Participating Site(s): MGH

Process Type: Laboratory Initial Application

Human Source Materials: Blood, Serum, Primary Cells, Cell Lines

rDNA: DsRed

Containment Level: BL1, BL2

Summary:
The goal of this research is to develop immunomodulatory strategies to generate monocytes capable of resolving inflammation and maintaining tissue homeostasis. The study involves isolating monocytes from human blood. Monocytes will also be treated with inflammation-resolving mediators (e.g., resolvins), sepsis

mimetics (e.g., LPS, Pam3CysSK4), and heat-killed *E. coli* and *S. auereus* to assess functional and phenotypic changes.

Meeting Discussion:
The reviewer presented a detailed summary of the proposed laboratory registration and requested the Lab review the Use of rDNA form to state that all genetically modified biological materials are obtained already modified, confirm that the gene or target sequence will be transcribed into RNA, and reflect the use of the MITO-DSRED plasmid. Following a brief discussion, the committee voted unanimously to approve with the condition the Lab will address the reviewer's request.

NIH Citation: III-E

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

Diagnosis, characterization, and treatment of sexually transmitted and bloodstream infections
2025B000076

Participating Site(s): MGH

rDNA: Yes

Process Type: Laboratory Initial Application

Human Source Materials: Blood, serum, primary cells, cell lines, urine, respiratory samples

Infectious Agents: *Neisseria gonorrhoeae, Neisseria meningitidis, Neisseria subflav, Escherichia coli, Bacillus subtilis, Klebsiella spp., Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium, Haemophilus influenzae, Acinetobacter baumannii, Streptococcus pyogenes, Streptococcus agalactiae* (Group B), *Streptococcus pneumoniae*

rDNA: *B. subtilis* (alrA and lptA)

Containment Level: BL1, BL2

Summary:
The goal of this research is to improve the diagnosis and treatment of bloodstream and sexually transmitted infections by developing rapid diagnostics, characterizing host-pathogen interactions, and discovering novel antimicrobials. The lab will extract nucleic acids from bacterial isolates and clinical samples (e.g., urine, swabs, blood, tissues) to develop and validate diagnostic tests, characterize microbiomes and host responses, and assess antimicrobial susceptibility to existing and new antibiotics. Bacterial isolates will be cultured and tested against candidate antibiotics, and cytotoxicity will be evaluated using human cell lines and primary cells. A CRISPRi knockdown library in Bacillus subtilis will be used for drug target discovery, and Neisseria gonorrhoeae will be genetically modified using natural transformation and inducible CRISPRi to validate antimicrobial targets.

Meeting Discussion:
The reviewer provided 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.

NIH Citation: III-D, III-E

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

CysLT1 and P2Y Receptors in Lung Inflammation
2011B000056

Participating Site(s): BWH

rDNA: Yes

Process Type: Laboratory Amendment

Human Source Materials: Cell Lines

Viral Vectors: Lentiviral vectors

rDNA: Cysltr1, Cysltr1, Ep1, Ep2, EP3, EP4, Gbeta, Ggamma, cAMP glosensor, RTK

Whole Animals: Mice –allergen (BWH IACUC - 2016N000294, 2016N000295)

Containment Level: BL1, BL2, BL1-N

Summary:
This amendment adds new recombinant DNA constructs to be transfected into HEK293 cells, including allergy-relevant GPCRs and signaling biosensors (e.g., cAMP GloSensor, NanoBiT reporters) for evaluating ligand-specific downstream signaling pathways. The overall goal of this project is to understand how the P2Y6 receptor suppresses inflammation in the respiratory tract, with the aim of improving our understanding and treatment of asthma. The added constructs are used to pharmacologically profile and functionally characterize GPCRs, particularly canonical G protein and non-canonical Gβγ-mediated signaling. The amendment also includes the use of lentiviral vectors (pLenti6/R4R2V5-DEST) to deliver shRNA targeting

CysLT1 receptor, P2Y6 receptor, and protein kinase C into human and mouse cells in vitro. These experiments aim to suppress gene expression and assess the function of these targets in dendritic cell activation and maturation.

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

NIH Citation: III-D, III-E

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

Porphyria research group laboratory protocol
2024B000156

Participating Site(s): MGH

Process Type: Laboratory Amendment

Human Source Materials: Cell lines

Viral Vectors: Lentiviral vectors

rDNA: genome-wide screening, gene knockouts, point mutations for genes involved with heme biosynthesis, erythroid regulation, iron metabolism, and oxidative stress response

Containment Level: BL2

Summary:
This amendment adds CRISPR-Cas9 editing experiments to the protocol, including both targeted editing and pooled genome-wide knockout screening. The overall goal of this project is to understand the mechanisms of disease in porphyria, develop quantitative biomarkers of disease severity, and identify genetic modifiers of disease penetrance, expression, and treatment response. Editing will be performed in primary human $CD34^+$ hematopoietic stem/progenitor cells and K562erythroleukemia cells using electroporation of CRISPR-Cas9 ribonucleoprotein complexes or lentiviral transduction. The amendment also includes the use of K562 cells obtained from a collaborator at Boston Children's Hospital that were edited using the same methods.

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

NIH Citation: III-D

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

Recombinant extracellular vesicles (rEV)
2019B000064

Participating Site(s): MGH

Process Type: Laboratory Five Year Resubmission

Human Source Materials: Cell Lines

rDNA: EGFP

Containment Level: BL1, BL2

Summary:
This resubmission continues research on the development of nanoplasmonic biosensors (nPLEX) for detecting and analyzing extracellular vesicles (EVs). The biosensors use nanohole arrays in gold films to amplify optical signals from EVs captured on the sensor surface. Because EVs are too small for conventional microscopy and lack universal fluorescent markers, the lab uses recombinant extracellular vesicles (rEVs) engineered to express GFP, which are received from collaborators. These rEVs are used to calibrate and validate the sensor system. The study also uses HEK293T cells engineered with a lentiviral vector to express GFP on the EV membrane, and LwaCas13a for RNA detection. These materials are received pre-modified and are not produced in-house. Changes since the initial registration include the use of a new HEK293 cell line engineered with a lentiviral vector to express GFP on the membrane and the addition of LwaCas13a for EV RNA detection using a plasmid obtained from Addgene.

Meeting Discussion:
The reviewer summarized the five-year resubmission and did not have any biosafety concerns. After a brief discussion, the committee did not have any questions and voted unanimously to approve without condition.

NIH Citation: III-E

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

COVID19 virus studies 2020B000058
Participating Site(s): MGH
Process Type: Laboratory Five Year Resubmission
Human Source Materials: Blood, Serum, Cell Lines, Saliva, BAL, Nasopharyngeal swabs, Unfixed Tissue, Saliva, CSF
Viral Vectors: Lentiviral vectors, VSV
rDNA: Spike proteins from SARS-CoV-2, SARS, MERS, OC43, NL63, HKU
Animal Materials: NHP Cell Lines
Containment Level: BL1, BL2
Summary: This resubmission continues research on COVID-19 virus studies using systems serology to investigate the role of antibodies and innate immunity in protection and survival during SARS-CoV-2 infection. The lab performs high-throughput functional and biophysical profiling of antibody responses using human, non-human primate (NHP), and mouse samples. These include blood, serum, PBMCs, respiratory samples, saliva, and cerebrospinal fluid from individuals infected with or vaccinated against SARS-CoV-2. The lab also produces replication-defective HIV and VSV pseudo-particles bearing beta-coronavirus spike proteins for use in neutralization assays.
Meeting Discussion: The reviewer presented a detailed summary of the five-year resubmission and did not have any biosafety concerns. The IBC Director noted that although the Lab operates at BL2+, the activities described in this registration are appropriate for BL2 containment and recommended approval at BL2. Following a brief discussion, the committee voted unanimously to approve the registration at BL2.
NIH Citation: III-D, III-E
Vote: (Admin Review) For: (22), Against: (0), Abstained: (0)
Reprogrammed cellular models of psychiatric disorders 2016B000024
Participating Site(s): MGH
Process Type: Laboratory Five Year Resubmission
Human Source Materials: Blood, Cell Lines
Viral Vectors: Lentiviral vectors, Adeno-associated viral vectors
rDNA: Ascl1, Brn2, Myt1L, miR9/124, ND2, Sox2, FoxG1, hHes1, Ngn2, PPARG2, Nlg, Nrx, GCaMP
Toxin: Tetrodotoxin
Animal Materials: NHP Cell Lines
Animals: Mice – human cells (MGH IACUC 2022N000078)
Containment Level: BL2, BL2+, BL2-N
Summary: This resubmission continues studies on cellular models of psychiatric disorders to better understand their biochemical mechanisms and discover therapeutic options. The lab reprograms and differentiates patient-derived fibroblasts and PBMCs into neuronal and glial cell types to study disease phenotypes and drug responses. Techniques include lentiviral and AAV vector transduction, CRISPR/Cas9 genome editing, and calcium imaging using GCaMP sensors. The lab also performs genome-wide CRISPR screens to identify genes involved in microglial phagocytosis and synaptic pruning, with a focus on schizophrenia-related pathways such as CSMD1 and C4 opsonization. Human PBMC-derived microglia are tested in vivo by injection into immunocompromised mice to assess brain integration. Comparative studies are also conducted using chimpanzee iPSC-derived microglia to explore evolutionary differences in disease mechanisms.
Meeting Discussion: The reviewer presented a detailed summary of the registration and did not have any biosafety concerns. The reviewer requested the Lab administratively update the Use of Viral Vectors form to confirm that BL2+ practices are used for working with viral vectors. Following a brief discussion, the committee voted unanimously to approve provided the Lab addresses the reviewer's request.
NIH Citation: III-D, III-E
Vote: (Admin Review) For: (22), Against: (0), Abstained: (0)

CMV Induced Transcriptional Networks & Regulation of Innate Immunity in Solid Organ Transplantation 2014B000062
Participating Site(s): MGH
Process Type: Laboratory Five Year Resubmission
Human Source Materials: Blood, Serum, Cell Lines, Unfixed tissues, Stool
Infectious Agents: Cytomegalovirus
Viral Vectors: Lentiviral vectors
rDNA: GFP, mCherry, CMV constructs
Containment Level: BL1, BL2
Summary: This resubmission continues research on the effects of cytomegalovirus (CMV) infection on innate immune function in the context of solid organ and bone marrow transplantation. The lab uses recombinant CMV strains (engineered to express fluorescent proteins) to infect human monocyte cell lines and primary cells, including PBMCs and iPSC-derived myeloid cells. The goal is to define transcriptional, proteomic, and functional changes in infected cells and to identify host dependency factors for CMV replication. Techniques include lentiviral CRISPR/Cas9 screening, flow cytometry, single-cell RNA-seq, and macrophage functional assays.
Meeting Discussion: The reviewer summarized the five-year resubmission and did not have any biosafety concerns. After a brief discussion, the committee did not have any questions and voted unanimously to approve without condition.
NIH Citation: III-D, III-E
Vote: (Approved) For: (21), Against: (0), Abstained: (0)

IV. Other Business:

Meeting Minutes	May 2025 MGB IBC Meeting Minutes
The committee reviewed and unanimously approved the May 2025 Meeting Minutes.	
General	Closed - non-recombinant General Business Session
The IBC Chair invited committee members to a closed session to discuss non-recombinant committee business.	
Administratively Approved	June 2025 MGB IBC Administrative Approvals
The committee reviewed the June 2025 MGB IBC Administrative Approvals without comment.	
Administratively Approved	June 2025 MGB IBC Administrative Actions
The committee reviewed the June 2025 MGB IBC Administrative Actions without comment.	
Policy	Viral Vector Discussion
Dr Schlimgen discussed the *NIH Guidelines* classification of viral vectors, informing them of the section of the *NIH Guidelines* that viral vectors belong to.	
General	Mass General to Serve as Authorized Treatment Center for First Gene Therapy for Sickle Cell Disease - Exa-cel
Dr. Schlimgen shared a recent article highlighting the FDA-approved, non-research use of gene therapy for the treatment of Sickle Cell Disease at Massachusetts General Hospital (MGH). This example illustrates how gene therapy protocols previously reviewed and approved by the IBC are now being implemented in clinical care settings. https://advances.massgeneral.org/research-and-innovation/article.aspx?id=1556	