IBC Meeting Minutes
December 18, 2025 (Thursday) at 11:00 A.M.
via Zoom Conference Bridge

IBC members present:

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

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

*RK- Left at 11:15am
**RML- Joined 11:30
***ER- Left at

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 November 20, 2025 Meeting Minutes**

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

Past Incidents that remain open:

1) 05/21/2025: BSL-3 PAPR incident. One person (who later traveled to Africa) had conversion of IGRA test. LTBI treatment
2) 07/08/2025: Needlestick in BSL-3. Potential TB exposure. 6-month follow-up
3) 10/23/2025: broken/cut skin under glove – while working with HIV infected cells – plastic or glass shard. Molecular clones of HIV (rNA). Fisher glove lot with defects. Reported to NIH. Opted for PEP
4) 11/05/2025: Issue reported – researcher cleaned up after working with pseudotyped lentivirus vectors without gloves last year sometime. Reported to NIH.

Recent incidents:

1) 11/24/2025: Mouse bite. Mouse with human PBMC xenotransplant. Source negative for BBP.
2) 11/26/2025: BSL-3 lab. 96 well plate incomplete sterilization. Wet sleeve noted. Repeat screening planned
3) 12/08/2025: Deep clean of lab. BSC pan with some tips and debris. Noted cut on finger after cleaning. BSC had been used for HIV (incl molecular clones) and HHV-6 work. Reported to NIH. Opted for PEP

- Year in review 19 events, down from the year before. Meeting with biosafety team and EHS- improved protocols. Productive year to improve

III. Protocols Reviewed Administratively

1) Investigator: Cecchini, S
   Title: Recombinant Adeno-Associated Viral Vector Large Scale Production
   IBC Registration: I-751-25, Amendment
   Training Verification: Acceptable

Brief Summary: We continue to produce rAAV at large scale at UMMS to help researchers to determine the best clinical candidate, we produce rAAV in suspension cell culture using max of 2 x 200L bioreactor scale. We can achieve production of 10e14 vg to 10e16 vg per run depending on the volume of the bioreactor used. Using two suspension systems: HEK293 cells and insect cells Sf9

- Producing rAAV of high quality and purity
- Clinical material from non-GMP environment

Qualification of vialing workflow, environment, and personnel practices and to provide robust sterility assurance during the operations. Growth-supporting media will be used to qualify a sterile vialing process ensuring the system reliability to detect potential microbial contamination. by confirming the media's ability to support recovery of standard challenge organisms.

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

2) Investigator: Parada, X
Title: Alexion IGAN-320
IBC Registration: **I-929-25, New**
Training Verification: Acceptable pending completion of PI training
Brief Summary: Ravulizumab (ALXN1210) is a long-acting C5 complement inhibitor under investigation for reducing proteinuria and slowing kidney function decline in adults with IgA nephropathy (IgAN). The study evaluates the efficacy and safety of ravulizumab versus placebo in a Phase 3, multicenter clinical trial.
Objectives:

- Evaluate efficacy of ravulizumab compared with placebo on proteinuria (interim endpoint).
- Evaluate efficacy of ravulizumab compared with placebo on eGFR decline (final endpoint).
- Assess safety, PK/PD, and immunogenicity.
- Assess kidney biomarkers and patient-reported outcomes.

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

3) Investigator: Zhou, W
Title: Immune Regulation in Intestinal Physiology, Inflammation, and Diseases
IBC Registration: **I-918-25, Amendment**
Training Verification: Acceptable
Brief Summary: The gastrointestinal (GI) tract plays an essential role in our overall health and well-being. It contains one of the largest immune systems which promotes tolerance to the nonharmful microbiota and protects against infection. However, dysregulated immune response drives numerous diseases. The goal of this project is to dissect, at the cellular and molecular level, 1) how immune homeostasis is achieved in the gut; 2) how dysregulation of these pathways impacts health and disease, and 3) how we can harness approaches to reinstate gut homeostasis, treat human diseases, and advance healthy life span.
To translate the findings from mouse models to humans, human gut biopsy or resection samples and feces will be used to investigate the immune response in gut health, inflammation, and diseases.

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

IV. Protocols to Discuss

1) Investigator: Flavahan, W
Title: Epigenetic Plasticity and Tumor Initiation and Progression
IBC Registration: I-781-25, Renewal
Training Verification: Acceptable pending completion of PI training
Brief Summary: Cancer is traditionally thought to be driven by genetic alterations to growth and tumor-suppressing pathways. This project seeks to characterize methods where epigenetic alterations, involving changes to the storage and chemical modifications made to the genome rather than its direct sequence, can affect the initiation and progression of cancer. Specifically, this project is interested in ways that defects in epigenetic silencing of potentially functional genetic elements can lead to aberrant gene reactivation, or how defects in epigenetic spatial compartmentalization of the genome can lead to gene activation, and how we can develop new sequencing technologies to characterize these changes.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This project seeks to characterize methods where epigenetic alterations, involving changes to the storage and chemical modifications made to the genome rather than its direct sequence, can affect the initiation and progression of cancer. Specifically, the investigator focuses on three main areas:

1) How defects in epigenetic silencing of potentially functional genetic elements result in aberrant gene reactivation.
2) How defects in epigenetic spatial compartmentalization of the genome lead to gene activation
3) How novel sequencing technologies can be developed to characterize these changes

Experimental Approach: This project seeks to understand the epigenetic changes in cancer cells using several methods:

1) Growth and manipulation of cancer cell lines. Genome editing will be done using CRISPR-Cas9 and related technologies.
2) Lentiviral delivery.
3) Characterization of human surgical specimens.
4) Detection of nucleic acid modifications in RNA and DNA using nanopore sequencing.
5) Construction of an in vitro metabolite biosensor using dCas9-based molecular sensor of epigenetically-relevant metabolites.

IBC Discussion and Vote

Discussion: Reviewer discussed that the renewal was well written and well described.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2+ as described in registration; BSL-2 Enhanced Flow Sorting**
NIH Guidelines: III-D, III-F

2) Investigator: Golenbock
Title: Toll Receptors in Health and Disease
IBC Registration: I-227-25, Renewal
Training Verification: Acceptable pending completion of PI training
Brief Summary: The overall goal of our laboratory is to understand how the innate immune system senses and responds to viral, bacterial, fungal, and parasitic pathogens. The main objective of these studies is to examine basic principles of the immune response to infection both in vitro and by manipulating the mouse model.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: Broadly, to understand how the innate immune system senses and responds to viral, bacterial, fungal, and parasitic pathogens. The main objective is to examine basic principles of the immune response to infection both in vitro and by manipulating the mouse model.

Experimental Approach: Using a combination of biochemical, molecular and genetic approaches to identify receptors and signaling molecules important in the innate immune response.
A combination of shRNA/siRNA approaches in human cell lines and mouse cell lines as well as the use of cells from mice with targeted deletions in these components will be used.
Live bacteria, live or UV inactivated viruses, fungi, and pathogen-derived products like lipopolysaccharide (LPS) will be used to treat cells in vitro. Downsteam assays examine activation of signal transduction pathways, transcription factor activation, and cytokine production in vitro or cells ex vivo. Additionally, disease models will be used to monitor the role of innate receptors/signaling molecules in vivo
For transgenic animals, ES cells from KOMP of with genes of interest targeted will be purchased, and these ES cells will be directly delivered to the transgenic core for generating gene targeted mouse strains. CRISPR technology will be used to synthesize gRNA and mRNA encoding Cas9 enzyme and generate mouse strains using the transgenic core's pronuclear injection.
For RNAi core, verified cDNA expression or shRNAs plasmids will be purchased from Thermo Scientific company which is made available to us through the UMASSMED freezer system/RNAiCore. Lentiviral based replication defective vectors expressing shRNA will be packaged with VSVg to transduce mouse immortalized macrophage cell lines or human cell lines. Adeno-associated viral plasmids or viral particles expressing gene of interest will be used for in vivo experiments with mouse models.
The CRISPR core will be used to design and construct the plasmids for deletion of gene of interest, and transfect into human THP1 cell line by electroporation.
The Flow core will be used to sort unfixed human, non-human primate, mouse cells / cell lines labeled with cell surface antibodies for cell population separation or cells infected with Plasmodium. Unfixed cells transfected or transduced with vectors expressing genes of interest will be sorted.
Mice infected with Plasmodium will be imaged.

IBC Discussion and Vote

Discussion: Reviewer discussed that the lab needs to verify that they no longer have plans to work with SARS CoV-2 or other corona virus work. Reviewer discussed the action items.
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

3) Investigator: Ionete, C
Title: Multiple Sclerosis Center Research Specimen Processing Lab
IBC Registration: **I-653-25, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The Multiple Sclerosis Center at university campus has a research lab that is used for clinical research protocols. Detect biomarkers of accurate MS diagnosis, detect biomarkers of MS activity.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The Multiple Sclerosis Center at university campus research lab is used for clinical research protocols to detect biomarkers of accurate MS diagnosis, and MS activity.

Experimental Approach: Human samples of blood, urine, stool, cerebrospinal fluid, and nasal swabs are processed within the lab. Samples may be clotted, spun, aliquoted and frozen or shipped immediately depending on the needs of the protocol. Human samples may be preparded for flow cytometry and stored for further biomarker analysis

IBC Discussion and Vote

Discussion: Reviewer discussed that this could have been reviewed administratively. Reviewer discussed the few action items.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2**
NIH Guidelines: **N/A**

4) Investigator: Khanna, H
Title: Pharmacology and mechanism of action of oligonucleotides-based therapies for retinal degeneration
IBC Registration: **I-449-25, Renewal**
Training Verification: Acceptable pending completion of PI training
Brief Summary: The project aims to investigate the pharmacokinetics of an ocular therapy administered via injection to the eye in rabbits, focusing on the absorption, distribution, metabolism, and excretion of the drug within the ocular tissues. By analyzing the drug's behavior over time, we seek to optimize its therapeutic efficacy and safety for potential clinical applications in treating ocular conditions.

Brief Summary and Review by Primary Reviewer

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

Experimental Approach: The experimental approach involves administering a therapeutic modality via ocular injection. Following the treatment, the animals will be euthanized at varying time points. The eyes will be dissected and processed for sectioning or for pharmacokinetic analysis.

IBC Discussion and Vote

Discussion: Reviewer discussed that the PI should provide better descriptions of the therapeutic modality is and it's biological function.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-1; ABSL-1**
NIH Guidelines: III-D, III-F

5) Investigator: Ram, S
Title: Complement activation and strategic design of Immunotherapeutics and vaccines against mucosal pathogens
IBC Registration: **I-315-25, Renewal (combining with the Rice I-253-20)**

Training Verification: Acceptable

Brief Summary: The emergence of ceftriaxone-resistance Neisseria gonorrhoeae (Ng) and threat of untreatable gonococcal infection have stimulated the need for novel therapeutics and vaccines against this organism and we have identified a bactericidal epitope of gonococcal lipooligosaccharide (LOS), the 2C7 epitope, that is a candidate vaccine target. Outer membrane vesicles of N. meningitidis (Nm) are currently used in licensed meningococcal vaccines and our study aims to test the efficacy of outer membrane vesicles prepared from strains of Nm that express gonococcal antigens including the 2C7 epitope (as LOS or as a peptide that mimics the 2C7 LOS epitope) for use as a combined vaccine against gonorrhoeae and meningitis. Complement inhibitors (antibodies or peptide inhibitors) are used therapeutically to treat numerous disease states (e.g. autoimmune diseases such as cold agglutin disease or paroxysmal nocturnal hemoglobinuria), however these antibodies interfere with activation of the complement and thus also dampen the ability of the immune system to kill invading microorganisms. Complement is required for efficient killing of Nm and Streptococcus pneumoniae (Sp) and we will determine the impact of complement inhibitors on complement activation in vitro by evaluating deposition of complement (C4b, C3b and MAC), direct complement-mediated killing and opsonophagocytic killing. Nontypeable Haemophilus influenzae (NTHi) continues to be a significant health burden causing a substantial portion (~30-50%) of acute otitis media and sinusitis in children and our studies are aimed at examining the interactions of complement with NTHi with the ultimate goal of developing rational and effective therapeutics.

Neisseria gonorrhoeae (*Ng*) is the causative agent of over 100 million new cases of gonorrhea each year, worldwide and the emergence of ceftriaxone-resistance and threat of untreatable gonococcal infection have prompted the need for novel therapeutics and vaccines against this organism. We have developed a novel vaccine that uses a peptide mimic (mimotope) to target the 2C7 epitope of gonococcal lipooligosaccharide (LOS) and our studies aim to (1) optimize the formulation of the 2C7 mimotope as a vaccine and advance this product through phase 1 studies, (2) understand the mechanism of action of the vaccine and gonococcal clearance (3) test the efficacy of this vaccine in various situations (e.g. different strains, co-infections) to ensure robust and broad coverage and (4) to explore novel vaccine platforms and antigen combinations that may improve vaccine effectiveness over the current lead formulation.

Our lab also currently aims to explore the utility of novel anti-gonococcal therapeutics that function by activating complement on the gonococcal surface and / or by thwarting the ability of *Ng* to evade complement mediated killing. Specifically, we are evaluating the mechanism of action and efficacy of (1) chimeric and humanized forms of mAb 2C7 that binds to Ng and activate complement on the cell surface, (2) novel immunotherapeutic molecules comprised of portions of human FH fused to IgG Fc (Fh/Fc) that block binding of FH and activate complement, and (3) novel analogs of sialic acid that specifically block the ability of gonococci to resist killing by complement in serum.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: The overall objective is the development of novel therapeutics and vaccines against Neisseria gonorrhoeae (Ng). A novel vaccine that uses a peptide mimic (mimotope) to target the 2C7 epitope of gonococcal lipooligosaccharide will be optimized including mechanism of action. The lab will also explore novel anti-gonococcal therapeutics that function by activating complement on the gonococcal surface and / or by thwarting the ability of Ng to evade complement mediated killing.

Experimental Approach: The proposed studies will (1) optimize the formulation of the 2C7 mimotope as a vaccine and advance this product through phase 1 studies, (2) understand the mechanism of action of the vaccine and gonococcal

clearance (3) test the efficacy of this vaccine in various situations (e.g. different strains, co-infections) to ensure robust and broad coverage and (4) to explore novel vaccine platforms and antigen combinations that may improve vaccine effectiveness over the current lead formulation.
The lab will also explore the utility of novel anti-gonococcal therapeutics that function by activating complement on the gonococcal surface and / or by thwarting the ability of Ng to evade complement mediated killing. Specifically, the mechanism of action and efficacy of (1) chimeric and humanized forms of mAb 2C7 that binds to Ng and activate complement on the cell surface, (2) novel immunotherapeutic molecules comprised of portions of human FH fused to IgG Fc (Fh/Fc) that block binding of FH and activate complement, and (3) novel analogs of sialic acid that specifically block the ability of gonococci to resist killing by complement in serum will be explored.

IBC Discussion and Vote

Discussion: Reviewer discussed that this is combining two separate IBC protocols. In the process of combining the Rice I-253-20 and Ram I-315-25 protocols, the lab copied and pasted a lot of unnecessary information including grant information. The lab is very experienced and very careful. The SOP's submitted were recently updated. An IBC member noticed a discrepancy in one of the animal addenda submitted that will require modification.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-2+; ABSL-2**
NIH Guidelines: III-D, III-E, III-F

6) Investigator: Thomson, T
Title: The Role of Transposable Elements in Physiological Processes.
IBC Registration: **I-930-25, New**
Reviewer: Greenough
Training Verification: Acceptable pending completion of PI training
Brief Summary: Use Drosophila and cell culture to measure transposon activity in tissue

Brief Summary and Review by Primary Reviewer

Overview and Objectives: To use Drosophila and cell culture to measure transposon activity in tissue.
How retrotransposons are selected and domesticated by host organisms to modulate synaptic plasticity is largely unknown. The Ty1 retrotransposon, Copia, forms virus-like capsids in vivo and transfers between cells. Copia is enriched at the Drosophila neuromuscular junction (NMJ) and transported across synapses, and disrupting its expression promotes both synapse development and structural synaptic plasticity. Proper synaptic plasticity is maintained in Drosophila by the balance of Copia and the Arc1 (activity-regulated cytoskeleton-associated protein) homolog. High-resolution cryogenic-electron microscopy imaging shows that the structure of the Copia capsid has a large capacity and pores like retroviruses but is distinct from domesticated capsids such as dArc1.

Experimental Approach: Most of the experiments revolve around putting exogenous sequences into Drosophila, many of the constructs made are tested in cell culture. Gene sequences are modified and inserted into plasmids The plasmids are tested in cell culture (usually for gene expression). Plasmids are then used to transform flies. Sequences are often tagged with GFP to measure expression and to purify proteins later.
There is no work with vertebrate animals or human sequences.

IBC Discussion and Vote

Discussion: Reviewer discussed the protocol was well written and straightforward. Reviewer discussed action items

Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL-1; ABSL-1**
NIH Guidelines: III-D, III-F

7) Investigator: Uthaman, G
Title: Understanding the regulation of Type II immune responses to Allergens
IBC Registration: **I-784-25, Renewal**
Training Verification: Acceptable
Brief Summary: IgE antibodies are key mediators of allergic disease. IgE can have devastating consequences when it triggers anaphylaxis, a life-threatening allergic reaction. How IgE is induced and maintained to allergens remains one of the major outstanding questions in immunology. Our central research focus is on the biology of two key immune cells (T cells and B cells) that are drivers of allergic responses. The overarching goal of our research is to understand at the cellular and molecular level how these cells of the immune system get activated, carry out their effector functions, and are regulated in allergic responses.

Brief Summary and Review by Primary Reviewer

Overview and Objectives: IgE antibodies are key mediators of allergic disease. IgE can have devastating consequences when it triggers anaphylaxis, a life-threatening allergic reaction. How IgE is induced and maintained to allergens remains one of the major outstanding questions in immunology. The lab's research focus is on the biology of two key immune cells (T cells and B cells) that are drivers of allergic responses. The overarching goal of their research is to understand at the cellular and molecular level how these cells of the immune system get activated, carry out their effector functions, and are regulated in allergic responses.

Experimental Approach: PCR will be performed on DNA obtained from ear punch biopsies of mice. Biopsies are digested in a buffer (10mM Tris, 10mM EDTA, 50mM NaCl, 0.5% SDS+ proteinase K). 2uL of digest is added to a standard PCR amplification kit regent (such as Go Taq Green Master Mix or Qiagen) and PCR is performed.
For qPCR, RNA material is obtained from isolated mouse cells using RNA isolation kits (Zymo) and qPCR will be performed by using iQ SYBR Green Supermix from Bio-Rad. Immunization Materials used are: Allergens (peanut, house dust mite extract, Alternaria alternata extract); TLR agonists (LPS, CPG), Adjuvants (Alum), purified proteins (peanut, ovalbumin), antibodies, toxins (Diphtheria toxin, cholera toxin). Mice will be sensitized with model antigen ovalbumin along with various allergens or immunogens. To induce food allergy cholera toxin will be administered through oral gavage once during allergen exposure. We will be using diphtheria toxin in a very limited number of experiments. The lab has a mouse strain in which a specific population of cells (T cells) express diphtheria toxin receptor (FoxP3-DTR) mouse. To understand the role of this cell in allergy we will administer diphtheria toxin to deplete these cells and test their function in various allergic sensitization.

IBC Discussion and Vote

Discussion: A member of the committee asked if the lab is just doing flow cytometry or flow sorting as this is something that gets confused frequently. The reviewer discussed the registration only mentions cytometry and no sorting.
Meeting Decision: Vote to approve upon completion of action items.
BSL/ABSL: **BSL- 2; ABSL-1; Administration to animals using BSL-2 precautions/sharps safety**
NIH Guidelines: III-E

8) Investigator: Winder, D

Title:	Neurobiology of Stress Reward Interactions
IBC Registration:	**I-881-23, Amendment**
Training Verification:	Acceptable pending completion of PI training
Brief Summary:	To add: 2 canine adenoviral vectors

Brief Summary and Review by Primary Reviewer

Overview and Objectives: This group aims to understand the brain circuits underlying addiction and to identify brain regions that could serve as potential therapeutic targets. Their research focuses on the extended amygdala, a brain region that plays a central role in behavioral responses to drugs of abuse and alcohol. They will examine how specific neural circuits are altered by alcohol exposure and withdrawal and will test the hypothesis that distinct molecular signaling pathways contribute to these changes.

Experimental Approach: Viral vectors and non-infectious viruses will be used to deliver genetic material into mouse brains in the form of reporters to test the roles of specific molecules within specific brain circuits in animal behaviors related to human mental illness. Agents will be delivered via an intracranial surgery. following recovery, the impact of the virally expressed construct on mouse behavior is assessed.

IBC Discussion and Vote

Discussion:	Reviewer discussed that this amendment was straightforward.
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

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

1) Drills and exercises

VI. Information from the field (Senior Biosafety Officer)

Dates to track:

1) End of year training/surveillance etc.
2) Reviews of manuals
3) Training emphasis needed – evident from recent incidents.

VII. Other Business

Acknowledgement Items:

1) **Caricchio 889-24: A Phase 1, Multicenter, Open-Label Study Of CC-97540 (BMS-986353), CD19-Targeted Nex-T Chimeric Antigen Receptor (CAR) T Cells, in Participants with Severe, Refractory Autoimmune Diseases: Systemic Lupus Erythematosus, Idiopathic Inflammatory Myopathy, Systemic Sclerosis, or Rheumatoid Arthritis (Breakfree-1)** *Protocol Amendment 11th 28-Oct-2025*

The purpose of this amendment is to incorporate follow up of newborn outcome language, to provide additional guidance around collection of synovial biopsies for RA participants, and to clarify imaging language at German sites.

Adjourned at 1:20pm