THE ROCKEFELLER UNIVERSITY INSTITUTIONAL BIOSAFETY COMMITTEE
July 29, 2025
By zoom

Attendees: Leslie Diaz, Gaitree McNab, Charles Rice, Jeremy Rock, Jennifer Rohr, Agata Smogorzewska, Amy Wilkerson, [redacted] (guest)

Chair's Remarks
- The Chair reported that the NIH OSP accepted annual roster update on July 8, 2025.

Approval of minutes: The minutes of the April 23, 2025, meeting were approved.

New NIH Guidance
- NIH "Implementation Update: Improving the Safety and Security of Biological Research" (NOT-OD-25-112) – The Chair reported on this update. She reminded the Committee that the University IRE is the Laboratory Safety Committee.
- NIH "Implementation Update: Promoting Maximal Transparency Under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules" (NOT-OD-25-082) – The Chair stated that the University IBC roster, available through the NIH OSP on line system, now lists the names as well as the roles of the IBC members. She reported that the University has created a public website to post approved IBC minutes as required under this Guideline. The minutes from this meeting will be the first that the University is required to post, once they are finalized.
- NIH "Implementation Update: Terminating or Suspending Dangerous Gain-of-function Research in Accordance with Executive Order on Improving the Safety and Security of Biological Research." (NOT-OD-25-127) – The Chair reported on this update. There was discussion of the current and potential effects on research conducted at the University.

Follow Up Actions from Last Meetings: The Chair said that all training that was noted as past due at the April meeting has been completed.

Conflict of Interest Statement: Members stated that they had no conflict with items of business in front of the Committee.

Annual Reports (see summary below): All reports were timely received. The Chair will follow up with the two HOLs (Fuchs and Casanova) regarding the past due training. There were no questions about the annual reports.

Amendments:
2023-04-006 Erich Jarvis PI Based Registration: The amendment request, submitted on May 22, 2025, to add *in vivo* use of glycoprotein-expressing helper Adenovirus and replication deficient glycoprotein-deleted rabies virus working with transgenic rodents at ABSL2 was approved administratively on May 27, 2025. Animals may be moved to ABSL1 72 hours post administration of the Adenovirus. The Committee noted that animals administered rabies virus must be maintained at ABSL2 and directed the Chair to convey that to the HOL.
2022-10-004 Shixin Liu PI Based Registration: The amendment request, submitted July 1, 2025, to add *E. coli* vectors, was approved administratively on July 1, 2025. The work is exempt from full Committee review requirements.
2023-04-006 Erich Jarvis PI Based Registration: The amendment request, submitted July 10, 2025, seeks to add new methods and materials to evaluate effect of modification of germ cell specific DAZL or CXC4 transcripts on germ cell development in quail embryos and generation of adult transgenic quails. This work is proposed to be conducted at the [redacted] The PI also seeks approval to add personnel. It was noted that the Laboratory maintains transgenic songbirds at the [redacted] as well. While noting that the proposed modification to the quail do not present threat to existing wild populations, the Committee discussed the procedures and facility design in place to ensure that transgenic birds are not released to the environment. The

Committee was satisfied that these provide appropriate containment. The Committee determined the work is covered by Section III-E-3 and approved the amendment.
2024-04-004 Tarun Kapoor PI Based Registration: The amendment request to add personnel was received and approved following administrative review on July 16, 2025.
2024-04-003 Charles Rice PI Based Registration: The amendment request to add personnel was approved following administrative review on July 21, 2025.

Exempt Renewals: The Committee was informed that the following renewals, which involve only work exempted from full Committee review, have been approved.
2025-07-005 Brian Chait PI Based Registration (renewal of 2022-07-012)
2025-07-006 Paul Nurse PI Based Registration (renewal of 2022-07-004). The Committee asked the chair to confirm that the listed personnel work only on the RU campus.
2025-07-010 Seth Darst PI Based Registration (renewal of 2022-07-011)

New/Renewed Registrations
2025-07-001 Charles Gilbert PI Based Registration (renewal of 2022-07-007)
There are no proposed changes to the currently approved covered research activities in the Gilbert Laboratory. The Laboratory has updated its personnel list. The Gilbert Laboratory uses replication incompetent AAV vectors and existing transgenic mice. It was noted that the Laboratory previously used Cynomolgus and rhesus macaques but that work is on hold and he currently does not maintain NHPs. The AAV is injected into the mice to label selected neurons with fluorescent probes for live animal imaging studies. The Committee notes that the proposed work includes activities covered by Sections III-D-4, III-E-1, III-F-1, III-F-2 and III-F-8 (Appendix C-VII and C-VIII) and determined that the proposed work with human cells and the proposed transfer of AAV to animals must be conducted at BSL2 and ABSL2 respectively. The Committee approved the registration.

2025-07-002 Michel Nussenzweig PI Based Registration (renewal of 2022-07-001)
There are no significant proposed changes to the currently approved covered research activities in the Nussenzweig Laboratory. The Laboratory has updated its inventory and personnel lists. The Nussenzweig Laboratory investigates the immune system using recombinant DNA and transgenic technologies to understand how immune cells cooperate in generating responses. It also focuses on discovering antibodies against HIV, Hepatitis B, and other viruses, as well as developing vaccine designs. The rDNA technology employed involves standard cloning and protein expression techniques. Serum and blood samples from individuals exposed to Hepatitis B, Zika, other flaviviruses, as well as from HIV-infected or treated individuals, are processed under BSL2 practices. Additionally, the Laboratory performs experiments in mice using different strains of the Influenza A virus. The Committee noted that the work with the Zika, Hepatitis B and HIV viruses, the lentiviral vectors, retroviruses and 293T cells must be conducted using BSL2/ABSL2 practices and procedures. The *in vitro* work covered under Sections III-D-3 and III-D-4-b and III-E-3 requires approval before initiation. Other work is covered under Sections III-F-1, III-F-2, III-F-3 and is exempt. Breeding of transgenic mice is covered under Section III-F-8, Appendix C-VIII. Use of existing transgenic mice is exempt and is covered under Appendix C-VII. The Committee approved the registration at the containment levels noted in the registration and above.

2025-07-003 Cori Bargmann PI Based Registration (renewal of 2022-07-005)
There are no proposed changes to the currently approved covered research activities in the Bargmann Laboratory. The Laboratory has updated the inventory and personnel list. The Bargmann Laboratory examines how genes affect the development and function of neural circuits in *C. elegans*. Plasmids generated in *E. coli* or PCR-amplified DNA are introduced into the nematodes by standard injection methods. The rDNA technology employed involves generating plasmids in *E. coli* through standard cloning techniques and purifying them using Qiagen columns or alkaline lysis minipreps. These plasmids, along with PCR-amplified DNA, are introduced into *C. elegans* to study the effects of genes on neural circuit development and function. The Laboratory also produces transgenic *C. elegans*. The Committee notes that aspects of the work are covered under Sections III-D-4-a which require approval by the IBC prior to initiation; remaining procedures described are exempt under Sections III-E-3, III-F-1, III-F-2 and III-F-5. The Committee noted that the Bargmann Laboratory facilities are designed to meet BSL2 requirements but

that the proposed research may be conducted at BSL1 containment. The Committee approved the registration.

2025-07-004 Robert Darnell PI Based Registration (renewal of 2022-07-003)

There are no significant proposed changes to the currently approved covered research activities in the Robert Darnell Laboratory. The Laboratory has updated its inventory and personnel lists. The Darnell Laboratory studies how dysregulation of RNA, the key intermediary between genomic DNA and proteins, contributes to human diseases. Using CLIP, they examine the regulation of RNAs by Ago-microRNA and RNA-binding proteins in the brain under normal and disease conditions. They employ homologous recombination in mice to create models of human disease with cell-type-specific variations of CLIP, aiming to generate biological insights and identify new diagnostic and therapeutic targets for neurological diseases. The Laboratory uses several types of rDNA technology in its work, including gene editing, CRISPR-mediated genome editing, and viral vector-based gene delivery systems. They create knock-in mouse models through homologous recombination in mouse ES cells, using targeting constructs which include conventional cloning from mouse BAC or CRISPR constructs. For molecular detection of SARS-CoV-2, heat-inactivated SARS-CoV-2 and CoV-229E serve as positive controls. Samples collected from potentially infected individuals in DRUL buffer, which inactivates the virus on contact, undergo RNA extraction and qRT-PCR testing. To study RNA-binding proteins (RBPs) in human neurons, they use a human pluripotent stem cell line expressing neurogenin-2 and CRISPR machinery to induce neurons. Imaging and sequencing methods map alternative splicing changes and their effects on synaptic physiology. CLIP-Seq is then used to identify RBP targets and define RNA-regulatory networks. In addition, the Laboratory has listed that lentiviral and retroviral vectors packaged in 293T cells will be used for *in vitro* and *in vivo* studies. The Committee notes that the methods and materials are covered under Sections III-D-3, III-E-1 and must be conducted at BSL2/ABSL2, the production of transgenic mice is covered under Section III-E-3 and may be conducted at BSL1/ABSL1. The proposed work also includes exempted work covered by Sections III-F-2, III-F-3, III-F-8, and Appendices C-VII and C-VIII. The Committee noted that the list of personnel on the registration does not include many lab members; they asked the Chair to confirm that the list includes all personnel who conduct work with rDNA and to update the list if others should be included. The Committee approved the registration on that condition.

2025-07-007 Jeffrey Friedman PI Based Registration (renewal of 2022-07-006)

There are no significant proposed changes to the currently approved covered research activities in the Friedman Laboratory. The Laboratory has updated Tables 1 and 4, and its personnel and inventory lists. The Friedman Laboratory investigates molecular mechanisms regulating food intake and body weight. Genetic studies in mice led to their discovery of leptin, a key hormone controlling body weight. Current research focuses on how leptin from adipose tissue acts on the hypothalamus to influence feeding behavior and the metabolic effects of obesity. To carry out these experiments, the Laboratory uses many different technologies including cloning of genes for *in vitro* expression, transfection, and infection of cell culture using replication deficient AAV, PRV, Adeno Virus, canine adenovirus, lentivirus, pseudorabies virus, herpes simplex virus and replication deficient rabies virus. For *in vivo* studies, transgenic mice are injected with replication deficient PRV expressing fluorescent proteins such as GFP, EGFP or mCherry for tracing of neurons. AAV, PRV and adenovirus are also used for gene expression in mice. They have worked with the mouse adapted strain of the Influenza A virus to study the effect of obesity on the viruses. The Committee noted that the Sections of the Guidelines that cover the different experiments include Sections III-D-1, III-D-2, III-D-3, III D-4-a and III-D-4-b which require approval of the IBC before initiation, III-E-1 and III-E-3 which require notification simultaneous with initiation and exempt under the Guidelines, III-F-1, III-F-2, III-F-3, III-F-4, III-F-5and III-F-8, Appendix C-VII, and CVIII. The work must be undertaken in a BSL2/ABSL2 facility using BSL2/ABSL2 practices. The Laboratory has discontinued *in vivo* work with the SARS-CoV-2 virus. While not indicated on the submitted registration, the Chair confirmed that the Laboratory does not work with embryos other than associated with creating transgenic mice. The Committee approved the registration.

2025-07-008 Sean Brady PI Based Registration (renewal of 2022-07-010)

There are no proposed changes to the currently approved covered research activities in the Brady Laboratory. The Laboratory has updated its inventory and personnel lists. In the Brady Laboratory, DNA from environmental

samples and sequenced bacterial pathogens is cloned into model bacteria, which are then screened for their ability to produce bioactive small molecules. Both the cloned biosynthetic pathways and the resulting molecules are studied in the Laboratory. The Laboratory employs various rDNA methods to identify novel bioactive small molecules encoded by cryptic biosynthetic gene clusters in both cultured and uncultured bacteria. For cultured bacterial pathogens, cryptic biosynthetic pathways, often sources of previously unknown signaling systems and toxins, are accessed using rDNA techniques. These gene clusters are cloned from native producers via large-insert cosmid/BAC libraries or transformation-assisted recombination (TAR) in yeast and then expressed in model hosts such as *E. coli*, *Pseudomonas spp.*, *Streptomyces spp.*, and others. If clusters remain silent under laboratory conditions, homologous recombination is used to insert inducible promoters to activate gene expression. For uncultured bacteria, environmental DNA (eDNA) extracted from diverse soils is cloned into broad host range cosmid or SAC vectors and initially expressed in *E. coli*. The resulting eDNA libraries are then transferred into phylogenetically diverse model bacteria to identify clones that produce or have the potential to produce novel small molecules. Natural product isolation and characterization involves growing transformed bacteria in small-scale cultures, extracting and screening metabolites by LCMS, scaling up cultures producing novel compounds, and purifying metabolites using various chromatographic methods, followed by structural and functional characterization. Gene cluster characterization employs random transposon mutagenesis and directed gene deletion strategies to study biosynthetic pathways. Mutants are examined for their ability to produce secondary metabolites, and in some cases, mutagenesis is performed directly in the native producing organism. The Committee noted the proposed work involves both Risk Group 1 and Risk Group 2 agents, is covered by Section III-D-1-a, requires approval before initiation and should be conducted using BSL2. Additionally, the Laboratory does rDNA work that is covered under Sections, III-F-2, III-F-4, III-F-5 and III-F-6 which are exempt from the Guidelines. The proposed work with pathogenic organisms must be conducted using BSL2 practices. Dr. Brady is past due for training. Dr. Diaz reported that the Brady Laboratory conducts work with mice involving administration of drug-resistant bacteria. The Committee approved the registration on condition that all personnel complete required training and that the HOL confirm that the *in vivo* work in mice does not fall under NIH Guidelines.

2025-07-009 Amy Shyer PI Based Registration (renewal of 2022-07-008)

There are no proposed changes to the currently approved covered research activities in the Shyer Laboratory. The Laboratory has updated its inventory and personnel lists. The Shyer Laboratory investigates how cells organize into tissue patterns during development to form functional organs, focusing on the physical dynamics of morphogenesis. Using the chicken embryo as a model, the Laboratory studies critical symmetry-breaking events that shape tissues and organs, aiming to integrate physical principles with known molecular pathways for a deeper understanding of morphogenesis. They combine classic embryological models with modern molecular manipulations and apply these principles to disease studies, particularly tumor morphogenesis, developing assays to examine the self-organizing behavior of tumor cell lines *in vitro*. The Laboratory employs several rDNA methods to manipulate gene expression in primary chicken cell lines, chicken embryos (embryonic day 10 and earlier), and commercial human or animal transformed cell lines. These include transient transfection using lipofectamine, lentiviral delivery of rDNA constructs, and CRISPR-Cas9 for targeted gene knockdown or knockout. Additionally, the Laboratory uses RCAS-A and RCAS-B avian retrovirus systems to introduce rDNA into chicken embryos. Genes of interest are cloned into replication-competent plasmids, transfected into DF1 chicken fibroblast cells to express the gene and produce recombinant virus, which is then used to infect chicken embryos or primary cells. These RCAS viruses are restricted to avian cells and cannot infect other species. Replication-incompetent lentiviral vectors from commercial sources, such as Addgene, are also utilized. The Committee noted that the proposed work includes activities covered by Sections III-D-1 and III-F-2. Work with lentivirus, RCAS vectors, VSVG and 293T cells must be conducted using BSL2 practices. It was noted that one person is past due for training. The Committee approved the registration on condition that all personnel complete required training.

Summary of Annual Reports Due

Protocol #	PI	Change in			Comments
		Materials	Methods	Personnel	

2023-07-001	Jue Chen			X	
2023-07-002	Priya Rajasethupathy			X	
2023-07-003	Katya Vinogradova	X	X	X	Added knockout and gene editing (including CRISPR/Cas9 knockout and base editing) in primary human immune cells, involving delivery either through lentiviral transduction or mRNA electroporation; added lentiviral vector VSVG.
2024-07-001	Leslie Vosshall			X	
2024-07-002	Elizabeth Campbell	X		X	Added Komagataella (Pichia) pastoris
2024-07-003	Hironori Funabiki	X	X	X	Generation and use of recombinant purified hepatitis B virus (HBV) circular DNA
2024-07-004	Hermann Steller				No changes
2024-07-005	Daniel Mucida	X	X	X	Added retrovirus MSCV to generate retroviral vector pMSCV-mCD4-PIG TCR-OTII to transduce the NFAT-GFP 58$\alpha^{-}\beta^{-}$ hybridoma cells with synthetic TCR constructs. The Platinum-E (Plat-E) retroviral packaging cell line (RV-101, Cell Biolabs) will be used for viral packaging of pMSCV-mCD4-PIG TCR vectors; added location
2024-07-006	Elaine Fuchs			X	Added RRB 8 space; personnel past due for training
2024-07-007	Luciano Marraffini			X	
2024-07-008	Jean-Laurent Casanova	X		X	Added pCMV6-IL10RB and pCMV3-IFNLR1; personnel past due for training