National Institutes of Health

Mini-Symposium Series on New Approach Methodologies for Preclinical HIV Research



NIH National Institutes of Health
Office of AIDS Research

Meeting Summary

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Meeting Summary

Overview

The National Institutes of Health (NIH) Mini-Symposium Series on New Approach Methodologies (NAMs) for Preclinical HIV Research was held virtually via Zoom as a three-session series, with approximately 250 attendees participating in each session. Collaborating NIH institutes, centers, and offices were: the Office of AIDS Research (OAR); National Institute of Allergy and Infectious Diseases (NIAID); Office of Research Infrastructure Programs (ORIP); National Institute on Drug Abuse (NIDA); National Institute of Mental Health (NIMH); *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD); and Office of Research Innovation, Validation, and Application (ORIVA). The sessions were:

- **Igniting the Pipeline: Preclinical Advances in NAMs for HIV**
  - **Date/Time:** August 31, 2026, 1:00 p.m. – 5:00 p.m. EDT
  - **Chairs:** Lis Caler, Ph.D., M.Phil. (OAR); Tania Lombo, Ph.D. (NIAID); Vasundhara Varthakavi, Ph.D., D.V.M. (NIDA); Dwight Yin, M.D., Ph.D. (NIAID)

- **Modeling Immunity to HIV: Bridging Preclinical Discovery to Clinical Evaluation**
  - **Date/Time:** September 10, 2026, 11:45 a.m. – 4:30 p.m. EDT
  - **Chairs:** Vasudev Rao, M.B.B.S., M.S. (NIMH); Uday Shankar, Ph.D. (NIH); Anjali Singh, Ph.D. (NIAID)

- **Preclinical Models and NAMs in HIV Research: Priority Use Models, Platform Readiness, and Validation Pathways**
  - **Date/Time:** September 18, 2026, 12:00 p.m. – 4:00 p.m. EDT
  - **Chairs:** David Chang, Ph.D. (OAR); Sai Majji, Ph.D. (NICHD); Youngjun Sui, Ph.D. (ORIP)

The Trans-NIH NAMs for HIV Working Group led the scientific planning, organization, and logistics for the three-meeting series (members of the Working Group are listed in Appendix A of this document). Across the series, more than 40 presenters, panelists, and moderators shared their perspectives through keynote presentations, expert panel discussions, and closing remarks focused on the development, application, integration, and validation of NAMs for HIV research. Additional information about the series, including an overview, session agendas, and speaker biographies, is available on the meeting registration website (session agendas also appear as Appendix B at the end of this document).

This series examined how human-relevant NAMs can strengthen preclinical HIV research, improve translation, and connect mechanistic research with product development and clinical evidence. Across the series, speakers emphasized that no single model can reproduce the full complexity of HIV and that the appropriate model or combination of models must be selected according to the scientific question and intended decision. Recurring themes included fit-for-purpose design, rigorous characterization, context-of-use definition, cross-laboratory reproducibility, access to human tissues, computational integration, ethical stewardship, and triangulated validation against clinical and *in vivo* evidence. The overarching goal was to establish a connected evidence ecosystem in which NAMs refine, prioritize, and interpret findings from animal and human research.

Mini-Symposium 1: Igniting the Pipeline: Preclinical Advances in NAMs for HIV

August 31, 2026

Welcome and Introduction to the Goals, Format, and Schedule of the Symposium Series

Lis Caler, Ph.D., M.Phil., OAR, NIH

Dr. Lis Caler opened the series by framing HIV as a uniquely complex modeling challenge that requires the deliberate selection and integration of complementary research systems. She explained that the series would assess the current HIV NAMs landscape, align applications with HIV research priorities, identify contexts in which human-based NAMs can add value alongside established preclinical approaches, and build collaborations that extend beyond the meetings. Dr. Caler emphasized that no single model can answer every question related to HIV acquisition, pathogenesis, immunity, prevention, treatment, persistence, comorbidities, and cure and that progress depends on matching the model or combination of models to a clearly defined question and decision context.

Opening Remarks: Advancing Human-Based Research Technologies

Nicole Kleinstreuer, Ph.D., Division of Program Coordination, Planning, and Strategic Initiatives, NIH

Dr. Nicole Kleinstreuer described the symposium as part of an NIH-wide transition toward human-based science and more integrated research strategies. She noted that human tissue models, organoids, microphysiological systems (MPS), computational systems biology, artificial intelligence (AI), and clinical evidence collectively provide opportunities to improve human relevance and accelerate translation. Dr. Kleinstreuer identified HIV-specific opportunities involving difficult-to-access tissues, biological sex, population heterogeneity, maternal and pediatric health, and chronic effects across the lifespan while stressing that multidisciplinary collaboration is needed to connect technological innovation with clinical and regulatory application.

Opening Remarks: NIH Prioritization, Validation, and Application of NAMs

Warren Casey, Ph.D., DABT, ORIVA, NIH

Dr. Warren Casey described NIH's commitment to prioritizing human-based research technologies and ORIVA's role in coordinating NIH-wide efforts to develop, validate, and scale the use of human-based science across the NIH biomedical research enterprise; facilitating interagency efforts to advance the development, validation, and implementation of non-animal approaches for regulatory testing of drugs and chemicals; and expanding training and infrastructure to support human-based research approaches. ORIVA comprises the Division of the National Interagency Center for the Evaluation of Alternative Test Methods and the Division for Accelerating Innovation in Biomedical Research. Dr. Casey highlighted the importance of transferable protocols; analytical characterization; context of use; and a continuum that links biomedical research to validation, qualification, and regulatory implementation. He also described NIH investments in shared capabilities and the Standardized Organoid Modeling (SOM) Center as a foundation for reproducible and accessible organoid research.

Keynote Presentation: Characterizing, Validating, and Standardizing 3D Models for Studies of HIV Pathogenesis and Persistence

Mary Kearney, Ph.D., National Cancer Institute, NIH

Dr. Mary Kearney introduced the HIV SOM Application Laboratory (HIV-SOMAL), which provides a framework for validating and benchmarking human organoid systems for HIV research. A component of the NIH-wide SOM initiative, HIV-SOMAL is partnering with leading investigators across NIH, academia, and industry to identify, evaluate, and standardize organoid systems with potential applications

in HIV research. HIV-SOMAL is working across relevant tissues and biological contexts to validate and standardize organoids for studies of HIV pathogenesis; explore mechanisms of HIV persistence during therapy; evaluate new interventions, drug resistance, transmission, and prevention; and develop personalized approaches to achieving HIV remission without antiretroviral therapy (ART). An HIV Models Collaboratory is being formed to develop models and address gaps in research. Dr. Kearney also identified open questions, including whether organoid models can address gaps in existing research models, answer key unanswered questions in the HIV field, advance the development of new assays and technologies, recapitulate human biology and HIV infection and persistence, and support the development of personalized therapies.

Session I: Where Are We?

NIH Landscape of NAMs in HIV Research

Tania Lombo, Ph.D., NIAID, NIH

Dr. Tania Lombo presented an NIH portfolio analysis identifying 274 active HIV projects incorporating NAMs in fiscal year 2026, representing less than 10 percent of the active NIH HIV portfolio. The portfolio was heavily weighted toward *in silico* methods (i.e., AI/machine learning [ML] and mathematical modeling/simulation), while organoids, 3D culture systems, MPS, and combined *in vitro–in silico* approaches were less prominent. Topic clusters included data science, neuro-HIV, maternal and pediatric therapeutics, vaccines and broadly neutralizing antibodies, reservoirs and cure, cancer, and mucosal immunity. Dr. Lombo emphasized the opportunity to more systematically connect computational prediction with experimental testing, benchmarking, reproducibility, and clinical translation.

Session II: Current Developments, Gaps, and Opportunities

NeuroHIV on a Chip: A Human-Relevant NAM

Michael Corley, Ph.D., M.A., University of California, San Diego

Dr. Michael Corley described an isogenic induced pluripotent stem cell (iPSC)–derived brain-on-chip model that separates perfused vascular and neural compartments while incorporating endothelial cells, neurons, astrocytes, microglia, and pericytes. The system enables controlled investigation of blood–brain barrier disruption, immune-cell trafficking, soluble mediators, inflammatory responses, and donor-specific biology. Preliminary studies reproduced cell type–specific interferon responses, detected HIV-associated signals across immune and central nervous system cell populations, and suggested aging-associated transcriptomic shifts. Dr. Corley emphasized that the model should be benchmarked against human tissues and identified limitations involving regional and reservoir fidelity, culture duration, and incomplete representation of real-world complexities. He also highlighted the ethical responsibilities associated with long-lived patient-derived resources, including consent, governance, stewardship, and future use.

Engineering Immunocompetent Neural Spheroids for Viral Infection Research

Emily Lee, Ph.D., National Center for Advancing Translational Sciences (NCATS), NIH

Dr. Emily Lee presented the Neural Microglia Integrated Multicellular iPSC-derived Cultured Spheroids (NeuroMIMICS) platform, which combines neurons, astrocytes, and microglia in neural spheroids. The system supports synchronized neural activity, microglial phagocytosis and motility, inflammatory responses, and pharmacologic manipulation. In early HIV studies conducted with HIV-SOMAL, M-tropic HIV-1 efficiently infected NeuroMIMICS; however, infection was limited in spheroids lacking microglia and with T-tropic viruses. The NeuroMIMICS platform offers opportunities to study neural infection, but additional work is needed to fully evaluate the system's capabilities and limitations. Dr. Lee outlined near-term next steps, which include transcriptomic and cytokine profiling, integration-site profiling,

characterization of latent versus active infection, assessment of reverse transcriptase activity, high-resolution microscopy, evaluation of microglial activation and migration, investigation of changes in neuronal activity and connectivity, and identification of additional cellular targets.

Modeling HIV Persistence and Cure in Human Lymphoid Organoids
Catherine Blish, M.D., Ph.D., Stanford University

Dr. Catherine Blish described tonsil- and spleen-derived lymphoid organoids that retain mature human immune cells, support HIV infection without artificial stimulation, spontaneously aggregate, and remain viable longer than conventional *ex vivo* lymphoid cultures. Her group used a transmitted-founder HIV strain to establish infection, evaluate susceptible cell populations, suppress replication with ART, and investigate rebound after treatment withdrawal. The experimental model offers research and translational applications in multiple areas, including HIV-susceptible and latently infected cells, vaccine development, cell-based therapies, new therapeutic agents, and insights into other immune-based diseases.

NAMs for HIV Research: A Stage-Specific 3D Feto–Maternal Interface Model for Viral Infection and Its Challenges and Future Horizons in Pathology and Therapeutics
Cristina Antich Acedo, Ph.D., NCATS, NIH

Dr. Cristina Antich Acedo presented a bioprinted human placenta model designed to reproduce stage-specific structural and functional changes across gestation. The model incorporates trophoblast and stromal components and demonstrated differences in barrier integrity, drug efflux, nutrient transport, hormonal secretion, and antiviral responses that were consistent with early- and late-gestation biology. Dr. Antich Acedo described the platform as a translational bridge for studying how HIV, inflammation, and antiretroviral (ARV) exposure may affect the placenta and fetus when direct study in pregnant people is constrained. Opportunities include mapping immune cascades, investigating placental dysfunction, conducting preclinical ARV screening, and developing personalized models; gaps include immune integration, multi-organ feedback, computational translation, and standardization and validation for safety-related applications.

Developing an Immunocompetent Lymph-Node-on-a-Chip Model for Cure Purposes
Guido Ferrari, M.D., Duke University

Dr. Guido Ferrari presented an immunocompetent lymph-node-on-a-chip model generated from lymph node stromal and immune cells obtained from transplant donors, including people with HIV. The platform allows for stromal expansion, immune-cell cryopreservation, experiment replication, and culture for up to several weeks while reproducing follicle-like organization and supporting immune-cell remodeling. Preliminary studies indicate that HIV reactivation from ART-suppressed participants is feasible and can be quantitatively measured within the platform, providing a means to inform the down-selection of combination cure strategies for implementation in both preclinical and clinical settings. Dr. Ferrari noted that the model can be used to evaluate the reproducibility of HIV infection and the establishment of viral latency, providing a platform for studying key aspects of HIV persistence. The research team plans to develop probes that enable real-time detection of viral replication, as well as cellular trafficking and rearrangement, without disrupting normal cellular phenotype and function. The team is now building an *in silico* model for further development in this space; future directions include modeling vaginal infection and its effects on lymph node follicle dynamics.

Building Partnerships for HIV NAMs: Opportunities With the Multiscale Immune System Modeling Center of Excellence

Keith Reeves, Ph.D., Duke University

Dr. Keith Reeves described a long-term vision in which the next generation of HIV NAMs will integrate advanced experimental systems with computational intelligence, creating predictive, continuously learning scientific platforms. The Multiscale Immune Systems Modeling Center supports AI/ML surrogate models, immune digital twins, agent-based models, mechanistic multiscale models, and *in silico* screening approaches while adhering to FAIR (findable, accessible, interoperable, and reusable) principles to support reproducible and standardized modeling. Dr. Reeves emphasized the importance of involving computational scientists at the beginning of study design so that experimental and computational models are developed around the same biological question. Proposed applications included transmission and prevention, reservoirs and cure, therapeutic optimization, and decision support. He envisioned a connected HIV NAM ecosystem that integrates organoids and tissue chips, combinatorial models and computational twins, virtual and synthetic HIV cohorts, animals and translational models, and human studies and clinical decisions.

Session III: Expert Panel Discussion and Closing Remarks

Research Questions Most Likely to Benefit From NAMs

NAMs can support factorial testing and prioritization before clinical or animal studies, but each model must be useful, informative, and predictive for a bounded question rather than presented as a complete representation of HIV disease. Panelists identified brain biology, mucosal transmission, tissue-specific behavior, therapeutic combination testing, and novel diagnostics and tools as areas where NAMs may provide information that is difficult to obtain directly from clinical or animal studies.

Complementarity With Established Models

Panelists emphasized the importance of parallel analyses across human tissues, human-based NAMs, nonhuman primate (NHP)–based NAMs, *in vivo* NHP studies, humanized mice, and clinical cohorts to gather appropriate data for a complete understanding of the biological question of interest. Panelists encouraged more direct cross-model studies, including matched human and NHP platforms and retrospective comparison with existing intervention datasets.

Translation and Model Development

Panelists recommended beginning with simple models, adding complexity only when required by the scientific question, and involving computational collaborators during study design. The desired trajectory is iterative: experimental findings inform computational models, predictions guide the next experiments, and results are compared with animal and human evidence. Potential translational uses include identifying intervention combinations, estimating human-relevant responses, improving diagnostics, and supporting personalized approaches.

Ethics and Stewardship

Panelists stressed that patient-derived organoids and renewable cell resources may remain scientifically valuable long after collection. Consent, privacy, ownership, future use, community engagement, and long-term stewardship therefore must be addressed at the outset in collaboration with bioethicists and affected communities rather than after a platform has been developed.

Closing Remarks

In his closing remarks, Dr. Dwight Yin, NIAID, NIH, remarked that the first mini-symposium highlighted NIH's efforts to advance a human-based research continuum that accelerates the translation of NAMs from discovery to regulatory application. Presentations demonstrated how organoids, organ-on-a-chip platforms, specialized tissue models, and computational approaches are providing human-relevant tools to study HIV infection, persistence, reservoirs, neuroinflammation, maternal–fetal transmission, and therapeutic responses. Participants emphasized the value of standardizing and validating these models, expanding experimental NAM platforms alongside computational approaches, and integrating multiple evidence streams to create a connected ecosystem that combines NAMs, computational models, preclinical studies, and clinical data to address critical HIV research questions and support translational decision-making.

Mini-Symposium 2: Modeling Immunity to HIV: Bridging Preclinical Discovery to Clinical Evaluation

September 10, 2026

Opening Remarks and Brief Recap of NAMs Mini-Symposium 1

Anjali Singh, Ph.D., NIAID, NIH

Dr. Anjali Singh provided opening remarks for the second mini-symposium. She stated that the session would provide a forum to share emerging evidence and insights, present existing capabilities, address key limitations and opportunities, and facilitate alignment of NAMs with their intended contexts of use. She explained that the HIV research landscape encompasses four interconnected areas: modeling HIV infection, pathogenesis, tissue reservoirs, and comorbidities; conducting human-centric discovery research and clinical product, platform, and regimen development; testing novel biomedical interventions for HIV prevention, treatment, and cure; and evaluating translational strategies across age groups, biological sexes, and vulnerable populations.

Keynote Presentation: Advancing HIV Research With NAMs

Melanie Ott, M.D., Ph.D., Gladstone Infectious Disease Institute

Dr. Melanie Ott discussed the role of organoids in bridging the human relevance gap in HIV research. She reviewed key milestones in organoid research and applications to virology, highlighting the discovery of iPSC technologies and development of organoids from human progenitor cells. She noted that organoids and spheroids have become a growing market in recent years. Her laboratory is focused on applications across models of the liver, airway, enteroid, and brain. Dr. Ott noted that HIV infects immune cells embedded within structured tissue environments, necessitating the use of integrated systems in this space. She briefly described her group's work using microfluidic co-culture models and mixed-brain organoids to study HIV infection. Dr. Ott also commented that model complexity must be added stepwise from human observations while preserving reproducibility and accessibility.

Session I: Modeling Immunity, Developmental Safety, Immune Pathways, and Comorbidities

Deciphering Human Immunology Through Immune Organoids and Functional MPS

Ankur Singh, Ph.D., Georgia Institute of Technology

Dr. Ankur Singh discussed MPS as reimagined through the lens of the immune system, outlining his group's efforts to recapitulate germinal center dynamics *in vitro*. His team has generated synthetic immune organoids derived from tonsil and blood cells and showed that polymer type, extracellular matrix, and mechanics regulate the germinal center response. The organoids reproduced germinal center–

like organization and *de novo* responses from naive B cells. This work has been applied to studies of impaired immunity in B-cell lymphoma survivors. Dr. Singh also described ongoing integrations with bone marrow, lung, and gut models to study immune responses across interconnected tissue systems.

In Vitro ***Modeling of Lymphoid Function in Spatially Organized Organs-on-Chip***
Rebecca Pompano, Ph.D., University of Virginia

Dr. Rebecca Pompano discussed approaches for modeling lymph nodes, which she noted are the starting point of most adaptive immune responses. Despite more than 20 years of development, lymphoid MPS remain limited by their primary focus on recall responses, challenges with live imaging, variable control of flow and gradients, and limited regional organization of cells. Her team has used a continuum of immune-function models—ranging from *in vitro* cell cultures and 3D organoid cultures to cell-based organs-on-chip, *ex vivo* tissues with or without chip technologies, and *in vivo* systems—to study and analyze immune function. Her artificial lymphoid chip mimics the organization and dynamics of human lymphoid tissue and supports migration, activation, plasmablast differentiation, and antibody production. Dr. Pompano stated that lymphoid MPS have immediate applications in immunotoxicology and in representing diverse patient populations; future development efforts should focus on advancing from polyclonal to antigen-specific responses, increasing throughput, improving spatial organization of cells, enabling human leukocyte antigen matching, and establishing connections with other tissues and organs.

A NAM Model of the Cervix Recapitulates Microbial, Immunologic, and Pathogenic Properties of Sexually Transmitted Infections
Jason Gleghorn, Ph.D., University of Delaware

Dr. Jason Gleghorn presented his work on modular cervical and vaginal MPS that recreate tissue morphology, physiology, and microbiota. Dr. Gleghorn's team has developed a 3D microphysiological model of the cervical epithelium that recapitulates key *in vivo* features of the mucosal surface and incorporates both optimal and non-optimal cervicovaginal microbiomes. The model reproduces important aspects of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections, demonstrating how the cervicovaginal microbiome influences infection outcomes. Ongoing advances include incorporating stromal and immune cell compartments, including macrophages, dendritic cells, natural killer cells, and T cells, as well as scaling the platform for high-throughput screening and broader use by domain experts.

Insights Into Viral Infection and Immunity From Human Immune Organoids
Lisa Wagar, Ph.D., University of California, Irvine

Dr. Lisa Wagar described tonsil-derived immune organoids that can be used to study mucosal and adaptive immune responses in a controlled, scalable system. The organoids are generated from cryopreserved immune cells, and outcomes can be assessed through flow cytometry, single-cell RNA sequencing, and other quantitative readouts. The model is designed to recapitulate key aspects of human immune function while supporting high-throughput experimentation and evaluation of vaccine-induced responses. Dr. Wagar's team has demonstrated that immune organoid models provide a valuable platform for studying human vaccine responses and identifying host and antigen factors that influence immunogenicity. Ongoing work focuses on understanding sources of inter-individual variation, modulating immune pathways to improve responses, and extending the model to additional pathogens and vaccine platforms. The model has been adapted for HIV infection, ARV treatment, and engineered B-cell studies.

Hi-DEF: A Unified Framework for Quantifying and Evaluating Immune Dysregulation at the System Level

Purvesh Khatri, Ph.D., Stanford University

Dr. Purvesh Khatri presented a computational NAM strategy that embraces biological and clinical heterogeneity across real-world patient populations. His group developed a workbench for *in silico* systems analysis using multicohort analysis, which has been applied to organ transplantation, infection, fibrosis, autoimmune diseases, neurodegenerative diseases, cancer, and vaccines. As a proof of concept, Dr. Khatri's group devised the Human immune Dysregulation Evaluation Framework (or Hi-DEF), which describes immune dysregulation at a systems level and can be used to assess diseases, risk factors, and drug responses. The approach identifies conserved patterns of immune dysregulation across healthy, chronic, and acute inflammatory conditions and may help predict treatment responses, supporting the goal of precision immunology and point-of-care assessment of immune status.

Session II: Modeling Disease Pathogenesis, Tissue Reservoirs, and Sanctuary Sites

Enhanced Human Antigen–Specific B-Cell Responses Using In Vitro *3D Tonsil Cultures Containing Stromal Cells*

Marit van Gils, Ph.D., University of Amsterdam

Dr. Marit van Gils presented a 3D hydrogel tonsil culture that permits matrix remodeling and allows for analysis via confocal imaging, flow cytometry, and spectral analysis. The goal of this work was to develop a human *in vitro* model that can be used to study antigen-specific human adaptive immunity and germinal center responses. Compared with 2D cultures, the system improved B- and T-cell viability, antigen-specific B-cell responses, and germinal center–like features while reducing excessive bystander activation. Future work will focus on optimizing gel stability and culture conditions, expanding the model to additional tissues, and using CRISPR/Cas9–engineered B cells to track and manipulate antigen-specific B-cell responses in a controlled manner.

Modeling Genome-Edited B-Cell Responses to Vaccination

James Voss, Ph.D., Scripps Research

Dr. James Voss described a strategy for inserting broadly neutralizing antibody sequences into the immunoglobulin heavy-chain locus of primary B cells so that vaccination can establish durable antibody memory. This reprogramming has been performed in mouse, NHP, and human cells. Dr. Voss outlined efforts to model *in vivo* behavior of reprogrammed B cells using secondary lymphoid organoids. Secondary lymphoid organoids reproduced the tendency of engineered primate B cells to differentiate into antibody-secreting cells rather than germinal center cells, suggesting value for screening immunogens and adjuvants. However, organoids currently model only early response stages and cannot replace *in vivo* assessment of trafficking, long-term memory, plasma-cell persistence, host rejection, off-target editing, and systemic safety.

Human Multi-Organ-on-a-Chip Systems to Evaluate Drug–Drug Safety for HIV Therapeutics

James Hickman, Ph.D., Hesperos, Inc.

Dr. James Hickman presented multi-organ MPS that can be applied to disease and toxicity modeling. The Hesperos Human-on-a-Chip® platform uses functional multi-organ *in vitro* systems to support therapeutic development and toxicity testing. The platform is designed to evaluate therapeutic index, reduce reliance on animal testing, and develop customized disease and toxicity models for drug discovery and safety assessment. Dr. Hickman's group has integrated liver, heart, nervous system, and other tissue models

and linked experimental data with pharmacokinetic/pharmacodynamic (PK/PD) and digital-twin models. Dr. Hickman noted that these systems could evaluate off-target effects in HIV models.

NAMs as Drug Development Tools in Reproductive Medicine

Ramkumar Menon, Ph.D., The University of Texas Medical Branch

Dr. Ramkumar Menon described organ-on-chip models spanning multiple fetal–maternal organs and interfaces. The Human Pregnancy–on-a-Chip platform is an integrated, humanized *in vitro* model designed to simulate key aspects of pregnancy, including parturition and preterm birth. The system aims to support preclinical evaluation of therapeutics during pregnancy and may help accelerate the generation of safety and efficacy data while reducing reliance on animal models. Dr. Menon also described a formal validation pathway involving independent laboratories and U.S. Food and Drug Administration review. The opportunity for HIV research involves studying maternal infection, fetal exposure, and immune activation. Dr. Menon presented data showing that the platform closely mirrors NHP tissue profiles across multiple organ systems, supporting its potential as a human-relevant alternative to animal models for studying pregnancy and evaluating therapeutics.

Modeling HIV Infection in 3D Cerebral Organoids: Opportunities and Considerations

Kelly Jordan-Sciutto, Ph.D., University of Pennsylvania

Dr. Kelly Jordan-Sciutto discussed the use of 3D neocortical organoids that contain integrated microglia for HIV research. This work provides a potential platform for studying viral movement, suppression, re-emergence, reservoir behavior, and neuropathogenesis. Dr. Jordan-Sciutto explained that microglial integration altered the processes of neurogenesis and gliogenesis, underscoring that immune components influence both the baseline model and disease responses. She concluded that the microglia successfully integrate into the 3D cortical organoids, adapt to their local cellular environment, support neurogenesis and gliogenesis in a stage-specific manner, and provide a physiologically relevant platform for studying HIV infection and neuroimmune interactions in the developing human brain. Areas for further development include improving the maturity and functionality of cell types, addressing batch-to-batch variability and reproducibility, increasing scalability, establishing standardized model systems, and enhancing the ability of models to capture complex biological processes.

Neuroimmunity in Motion: A Human 3D Neurovascular Model for Tracking Neuroinflammation in Real Time

Lishomwa Ndhlovu, M.D., Ph.D., Weill Cornell Medicine

Dr. Lishomwa Ndhlovu presented an immune-competent 3D neurovascular model with built-in sensing to recapitulate the native architecture of the brain. He identified persistent gaps in blood–brain barrier models for HIV neuropathogenesis, which include incomplete representation of key immune cell populations; reliance on endpoint-only measurements; limited ability to study viral reservoirs and ARV drug penetration; and inadequate modeling of chronic inflammation, aging, and comorbidities that contribute to HIV-associated neurocognitive disorders. Dr. Ndhlovu stated that the chip forms a physiologically realistic, reproducible barrier. The platform is positioned for studies of HIV neuroinflammation, ARV penetration, reservoir biology, aging, and comorbidities.

Session III: Expert Panel Discussion and Closing Remarks

Integration Across Systems

The discussion highlighted the potential value and challenges of connecting tissue-based models, multi-organ platforms, clinical datasets, and computational analysis. Multi-organ systems can capture biological dynamics that isolated models miss, but individual components must be sufficiently characterized before

extensive integration. Additionally, researchers can leverage existing human data to inform key areas of NAMs development.

Validation, Context of Use, and Regulatory Readiness

It was noted that efficacy applications may reach decision utility sooner than safety applications, for which regulators require stronger assurance that serious adverse effects will not be missed. MPS safety data can inform the design of animal studies and clinical trials. Panelists discussed the importance of model validation—defining a precise context of use, demonstrating human relevance, technically characterizing model performance, and establishing fitness for purpose—across both efficacy and safety applications. Standardization across laboratories was also identified as a prerequisite for confidence.

Longitudinal Processes

HIV persistence, aging, and rebound unfold over months or years, whereas many models operate for days or weeks. Panelists noted that *in vitro* kinetics may not map directly to calendar time in humans and that accelerated phenotypes must be biologically justified—considering the research question and context of use—rather than assumed equivalent. Approaches to this gap include longer cultures, patient-derived tissues that already contain years of disease history, repeated functional monitoring, retrospective comparison with clinical and animal studies, and mathematical models that extrapolate carefully from measured responses.

Closing Remarks

In his closing remarks, Dr. Vasudev Rao, NIMH, NIH, noted that the second mini-symposium focused on the application of NAMs across diverse tissues, organ systems, and research contexts, highlighting the complexity of modeling HIV in interconnected biological systems. Key themes included the use of central nervous system models, such as cerebral organoids and blood–brain barrier chips, to study neuropathogenesis and neuroinflammation; mucosal, gastrointestinal, reproductive tract, and placental models to investigate reservoirs, transmission, coinfections, and maternal–fetal health; and lymphoid, tonsil, and lymph node–on-a-chip systems to examine immune responses, HIV persistence, latency, and vaccine development. Speakers also discussed multi-organ and computational platforms for evaluating drug responses and integrating data across populations. Across these applications, participants emphasized the importance of selecting fit-for-purpose models, incorporating biological and clinical heterogeneity, capturing tissue and organ connectivity, validating findings through complementary lines of evidence, and prioritizing functional readouts to ensure translational relevance.

Mini-Symposium 3: Preclinical Models and NAMs in HIV Research: Priority Use Models, Platform Readiness, and Validation Pathways

September 18, 2026

Welcome and Opening Remarks

Yongjun Sui, Ph.D., ORIP, NIH

Dr. Yongjun Sui framed the third mini-symposium as the bridge from platform capability to credible use. She emphasized that readiness and validation cannot be judged without defining the decision that a model is intended to support. Dr. Sui observed that the third mini-symposium was organized as an evidence pathway that addressed three overarching questions: where HIV NAMs should be applied, how findings translate across model systems, and what evidence is needed to establish the usability and validity of the platforms. The discussions were intended to define a clearer path toward adoption-ready HIV NAMs by identifying priority use cases; establishing criteria for platform readiness; outlining principles for

integrating NAMs with animal and clinical data; and highlighting opportunities for standards development, validation, and collaboration to advance the field. Dr. Sui encouraged participants to ask what decision is being informed, why a particular model is appropriate, what it should be compared with, and what uncertainty remains.

Brief Recap of Mini-Symposia 1 and 2: Key Gaps, Model Systems, and Unresolved Translational Questions

David Chang, Ph.D., OAR, NIH

Dr. David Chang summarized the expansion of the HIV NAM toolbox across organoids, tissue chips, immune models, multi-organ systems, and computational models. He emphasized that human relevance depends on capturing the necessary biology (e.g., tissue context, cellular organization, human heterogeneity) rather than maximizing complexity. Dr. Chang also emphasized that the future of HIV NAMs lies in integration rather than replacement, with human-relevant models serving as one component of a connected evidence framework that combines computational approaches, established preclinical models, and clinical and real-world data to strengthen confidence through convergent validation. He emphasized that the primary challenge has shifted to establishing model readiness and validation and highlighted the need for clearly defined contexts of use, biologically meaningful benchmarks, scalability, reproducibility, standardization, human-based validation, longitudinal performance, and evidence of predictive value. The goal is not to develop a single "perfect" HIV model but rather to establish a fit-for-purpose, human-relevant evidence ecosystem that integrates complementary NAMs and other data sources to address specific research questions and support decision-making.

Session I: Priority Use Models for HIV NAM Adoption and Preclinical Integration

Modeling Mucosal HIV: Integrating Clinical Cohorts, Organoids, and Preclinical Models

Douglas Kwon, M.D., Ph.D., Ragon Institute of MGH, Massachusetts Institute of Technology and Harvard University, and Harvard Medical School

Dr. Douglas Kwon integrated data from the Females Rising through Education, Support and Health (or FRESH) cohort, epithelial co-cultures, vagina-on-chip systems, patient-derived intestinal organoids, and humanized mice to investigate mucosal HIV susceptibility and tissue injury. He explained that vaginal microbiomes dominated by *Lactobacillus* bacteria are associated with a range of favorable reproductive and sexual health outcomes, including improved pregnancy outcomes and lower rates of HIV and other infections and reproductive health conditions. Dr. Kwon's team also is investigating the relationship between HIV-associated gut impairment and disease progression. This work demonstrated that clinical data can guide the development and validation of NAMs for mucosal HIV research, while co-culture and patient-derived organoid models provide mechanistic insights into host-microbe and immune interactions, highlighting both the promise of these systems and the need for context-specific validation and recognition of their limitations in fully recapitulating human biology.

New Approaches to HIV Cure

Robert Siliciano, M.D., Ph.D., The Johns Hopkins University School of Medicine

Dr. Robert Siliciano discussed his work on the latent HIV reservoir and assays used to distinguish replication-competent or intact proviruses from defective proviruses. He explained that despite extensive HIV cure research, no strategy other than stem cell transplantation has consistently achieved a significant and sustained reduction in intact proviruses. Dr. Siliciano emphasized that achieving an HIV cure requires preventing viral rebound from the stable reservoir of latently infected $CD4^+$ T cells and noted that progress is hindered by challenges in studying and isolating these cells; limitations of current *ex vivo* and *in vitro* models in recapitulating the profoundly quiescent state of latent HIV infection; and the complex

interactions between rebound virus and host immune responses, including autologous neutralizing antibodies. NAM opportunities include studying activation, proliferation, latency reversal, antigen response, and neutralization in tissue context, but models must focus on intact rebound-capable virus, represent long-term reservoir biology appropriately, and not confuse percentage reductions with clinically meaningful log-scale change.

Session II: Human-Relevant Platforms and Cross-Model Translation in HIV Research

Dissecting Human Inflammatory Diseases: Lessons From HIV-1

Lishan Su, Ph.D., University of Maryland School of Medicine

Dr. Lishan Su presented his research on HIV-associated inflammaging, highlighting how persistent HIV infection and ART can contribute to accelerated aging and increased risk of age-related end-organ diseases through such interconnected processes as immunosenescence, mitochondrial damage, epigenetic changes, clonal hematopoiesis, stem cell exhaustion, and metabolic dysregulation. He also discussed the use of HIV/ART as a model for studying inflammatory diseases and identifying potential therapeutic targets. Dr. Su noted that humanized mouse models support HIV infection and reproduce key aspects of HIV-associated immunopathogenesis across multiple organ systems, making them a valuable platform for *in vivo* studies. He emphasized that researchers must understand the strengths and limitations of each experimental system, using complementary approaches and validating key findings in patient-derived cells and organoid-based NAMs to ensure relevance to human disease.

From Patient to Pipette to Predicting Clinical Outcomes: How NAMs Can Be Harnessed to Advance HIV Research

J. Zachary Porterfield, M.D., Ph.D., University of South Florida (USF) and USF Health

Dr. J. Zachary Porterfield described connections between deeply characterized clinical cohorts, animal models, and tonsil-derived organoids to investigate the role of germinal centers as sites of HIV persistence and immune dysfunction. He explained that organoids are well-suited for acute infection studies, and researchers can apply key insights toward work on chronic HIV. NHP model data point to opportunities to test interventions that preserve germinal center structure and function, suggesting applications for modularity in organoids. Dr. Porterfield emphasized the potential of NAMs to bridge human clinical data, organoid systems, animal models, and computational approaches, creating a more integrated framework for prediction and translational research. Such approaches may help improve understanding of individual responses and support the development of more informative and effective clinical studies.

Beyond Replacement: Integrating NHP Models and NAMs to Advance HIV Research

Mirko Paiardini, Ph.D., Emory University

Dr. Mirko Paiardini spoke on the value of integrating human-relevant NAMs with established NHP models to enhance mechanistic understanding and translational relevance while highlighting both the opportunities and current limitations of these complementary approaches in HIV cure research.
Dr. Paiardini highlighted findings from anti-IL-10 studies in NHPs that revealed adverse events unlikely to have been detected in other experimental systems, underscoring the unique role of NHP models in generating critical safety data. These observations illustrated how NHP research contributes essential knowledge for HIV cure research and biomedical advances, even when studies do not directly lead to new therapies. He proposed a complementary, iterative framework that integrates NHP models and NAMs, including immunologic, virologic, toxicity, and computational modeling approaches. Dr. Paiardini underscored the value of using NAMs to refine, prioritize, and interpret NHP studies and using NHP studies to address scientific questions that remain beyond the capabilities of current NAMs.

Session III: Validation and Context of Use for HIV NAMs

Resource Development and Validation Landscape for NAMs

Oleg Mirochnitchenko, Ph.D., ORIP, NIH

Dr. Oleg Mirochnitchenko summarized infrastructure needs identified through a recent ORIP workshop and applied them to HIV NAMs development. Several key themes emerged from Day 1 of the workshop, including the critical role of research infrastructure, validation frameworks, shared resources, and data standards in supporting the development and adoption of NAMs. Speakers emphasized that no single model can address all research questions and that integrating complementary model systems while accounting for human biological complexity and variability is essential for generating more predictive and translationally relevant science. Additional themes from Day 2 of the workshop focused on the infrastructure, workforce, and partnerships needed to support broader adoption of NAMs. Speakers highlighted the importance of centralized resources, data accessibility, computational modeling, and automated platforms to improve the scalability, reproducibility, and utility of NAMs.
Dr. Mirochnitchenko emphasized that poorly defined research models and resources can introduce hidden biological variability, limiting the reproducibility, comparability, and translation of findings. He concluded that the strongest strategy for HIV research is an integrated, fit-for-purpose portfolio that combines human NAMs, animal models, computational approaches, and clinical data.

From Models to Mothers: NAMs to Advance ARV Safety in Pregnancy

Mackenzie Cottrell, Pharm.D., M.S., University of Oklahoma College of Pharmacy

Dr. Mackenzie Cottrell compared *in vivo*, *ex vivo*, *in vitro*, and *in silico* models for anticipating ARV transfer and safety during pregnancy. Tenofovir and dolutegravir examples showed useful concordance among preclinical and clinical evidence, whereas cabotegravir illustrated how *ex vivo*, computational models, and clinical data can yield different predictions and why emerging human observations are essential for adjudication. She emphasized that cord-blood exposure is not equivalent to fetal tissue exposure or fetal safety and that toxicity thresholds remain poorly defined. Short-term priorities include using drugs with known clinical transfer and safety data to standardize and validate placenta-on-chip platforms. Dr. Cottrell concluded that *ex vivo* and *in vitro* models can help bridge species differences, but greater standardization is needed before these systems can be widely applied in drug development. Because no single model fully recapitulates the human placenta, a multimodel approach that integrates *in vivo* and *in vitro* data is necessary to support translational research and decision-making.

Extended Expert Panel Discussion and Closing Remarks

Prioritizing Unmet Needs

Panelists remarked that many priorities exist in this space based on research questions of interest. They underscored the importance of mucosal models of immunity, microbiota, and infection, as well as physiologically based PK/PD modeling, teratogenicity prediction, and validation of organ-on-chip models with known drugs. They also emphasized the importance of prioritizing bounded use cases where applicable.

Defining Context of Use and Necessary Complexity

Panelists stated that model design must be anchored to the *in vivo* biology of the research question. Cure models may require reservoir composition, activation, tissue microenvironment, migration, and immune control; transmission models may require epithelial barriers, mucus, microbiota, hormones, and target cells. Panelists emphasized characterizing the actual cell composition and how it changes over time,

documenting donor clinical histories, and accepting that a useful model does not need to be perfect if its boundaries are known.

Short-Term Validation Opportunities

Panelists recommended repeating retrospective interventions that already have NHP and human clinical outcomes. Latency-reversing agents, broadly neutralizing antibodies, transmission studies, and other well-characterized interventions could be tested across NAMs to determine whether they reproduce efficacy, safety, and mechanistic findings. Stored human and animal specimens and cross-model analyses were described as key opportunities that require coordinated funding and multiple laboratories.

Connected Evidence and Near-Term Translational Use

When asked where a NAM could realistically change a decision within the next few years, panelists favored retrospective and prospective cross-model testing of interventions with known clinical and animal outcomes. They emphasized that trust will require standardized production, benchmarking, transparent limitations, reproducibility across laboratories, clinically relevant PK/PD, and evidence that the model changes or improves a real decision.

Confidentiality and Ethics

Panelists described de-identification, restricted access to identifiable information, barcoding, encryption, and secure storage as methods to preserve confidentiality. They noted that long-lived organoid resources raise questions about the duration and scope of consent and confidentiality and that rapid-autopsy programs are working with bioethicists. The panel emphasized that consent must anticipate reuse, sharing, future technologies, and the possibility that a patient-derived model may persist for decades.

Human Tissues, Cohorts, and Biobanks

Panelists identified access to well-characterized human tissue as an urgent resource need. Recruiting people with HIV for fresh lymphoid and mucosal samples, maintaining longitudinal cohorts, obtaining clinical metadata, and rapidly processing specimens require dedicated coordinators, clinicians, laboratories, and community relationships. Panelists noted that cohort maintenance is difficult to fund even though it underpins discovery science. Shared resources, such as the Human Tissues and Organs for Research Resource and HIV-SOMAL, were highlighted as important infrastructure.

Cryopreservation and Donor Heterogeneity

Panelists reported that thymus and spleen fragments can be cryopreserved successfully and that some explant and organoid approaches can be recovered from frozen material, although performance depends on the tissue, how it is prepared, and the intended assay. To manage human variability, the panel recommended defining a robust signal for a specific question, identifying quality-control criteria, recording donor characteristics, and eventually using automated high-throughput experiments across many donors. Variation was viewed as biologically informative and potentially central to personalized therapies.

Closing Remarks

In her closing remarks, Dr. Stephanie Murphy, ORIP, NIH, summarized the progression of the mini-symposium series—from exploring advances in NAMs and their applications in HIV research to examining the complexity of human immunity and translation to clinical settings and ultimately to addressing the evidence, validation, and implementation challenges needed for broader adoption. She

emphasized that no single model can answer every research question and that progress will depend on integrating NAMs with established preclinical approaches, ensuring scientific rigor through validation and standardization, strengthening connections between model systems and human biology, and fostering sustained collaboration across disciplines. Looking ahead, she highlighted the need to identify priority contexts of use, build confidence in emerging platforms, improve translation across models, and develop partnerships that advance human-relevant evidence and accelerate progress in HIV research.

Appendix A: Trans-NIH NAMs for HIV Working Group Members

Elisabet Caler, Ph.D., M.Phil., OAR

David Chang, Ph.D., OAR

Tania Lombo, Ph.D., NIAID

Sai Majji, Ph.D., NICHD

Margaret Ochocinska, Ph.D., DPCPSI

Amy Palin, Ph.D., NIAID

Marina Protopopova, Ph.D., NIAID

Vasudev Rao, M.B.B.S., M.S., NIMH

Uday Shankar, Ph.D., NIAID

Anjali Singh, Ph.D., NIAID

Yongjun Sui, Ph.D., ORIP

Vasundara Varthakavi, Ph.D., D.V.M., NIDA

Sujata Vijh, Ph.D., NIAID

Dwight Yin, M.D., Ph.D., NIAID

Appendix B: Mini-Symposium Series Agendas

Mini-Symposium 1: Igniting the Pipeline: Preclinical Advances in NAMs for HIV

August 31, 2026
1:00–5:00 p.m. EDT

Time	Presentation
1:00–1:10 p.m.	**Welcome and Introduction to the Goals, Format, and Schedule of the Symposium Series** Lis Caler, Ph.D., M.Phil., Office of AIDS Research (OAR), NIH
1:10–1:35 p.m.	**Opening Remarks**
	Advancing Human-Based Research Technologies Nicole Kleinstreuer, Ph.D., Division of Program Coordination, Planning, and Strategic Initiatives, NIH **NIH Prioritization, Validation, and Application of NAMs** Warren Casey, Ph.D., DABT, Office of Research Innovation, Validation, and Application, NIH
1:35–2:00 p.m.	**Keynote Presentation**
	Characterizing, Validating, and Standardizing 3D Models for Studies of HIV Pathogenesis and Persistence Mary Kearney, Ph.D., National Cancer Institute (NCI), NIH
2:00–2:15 p.m.	**Session I: Where Are We?**
2:00–2:08 p.m.	**NIH Landscape of NAMs in HIV Research** Tania Lombo, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID), NIH
2:08–2:15 p.m.	**Break**
2:15–4:20 p.m.	**Session II: Current Developments, Gaps, and Opportunities**
2:15–2:35 p.m.	**NeuroHIV on a Chip: A Human-Relevant NAM** Michael Corley, Ph.D., M.A., University of California, San Diego (UCSD)
2:35–2:55 p.m.	**Engineering Immunocompetent Neural Spheroids for Viral Infection Research** Emily Lee, Ph.D., National Center for Advancing Translational Sciences (NCATS), NIH
2:55–3:15 p.m.	**Modeling HIV Persistence and Cure in Human Lymphoid Organoids** Catherine Blish, M.D., Ph.D., Stanford University

Time	Presentation
3:35–3:55 p.m.	**NAMs for HIV Research: A Stage-Specific 3D Feto–Maternal Interface Model for Viral Infection and Its Challenges and Future Horizons in Pathology and Therapeutics** Cristina Antich Acedo, Ph.D., NCATS, NIH
3:55–4:15 p.m.	**Developing an Immunocompetent Lymph-Node-on-a-Chip Model for Cure Purposes** Guido Ferrari, M.D., Duke University
4:15–4:20 p.m.	**Building Partnerships for HIV NAMs: Opportunities With the Multiscale Immune System Modeling Center of Excellence** Keith Reeves, Ph.D., Duke University
4:20–5:00 p.m.	**Break**
4:20–4:50 p.m.	**Session III: Expert Panel Discussion and Closing Remarks**
4:50–5:00 p.m.	**Expert Panel Discussion** Mary Kearney, Ph.D., NCI, NIH; all speakers; and invited experts Sara Gianella Weibel, M.D., UCSD; Brandon Keele, Ph.D., NCI, NIH; and Frank Maldarelli, M.D., Ph.D., NCI, NIH
	Closing Remarks Dwight Yin, M.D., Ph.D., NIAID, NIH

Mini-Symposium 2: Modeling Immunity to HIV: Bridging Preclinical Discovery to Clinical Evaluation

September 10, 2026
11:45 a.m.–4:30 p.m. EDT

Time	Presentation
11:45 a.m.–12:00 p.m.	**Opening Remarks and Brief Recap of NAMs Mini-Symposium 1** Anjali Singh, Ph.D., NIAID, NIH; Uday Shankar, Ph.D., NIAID, NIH; and Vasudev Rao, M.B.B.S., M.S., National Institute of Mental Health (NIMH), NIH
12:00–12:20 p.m.	**Keynote Presentation**
	Advancing HIV Research With NAMs Melanie Ott, M.D., Ph.D., Gladstone Infectious Disease Institute
12:20–2:10 p.m.	**Session I: Modeling Immunity, Developmental Safety, Immune Pathways, and Comorbidities**

Time	Presentation
12:20–1:20 p.m.	**Deciphering Human Immunology Through Immune Organoids and Functional MPS** Ankur Singh, Ph.D., Georgia Institute of Technology ***In Vitro* Modeling of Lymphoid Function in Spatially Organized Organs-on-Chip** Rebecca Pompano, Ph.D., University of Virginia **A NAM Model of the Cervix Recapitulates Microbial, Immunologic, and Pathogenic Properties of Sexually Transmitted Infections** Jason Gleghorn, Ph.D., University of Delaware
1:20–2:00 p.m.	**Insights Into Viral Infection and Immunity From Human Immune Organoids** Lisa Wagar, Ph.D., University of California, Irvine **Hi-DEF: A Unified Framework for Quantifying and Evaluating Immune Dysregulation at the System Level** Purvesh Khatri, Ph.D., Stanford University
2:00–2:10 p.m.	**Break**
2:10–4:00 p.m.	**Session II: Modeling Disease Pathogenesis, Tissue Reservoirs, and Sanctuary Sites**
2:10–3:00 p.m.	**Enhanced Human Antigen–Specific B-Cell Responses Using *In Vitro* 3D Tonsil Cultures Containing Stromal Cells** Marit van Gils, Ph.D., University of Amsterdam **Modeling Genome-Edited B-Cell Responses to Vaccination** James Voss, Ph.D., Scripps Research **Human Multi-Organ-on-a-Chip Systems to Evaluate Drug–Drug Safety for HIV Therapeutics** James Hickman, Ph.D., Hesperos, Inc.
3:00–3:50 p.m.	**NAMs as Drug Development Tools in Reproductive Medicine** Ramkumar Menon, Ph.D., The University of Texas Medical Branch **Modeling HIV Infection in 3D Cerebral Organoids: Opportunities and Considerations** Kelly Jordan-Sciutto, Ph.D., University of Pennsylvania **Neuroimmunity in Motion: A Human 3D Neurovascular Model for Tracking Neuroinflammation in Real Time** Lishomwa Ndhlovu, M.D., Ph.D., Weill Cornell Medicine

Time	Presentation
3:50–4:00 p.m.	**Break**
4:00–4:30 p.m.	**Session III: Expert Panel Discussion and Closing Remarks**
	Key Takeaways, Gaps in the Current NAMs Landscape, and Actionable Recommendations for Future Collaborative Research and Development Opportunities James Hickman, Ph.D., Hesperos, Inc. Lorna Ewart, Ph.D., Emulate **Closing Remarks** Vasudev Rao, M.B.B.S., M.S., NIMH, NIH

Mini-Symposium 3: Preclinical Models and NAMs in HIV Research: Priority Use Models, Platform Readiness, and Validation Pathways

September 18, 2026
12:00–4:30 p.m. EDT

Time	Presentation
12:00–12:10 p.m.	**Welcome and Opening Remarks** Yongjun Sui, Ph.D., Office of Research Infrastructure Programs (ORIP), NIH
12:10–12:20 p.m.	**Brief Recap of Mini-Symposia 1 and 2: Key Gaps, Model Systems, and Unresolved Translational Questions** David Chang, Ph.D., OAR, NIH
12:20–1:20 p.m.	**Session I: Priority Use Models for HIV NAM Adoption and Preclinical Integration**
12:20–12:45 p.m.	**Modeling Mucosal HIV: Integrating Clinical Cohorts, Organoids, and Preclinical Models** Douglas Kwon, M.D., Ph.D., Ragon Institute of MGH, Massachusetts Institute of Technology and Harvard University, and Harvard Medical School
12:45–1:10 p.m.	**New Approaches to HIV Cure** Robert Siliciano, M.D., Ph.D., The Johns Hopkins University School of Medicine
1:10–1:20 p.m.	**Break**
1:20–2:45 p.m.	**Session II: Human-Relevant Platforms and Cross-Model Translation in HIV Research**

Time	Presentation
1:20–1:45 p.m.	**Dissecting Human Inflammatory Diseases: Lessons From HIV-1** Lishan Su, Ph.D., University of Maryland School of Medicine
1:45–2:10 p.m.	**From Patient to Pipette to Predicting Clinical Outcomes: How NAMs Can Be Harnessed to Advance HIV Research** J. Zachary Porterfield, M.D., Ph.D., University of South Florida (USF) and USF Health
2:10–2:35 p.m.	**Beyond Replacement: Integrating NHP Models and NAMs to Advance HIV Research** Mirko Paiardini, Ph.D., Emory University
2:35–2:45 p.m.	**Break**
2:45–3:35 p.m.	**Session III: Validation and Context of Use for HIV NAMs**
2:45–3:10 p.m.	**Resource Development and Validation Landscape for NAMs** Oleg Mirochnitchenko, Ph.D., ORIP, NIH
3:10–3:35 p.m.	**From Models to Mothers: NAMs to Advance ARV Safety in Pregnancy** Mackenzie Cottrell, Pharm.D., M.S., University of Oklahoma College of Pharmacy
3:35–4:30 p.m.	**Extended Expert Panel Discussion and Closing Remarks**
3:35–4:25 p.m.	**Integrating Preclinical Models With NAMs for HIV Research and Product Development** All speakers
4:25–4:30 p.m.	**Closing Remarks** Stephanie Murphy, V.M.D., Ph.D., ORIP, NIH