

IHV2023 25th Anniversary and Dr. Robert Gallo Scientific Legacy Symposium & Gala



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IHV 25th Anniversary and Dr. Robert Gallo Scientific Legacy Symposium & Gala

Dear Colleagues and Friends,

You are invited to join us on Thursday and Friday, September 28-29 for the **IHV 25th Anniversary and Dr. Robert Gallo Scientific Legacy Symposium**. Delayed by COVID-19, this year's event will celebrate the 25th anniversary of the founding of the Institute of Human Virology and will recognize Dr. Robert Gallo for his lasting scientific contributions.

The focus of IHV2023 is "Viruses of Yesterday, Today, and Tomorrow" and will include a welcome message from Robert Gallo, MD, IHV Director Emeritus and Co-Founder of the Institute, the Homer & Martha Gudelsky Distinguished Professor in Medicine, Special Advisor to the Dean, Co-Founder, and Chair of the Scientific Leadership Board of the Global Virus Network, along with a brief commentary on his historic scientific discoveries on HTLV-1, HTLV-2, HIV, and herpes 6 viruses.

Expert opinions and presentations will feature John Nkengasong, MD, MSc, U.S. President's Emergency Plan for AIDS Relief (PEPFAR) Ambassador; CDC Director Rochelle Walensky MD, MPH; and Anthony Fauci, MD, among many other notable scientific and clinical researchers, highlighting their discoveries of new viruses and describing new insight into the pathogenesis of viral infections.

Sessions include: Viruses of Yesterday; Viruses of Today; Viruses of Tomorrow; New Treatments for Human Disease

An exciting 25th Anniversary Reception and Gala will take place at the close of Thursday's session. We will be celebrating the Scientific Legacy of Dr. Robert Gallo, as well as recognizing this year's IHV Lifetime Achievement Awardee for Scientific Contributions and Drug Development, William Haseltine, PhD.

The Reception will be held at the Four Seasons beginning at 6:00 pm, followed by dinner at 6:45 pm.

We look forward to welcoming you to Baltimore this September as we continue our annual tradition of excellent science and provocative discussion on our 25th anniversary.

Sincerely,



Peter Palese, PhD

Co-Chair, IHV2023 Scientific Organizing Committee Horace W. Goldsmith Professor Department of Microbiology Professor, Department of Medicine Icahn School of Medicine at Mount Sinai Member, IHV Board of Advisors Member, IHV Scientific Advisory Board Center of Excellence Director, Global Virus Network



Mark H. Kaplan, MD

Co-Chair, IHV2023 Scientific Organizing Committee Professor Emeritus Division of Infectious Disease Department of Medicine University of Michigan Health System Michigan Medicine Member, IHV Board of Advisors Member, IHV Scientific Advisory Board Member, Global Virus Network



Shyam Kottilil, MBBS, PhD

Interim IHV Director Director, Division of Clinical Care & Research Chief, Division of Infectious Diseases Professor of Medicine Institute of Human Virology University of Maryland School of Medicine Senior Advisor, Global Virus Network



The Institute of Human Virology (IHV) was established to create and develop a world-class center of excellence focusing on chronic viral diseases, especially HIV/AIDS, and virally-linked cancers.

The IHV is dedicated to the discovery, research, treatment, and prevention of these diseases.

Its unique structure seeks to connect cohesive, multi-disciplinary research and clinical programs so that new treatments are streamlined from discovery to patient.

The IHV serves patients locally and the scientific community globally

Shyamasundaran Kottilil, MBBS, PhD

Interim IHV Director Director, Division of Clinical Care and Research

George K. Lewis, PhD

IHV Deputy Director Director, Division of Vaccine Research

Manhattan Charurat, PhD

Director, Division of Epidemiology and Prevention Director, Center for International Health, Education, and Biosecurity (Ciheb)

> Lishan Su, PhD Director, Division of Virology, Pathogenesis and Cancer Interim Director, Division of Immunotherapy

> > Anthony Amoroso, MD Director, Clinical Innovations Program

> > > Robert C. Gallo, MD IHV Emeritus Director



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The Institute of Human Virology (IHV) wishes to thank the following individuals for their hard work and thoughtful efforts in developing this year's scientific program.



Peter Palese, PhD Icahn School of Medicine at Mount Sinai

Dr. Palese is Professor and Chair of the Department of Microbiology at the Icahn School of Medicine in New York. His research includes work on the replication of RNA-containing viruses with a special emphasis on influenza viruses, which are negative-strand RNA viruses. Specifically, he established the first genetic maps for influenza A, B, and C viruses; identified the function of several viral genes; and defined the mechanism of neuraminidase inhibitors (which are now FDA-approved antivirals).

Dr. Palese also pioneered the field of reverse genetics for negative strand RNA viruses, which allows the introduction of site-specific mutations into the genomes of these viruses. This technique is crucial for the study of the structure/ function relationships of viral genes, for investigation of viral pathogenicity, and for development and manufacture of novel vaccines. In addition, an improvement of the technique has been effectively used by him and his colleagues to reconstruct and study the pathogenicity of the highly virulent but extinct 1918 pandemic influenza virus. His recent work in collaboration with Dr. Garcia-Sastre has revealed that most negative strand RNA viruses possess proteins with interferon antagonist activity, enabling them to counteract the antiviral response of the infected host. Dr. Palese and colleagues are now aiming at developing a Universal Influenza Virus Vaccine, which is long-lasting and effective against all strains of influenza.

Dr. Palese is a member of the National Academy of Sciences, the National Academy of Medicine, and the American Academy of Arts and Sciences.



Mark H. Kaplan, MD University of Michigan Health System

Dr. Kaplan, formerly the Jane and Dayton T. Brown Professor at New York University School of Medicine, was at North Shore University Hospital for 25 years as Chief of Infectious Diseases, founding and serving as Director of the Center for AIDS Research and Treatment. Currently, he is Professor of Clinical Medicine at the University of Michigan Health System Department of Medicine, Infectious Diseases Division, where he conducts research on AIDS lymphoma, human endogenous retrovirus activation in HIV, and ELF-3 in breast cancer. He has published 144 peerreviewed papers in infectious diseases, along with several books and book chapters on pathogenesis, diagnosis, and treatment of infectious diseases. For years he has been named one of the "Best Doctors" in New York, in the Northeast, and in America.



Communications and Press Policy

IHV2023 is open to credentialed press.

One-on-one interviews with scientists and media may be arranged by contacting Nora Samaranayake, Chief, Communications & Public Affairs Officer, Institute of Human Virology, <u>nsam@ihv.umaryland.edu</u>.

Those registering for the meeting as "press" must provide their credentials within three days of registration to Nora Samaranayake, Chief, Communications & Public Affairs Officer, Institute of Human Virology, nsam@ihv.umaryland.edu.



The Institute of Human Virology wishes to recognize, with gratitude, the following sponsors.

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Institute of Human Virology at the University of Maryland School of Medicine Legacy Award for Transformative Scientific Discoveries



Robert C. Gallo, MD

The Institute of Human Virology (IHV) was co-founded and directed by Robert C. Gallo, MD, the eminent scientist who became world famous in 1984 when he co-discovered HIV as the cause of AIDS. Little was known then of the mysterious disease that was fast becoming the deadliest in medical history. Since, Dr. Gallo has spent much of his career trying to put an end to this raging epidemic and other viral, chronic illnesses.

Though best known for his co-discovery of HIV, Dr. Gallo and his team pioneered the development of the HIV blood test, which enabled health care workers for the first time to screen for the AIDS virus - leading to a more rapid diagnosis while simultaneously protecting patients receiving blood transfusions. His research also helped physicians develop HIV therapies to prolong the lives of those infected with the virus. In 1996, his discovery that a

natural compound known as chemokines can block HIV and halt the progression of AIDS was hailed by Science magazine as one of that year's most important scientific breakthroughs. This also helped others identify CCR5 as the HIV co-receptor since these chemokines were known to bind to CCR5.

Prior to the AIDS epidemic, Dr. Gallo was the first to identify a human retrovirus and the only known human leukemia virus - HTLV - one of few known viruses shown to cause a human cancer. In 1976, he and his colleagues discovered Interleukin-2, a growth regulating substance now used as therapy in some cancers and sometimes AIDS. And in 1986, he and his group discovered the first new human herpes virus in more than 25 years (HHV-6), which was later shown to cause an infantile disease known as Roseola and currently is hypothesized as a strong suspect in the origin of Alzheimer's disease.

Dr. Gallo's legacy continues at the IHV, a first-of-its-kind virology center that combines the disciplines of research, patient care and prevention programs in a concerted effort to speed the pace of medical breakthroughs. IHV was co-founded in 1996 by Dr. Gallo alongside his now longtime colleagues, William Blattner, MD, who is now retired, and Robert Redfield, MD, associate director of the IHV and director of IHV's Division of Clinical Care and Research. The Institute is a part of the University of Maryland School of Medicine and affiliated with the University of Maryland Medical Center. IHV's patient base includes approximately 6,000 in Baltimore and Washington, D.C., and more than 1.3 million in African and Caribbean nations. In particular, IHV is internationally renowned for its basic science and vaccine research, which includes a preventive HIV vaccine candidate in human clinical trials and funded largely by the Bill & Melinda Gates Foundation. The Institute has five Divisions comprising Basic Science, Vaccine Research, Immunotherapy, Clinical Care and Research, and Epidemiology and Prevention, and four Scientific Core Facilities.

In 2011, Dr. Gallo co-founded the Global Virus Network (GVN) to position the world to rapidly respond to new or re-emerging viruses that threaten mankind, to bring together and achieve collaboration amongst the world's leading virologists, and to support training of the next generation of medical virologists.

Prior to becoming director of the Institute in 1996, Dr. Gallo spent 30 years at the National Institutes of Health's National Cancer Institute, where he was head of its Laboratory of Tumor Cell Biology. A Connecticut native, his interest in science and medicine was first stirred by the loss of his 6-year-old sister to leukemia when he was just 12 years old. The physicians who cared for her made a lasting impression and Dr. Gallo would later make scientific research - and the opportunity to help put an end to deadly diseases - his life's work.

IHV2023 25th Anniversary and Dr. Robert Gallo Scientific Legacy Symposium & Gala

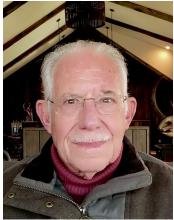


Lifetime achievements in Dr. Gallo's legendary career include discoveries that have led to both diagnostic and therapeutic advances in cancer, AIDS and other viral disorders while his vision remains unprecedented in the field of virology.

Dr. Gallo's research has brought him international recognition as well as election into the National Academy of Sciences and the Institute of Medicine. He has been awarded honors for his contribution to science from countries around the world and holds 35 honorary doctorates. Dr. Gallo was the most referenced scientist in the world in the 1980s and 1990s, during which he had the unique distinction of twice winning America's most prestigious scientific award - the Albert Lasker Award in Medicine - in 1982 and again in 1986. Dr. Gallo is the author of more than 1,200 scientific publications and the book "Virus Hunting - AIDS, Cancer & the Human Retrovirus: A Story of Scientific Discovery."



2023 IHV 25th Anniversary Lifetime Achievement Award for Scientific Contributions and Drug Development



William Haseltine, PhD

William Haseltine, PhD, is an American scientist, businessman, author, and philanthropist. He is known for his groundbreaking work on HIV/AIDS, the human genome, and the COVID-19 pandemic. He was a Professor at Harvard Medical School, where he founded two research departments on cancer and HIV/AIDS.

Dr. Haseltine helped create the biotechnology companies ProScript Inc. that developed a treatment multiple myeloma and other cancers, and Dendreon that developed the first approved cell-based cancer therapy for treating metastatic prostate cancer. Haseltine co-founded Human Genome Sciences, which developed a number of drugs for treating diabetes and its complications, cancers, obesity, and anthrax.

After completing the sequence of the HIV genome, Dr. Haseltine's laboratory then showed that damage to certain viral genes killed the virus, identifying good antiviral drugs. The first HIV-specific protease inhibitor, Nelfinavir, was developed as a part of a collaboration between the Haseltine laboratory, Cambridge BioSciences — another company founded by Dr. Haseltine —, and Agouron Pharmaceuticals. He founded additional biotechnology companies including The Virus Research Institute, LeukoSite, Diversa, X-VAX, and Demetrix.

Dr. Haseltine successfully advocated for Congress to HIV/AIDS research through the NIH. He publicly advocated for destigmatizing HIV infection. He played an important early role in creating the International Society for AIDS Research, now the International AIDS Society, and was the Founding Editor of the scientific journal AIDS Research and Human Retroviruses. Dr. Haseltine went on to co-found E-Biomed: The Journal of Regenerative Medicine and The Society for Regenerative Medicine to help expand the field of regenerative medicine.

Committed to philanthropy, Dr. Haseltine founded two non-profit foundations. He is President of the Haseltine Foundation for Science and the Arts, and Chairman and President of ACCESS Health International, an organization dedicated to improving access to high-quality health outcomes worldwide through medical technology. In 2001 he was listed by Time Magazine as one of the world's 25 most influential businesspeople, and in 2015 by Scientific American as one of the 100 most influential leaders in biotechnology. He is the author of more than two hundred peer-reviewed manuscripts and fifteen books.



Previous Recipients of IHV Lifetime Achievement Awards

LIFETIME ACHIEVEMENT AWARD FOR SCIENTIFIC CONTRIBUTIONS

- 1999 George Klein, MD, Karolinska Institute, Stockholm, Sweden
- 2000 Maurice Hilleman, PhD, Merck Research Laboratories, Sumneytown, Pennsylvania, USA
- 2001 Hilary Koprowski, MD, Thomas Jefferson University, Philadelphia, Pennsylvania, USA
- 2002 Alexander Rich, MD, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA
- 2003 Jan Svoboda, PhD, DSc, Institute of Molecular Genetics, Prague, Czech Republic
- 2004 Paul Zamecnik, MD, Massachusetts General Hospital, Boston, Massachusetts, USA
- 2005 Manfred Eigen, PhD, Max Planck Institute, Göttingen, Germany
- 2006 Maxine Singer, PhD, National Institutes of Health, Bethesda, Maryland, USA
- 2008 Isaac P. Witz, PhD, Tel Aviv University, Tel Aviv, Israel
- 2010 Rino Rappuoli, PhD, Novartis Vaccines, Sienna, Italy
- 2011 Max Essex, DVM, PhD, Harvard AIDS Institute, Boston, Massachusetts, USA
- 2012 Thomas A. Waldmann, MD, National Cancer Institute, Bethesda, Maryland, USA
- 2013 Vadim I. Agol, MD, PhD, DSc, Russian Academy of Medical Sciences, Moscow, Russia
- 2014 William Paul, MD, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA
- 2015 Harald zur Hausen, MD, Nobel Laureate, Gelsenkirchen, Germany
- 2016 Peter Vogt, PhD, Scripps Research Institute, La Jolla, California, USA
- 2017 Peter Palese, PhD, Icahn School of Medicine at Mount Sinai, New York, New York, USA
- 2019 Warner C. Greene, MD, PhD, Gladstone Center for HIV Cure Research

LIFETIME ACHIEVEMENT AWARD FOR PUBLIC SERVICE

- 2004 Stewart Greenebaum, Greenebaum and Rose Associates, Inc., Baltimore, Maryland, USA
- 2006 Martin Delaney, Project Inform, San Francisco, California, USA
- 2008 John D. Evans, Evans Telecommunication Company, Miami, Florida, USA
- 2008 The Honorable Robert K. Gray, Gray and Company II, Miami, Florida, USA
- 2010 Harry Huge, Esq., The Harry and Reba Huge Foundation, Charleston, South Carolina, USA
- 2011 Bernadine Healy, MD, In Memoriam, Former Director, National Institutes of Health, Bethesda, MD, USA
- 2012 Yi Zeng, PhD, China Centers for Disease Control, Beijing, China
- 2013 José G. Esparza, MD, PhD, Bill & Melinda Gates Foundation, Seattle, Washington, USA
- 2014 John Martin, PhD, Gilead Sciences, Inc., Foster City, California, USA
- 2015 Anthony S. Fauci, MD, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA
- 2016 Raymond Schinazi, PhD, Hon DSc, Emory University, Atlanta, Georgia, USA
- 2017 Quarraisha Abdool Karim, PhD, Center for the AIDS Programme of Research in South Africa, Durban, South Africa
- 2017 Salim Abdool Karim, MBChB, PhD, DSc, Center for the AIDS Programme of Research in South Africa, Durban, South Africa
- 2019 The Honorable Parris N. Glendening, Smart Growth America's Leadership Institute, Governors' Institute on Community Design
- 2019 The Honorable Kathleen Kennedy Townsend, Economic Policy Institute

ONE-TIME LIFETIME ACHIEVEMENT AWARD FOR EXCELLENCE IN TEACHING

2010 Michele LaPlaca, MD, Institute of Microbiology of the University of Bologna, Bologna, Italy

LIFETIME ACHIEVEMENT AWARD FOR EXCELLENCE IN MEDICAL EDUCATION, CLINICAL CARE AND CLINICAL RESEARCH

- 2012 John G. Bartlett, MD, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland
- 2018 Henry Masur, MD, Chief of Critical Care Medicine Department, NIH Clinical Center, Bethesda, Maryland, USA

LIFETIME ACHIEVEMENT AWARD FOR EXCELLENCE IN CLINICAL RESEARCH

2018 Kiyoshi Takatsuki, MD, PhD, Professor Emeritus, Kumamoto University, Kumamoto, Japan



Evening Events Schedule

Thursday, September 28, 2023

6:00 pm

Gala Reception Grand Prefunction

6:45 pm

Gala Dinner and Awards Ceremony Grand Ballroom A



Program Overview

Thursday, September 28, 2023

9:00am – 12:00 pm	Session A - Viruses of Yesterday
10:20 – 10:30 am	Coffee Break
12:00 pm – 1:00 pm	Lunch Break
1:00 – 4:00 pm	Session B – Viruses of Today
2:30 – 2:40 pm	Coffee Break
6:00 pm	Gala Reception
6:45 pm	Lifetime Achievement Award Dinner
Friday, September 29, 2023	
9:00 am – 12:00 pm	Session C – Viruses of Tomorrow
10:25 – 10:35 am	Coffee Break
12:00 – 1:00 pm	Lunch Break
1:00 – 4:00 pm	Session D – New Treatments for Human Disease
2:30 – 2:40 pm	Coffee Break



Speaker Schedule

Thursday, September 28, 2023

Session A:

Viruses of Yesterday

Grand Ballroom B Chairpersons and Discussants: William Blattner, MD, Salt Run Global Health and Research Man Charurat, PhD, MHS, Institute of Human Virology

- 9:00 Robert Gallo, MD, Institute of Human Virology, University of Maryland School of Medicine, U.S. *Welcome, Session Comments/One Man Four Viruses HTLV-1, HTLV-2, HIV, Herpes 6*
- 9:20 Jeffrey Cohen, MD, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health A-101 Development of Vaccines for Herpesviruses
- 9:50 Diane E. Griffin, MD, PhD, W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD A-102 Measles: Immunity and Immunosuppression

Coffee Break, 10:20 AM - 10:30 AM Grand Prefunction

- 10:30
 Ambassador Dr. John N. Nkengasong, U.S. Global AIDS Coordinator and Special Representative for
Global Health Diplomacy The United States President's Emergency Plan for AIDS Relief
 A-103

 PEPFAR 20th Anniversary and its role in Pandemic Preparedness
 A-103
- 11:00 Genoveffa Franchini, MD, Animal Models and Retroviral Vaccines Section, Vaccine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA A-104 Innate and adaptive immunity to prevent SIV/HIV infection
- 11:30 William Blattner, MD, Salt Run Global Health and Research *Round Table Discussion*

Lunch Break, 12:00 PM - 1:00 PM

Session B:

Viruses of Today

Grand Ballroom B Chairpersons and Discussants: Peter Palese, PhD, Icahn School of Medicine at Mount Sinai Susan Weiss, PhD, University of Pennsylvania

1:00 Andrea Carfi, PhD, Chief Scientific Officer, Moderna Genomics *mRNA/LNP: a disruptive technology for infectious disease vaccines and beyond*

B-101



IHV2023 25th Anniversary and Dr. Robert Gallo Scientific Legacy Symposium & Gala



Lunch Break, 12:00 PM - 1:00 PM

Session D:

New Treatments for Human Disease

Grand Ballroom B Chairpersons and Discussants: Warner C. Greene, MD, PhD, Gladstone Institute of Virology George Lewis, PhD, Institute of Human Virology

1:00	Shyamasundaran Kottilil, MBBS, PhD, Interim IHV Director; Director, Division of Clinical Care & Research; Chief, Division of Infectious Diseases; Professor of Medicine, Institute of Human Virology, University of Maryland School of Medicine; Senior Advisor, Global Virus Network <i>Novel Antiviral Therapeutics for hepatits viruses</i>	D-101	
1:15	Howard Gendelman, MD, University of Nebraska College of Medicine At the crossroads of viral infection of CD4+ T cells and mental health	D-102	
1:30	Warner C. Greene, MD, PhD, Gladstone Institute of Virology Direct infection of microglia in human brain organoids induces inflammation leading to bystander neuron dysfunction and death: Implications for HIV-associated neurocognitive disorder (HAND)	D-103	
2:00	Mario Stevenson, PhD, Department of Medicine, University of Miami, Miller School of Medicine, Miami, FL, USA HIV-1 Persistence in Myeloid Cell Reservoirs	D-104	
Coffee Break, 2:30 AM - 2:40 AM Grand Prefunction			
2:40	Michel Nussenzweig, MD, PhD, Rockefeller University Antibodies in HIV-1 Vaccine and Therapy	D-105	
3:10	Warner C. Greene, MD, PhD, Gladstone Institute of Virology Round Table Discussions		
3:40	Robert Gallo, MD, Institute of Human Virology		

The Future of the IHV

Adjourn, 4:00 PM



- A-101 Jeffrey Cohen, MD, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health Development of Vaccines for Herpesviruses
- A-102 Diane E. Griffin, MD, PhD, W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD *Measles in the 21st Century*
- A-103 Ambassador Dr. John N. Nkengasong, U.S. Global AIDS Coordinator and Special Representative for Global Health Diplomacy The United States President's Emergency Plan for AIDS Relief *PEPFAR 20th Anniversary and its role in Pandemic Preparedness*
- A-104 Genoveffa Franchini, MD, Animal Models and Retroviral Vaccines Section, Vaccine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA Innate and adaptive immunity to prevent SIV/HIV infection
- **B-101** Andrea Carfi, PhD, Chief Scientific Officer, Moderna Genomics *mRNA/LNP: a disruptive technology for infectious disease vaccines and beyond*
- **B-102** Susan R Weiss, PhD, Perelman School of Medicine, University of Pennsylvania Human coronaviruses induce diverse interferon signaling responses in primary nasal epithelial cells
- **B-103** Ralph S. Baric, PhD, Departments of Epidemiology, Microbiology and Immunology, University of North Carolina at Chapel Hill *Challenges in Pan Betacoronavirus Countermeasure Design*
- B-104 Anthony S. Fauci, MD, Georgetown University: School of Medicine and McCourt School of Public Policy Pandemic Preparedness and Response: Lessons from COVID-19
- C-101 Rachel Roper, PhD, East Caroline University, Brody Medical School Monkeypox Infections, Therapeutics and Vaccines
- **C-102** Emma Thomson, PhD, MRC, University of Glasgow Center for Virus Research Adeno-associated virus 2 infection in children with non-A–E hepatitis
- C-103 Erica Ollmann Saphire, PhD, MBA, La Jolla Institute for Immunology Antibodies against Emerging Infections: A Global Collaboration
- C-104 Bruce Walker, MD, Ragon Institute of MGH, MIT and Harvard HIV Controllers as a model for therapeutic and prophylactic vaccines
- C-105 Gavin Cloherty, PhD, Head of Infectious Disease Research and the Abbott Pandemic Defense Coalition, Diagnostics Discovery of New Agents of Disease
- D-101 Shyamasundaran Kottilil, MBBS, PhD, Interim IHV Director; Director, Division of Clinical Care & Research; Chief, Division of Infectious Diseases; Professor of Medicine, Institute of Human Virology, University of Maryland School of Medicine; Senior Advisor, Global Virus Network Novel Antiviral Therapeutics for hepatits viruses
- D-102 Howard E. Gendelman, MD, University of Nebraska Medical Center At the crossroads of viral infection of CD4+ T cells and mental health
- **D-103** Warner C. Greene, MD, PhD, Gladstone Institute of Virology Direct infection of microglia in human brain organoids induces inflammation leading to bystander neuron dysfunction and death: Implications for HIV-associated neurocognitive disorder (HAND)
- D-104 Mario Stevenson, PhD, Department of Medicine, University of Miami, Miller School of Medicine, Miami, FL, USA HIV-1 Persistence in Myeloid Cell Reservoirs
- D-105 Michel Nussenzweig, MD, PhD, Rockefeller University Antibodies in HIV-1 Vaccine and Therapy



A-101 Development of Vaccines for Herpesviruses

Jeffrey Cohen, MD, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Of the 8 human herpesviruses, vaccines are available only for onevaricella-zoster virus. mRNA vaccines for herpes simplex virus (HSV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV) are in clinical trials in which multiple viral glycoproteins from each virus are expressed. In addition both a CMV glycoprotein subunit protein vaccine and a nonreplicating vectored vaccine are in trials for CMV. Our lab has developed vaccines for EBV in which viral glycoproteins are fused to ferritin and self-assemble into nanoparticles containing a dense, symmetrical array of antigen. These nanoparticles have neutralizing antibody epitopes that are optimally spaced to cross-link B cell receptors and they induce higher neutralizing antibody titers than the corresponding soluble glycoproteins in animal models. Passive transfer of antibody from vaccinated mice into humanized mice protect the latter from EBV viremia and lymphoma after challenge with the virus. We are performing a clinical trial of one of these vaccines. In addition, we have developed monoclonal antibodies to EBV glycoproteins and have shown that they can protect mice from viremia and EBV lymphoma after challenge with the virus. Such monoclonal antibodies might be useful to prevent EBV disease in immune compromised persons who may not respond well to vaccines.



Jeffrey Cohen received his M.D. from The Johns Hopkins University and was a resident in medicine at Duke University. Following a fellowship at the National Institutes of Health (NIH), he was a clinical fellow in infectious diseases at the Brigham and Women's Hospital and an instructor in medicine at Harvard University. He returned to NIH, where he is chief of the Laboratory of Infectious Diseases. He is a member of the American Association of Physicians, the American Society for Clinical Investigation, and an Associate Editor of Field's Virology.

Dr. Cohen's laboratory focuses on vaccine development for human herpesviruses, and treatment and identification of cellular mutations in patients

with severe herpesvirus infections. Clinical projects complement the laboratory studies including a phase I study of an Epstein-Barr virus vaccine, studies of patients with severe virus infections, and studies of immune responses in persons after infection or vaccination.

A-102 Measles in the 21st Century

Diane E. Griffin, MD, PhD, W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Measles is a highly infectious, aerosol-transmitted rash disease that continues to be an important cause of childhood mortality despite the availability of a safe, effective live virus vaccine. Measles virus (MeV) infects lymphocytes and macrophages as well as epithelial and endothelial cells and has profound effects on the immune system. Measles increases susceptibility to other infections, but life-long immunity is established after recovery. Our studies have shown that MeV RNA persists long after infectious virus is cleared with continued stimulation of virus-specific T cell and antibody responses. While antibody to MeV is increasing and maturing, levels of antibody to other pathogens decrease. Measles vaccine replicates less well in lymphoid tissue and does not have these effects, but needs to be delivered to a high proportion of the population to prevent outbreaks.



Diane E. Griffin is University Distinguished Service Professor and former Chair of the W. Harry Feinstone Department of Molecular Microbiology and Immunology at Johns Hopkins Bloomberg School of Public Health. Dr. Griffin is a virologist recognized for her work on the pathogenesis of viral infections. She is known particularly for her studies on measles and alphavirus encephalomyelitis that have delineated the role of the immune response in virus clearance, vaccine-induced protection from infection, tissue damage and immune suppression. Dr. Griffin graduated from Augustana College, Rock Island, Illinois with a B.A. in biology and from Stanford University School of Medicine with an M.D and Ph.D. in immunology, followed by a residency in internal medicine.

internal medicine. She was a postdoctoral fellow in virology and infectious diseases at Johns Hopkins University School of Medicine and joined the faculty in 1974. She has been president of the American Society for Virology and of the American Society for Microbiology and is a member of Global Virus Network, the National Academy of Sciences and the National Academy of Medicine.



A-103 PEPFAR 20th Anniversary and its role in Pandemic Preparedness

Ambassador Dr. John N. Nkengasong, U.S. Global AIDS Coordinator and Special Representative for Global Health Diplomacy The United States President's Emergency Plan for AIDS Relief

The PEPFAR program has been without a doubt one of the most successful global health programs in history. At the turn of the millennium, HIV/AIDS had driven life expectancies down 10-30 years in many high burden countries. The creation of PEPFAR (and the Global Fund) served as a critical inflection point in the fight, and after 20 years, and hundreds of billions of dollars invested, HIV is on the decline, especially in high burden countries. However, persistent gaps remain at the last mile - especially for vulnerable groups such as children, adolescent girls and young women, and key populations. With the launch of the new Bureau of Global Health Security and Diplomacy at the State Department, PEPFAR's future role in not only ending the HIV/AIDS pandemic as a public health threat, but also sustainably strengthening public health systems comes into focus even more. Ambassador Nkengasong will reflect on lessons from PEPFAR over the past 20 years in how to control one of the most complex diseases in history, while also exploring ways health systems and institutions that PEPFAR support are better equipped to fight, prevent, detect, and control the pandemics of the future.



Dr. John N. Nkengasong is an Ambassador at Large and serves as the U.S. Department of State's U.S. Global AIDS Coordinator and Special Representative for Global Health Diplomacy. In this role, Dr. Nkengasong oversees the U.S. President's Emergency Plan for AIDS Relief – PEPFAR; which is the largest commitment by any nation to address a single disease in history, prevent millions of HIV infections, save lives, and make progress toward ending the HIV/AIDS pandemic. Previously, Dr. Nkengasong served as the first director of the Africa Centres for Disease Control and Prevention. Through his leadership, a framework for transforming Africa CDC into a full autonomous health agency of the Africa Union was established. As Africa CDC director, Dr. Nkengasong also led the COVID-19 response in Africa, coordinating with heads

of state and governments across the continent, among other achievements to fight the COVID-19 pandemic, he helped secure 400 million doses of COVID-19 vaccines at the height of vaccine scarcity. During his tenure, he was appointed as one of the World Health Organization's special envoys on COVID-19 preparedness and response. Dr. Nkengasong also served as acting deputy principal director of the Center for Global Health, as well as the Division of Global HIV and TB's chief of the International Laboratory Branch at the U.S. Centers for Disease Control and Prevention.

As a world-renowned public health leader, Dr. Nkengasong's contributions to global health have been recognized by numerous prestigious awards and honors including the Bill and Melinda Gates Foundation, 2020 Global Goalkeeper Award; Time Magazine, 2021 Time 100 List of Most Influential People; Fortune magazine, 2021 World's 50 Greatest Leaders; Bloomberg, 2021 Bloomberg 50 Influential People; and U.S. Centers for Disease Control and Prevention, Shepard Award and William Watson Medal of Excellence. Last year, he was invited to join the National Academy of Medicine and he became the first laureate of the Virchow Prize for Global Health. In 2023, he received the African of the Year Award from All Africa Business Leaders Award in partnership with CNBC Africa and Forbes Africa. Dr. Nkengasong also holds the rare honor of being knighted by the governments of Sénégal, Côte d'Ivoire, and Cameroon.

A-104 Innate and adaptive immunity to prevent SIV/HIV infection

Genoveffa Franchini, MD, Animal Models and Retroviral Vaccines Section, Vaccine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA

The highest burden of people living with HIV and of new HIV infections and AIDS is in Africa, with 61% of the 5000 new daily infections occurring in sub-Saharan Africa, and of these 80% are in adolescent girls (age 15-19) who scarce access to antiretroviral therapy. The potential of the ALVAC/ SIV vaccine modality boosted with gp120 (formulated in alum or MF59) has been reproduced in macaques by recapitulating the limited success of RV 144, and by predicting the futility in the HVTN-702 trial in South Africa. The efficacy of ALVAC-based HIV vaccine candidates has been increased in macagues by modifying the vaccine platform, by shortening the vaccine regimen and by exposing Variable region 2 (V2), located at the apex of the viral spike, in an α-helix conformation via the deletion of Variable Region 1 (V1). This vaccine regiment will be first in humans in the CLEAR trial at the NCI in year 2025. Vaccine efficacy is linked the engagement of the CCR2/ CCL2 anti-inflammatory axis, M2-like monocytes mediating efferocytosis, a function that avoids inflammation by clearing apoptotic cells. Vaccine efficacy is further increased, from 65% to 92.7%, by adding a topical vaginal gel with S-acyl-2 mercaptobenzamide thioester (SAMT-247) 2. SAMT-247 synergizes with vaccination by increasing protective immunity and the combination is more efficacious than vaccine alone (p=0.006).

A gel delivery of SAMT-247 limits compliance. The development of IntraVaginal Ring (IVR) with sustained delivery of SAMT-247 to prevent HIV transmission to women may overcome this limitation.

Ref: ¹Bissa M. et al Nat. Comm, 2023; ²Rahman M.A.et al Nat Microbiol, 2023.



Genoveffa Franchini obtained her MD at the age of 25 from the University of Modena, Italy. She is Board. Certified in Hematology and did her postdoctoral training under the mentorship of Drs F. Wong-Staal, and R.C Gallo at the NIH. She is the head of the Animal Models and Retroviral Vaccines Section at the National Cancer Institute, NIH. She has published more than 300 per-reviewed papers in reputed journals and has been serving on editorial board of several journal and participated in advisory board for American Academic Institutions. Dr. Franchini has pioneered research on oncogenes and the molecular virology of human retroviruses (HTLVs and HIVs). Her work has furthered the understanding of HIV and HTLV-1 pathogenesis, leading to the identification and characterization of new viral genes for HIV and HTLV-1. and their functions.

Her accomplishments in HIV vaccine development include the pre-clinical work on the Canarypox (ALVAC) based HIV vaccine, the first vaccine to demonstrate significant, though limited, protection against HIV acquisition in the RV144 HIV vaccine trial that enrolled 16,000 volunteers in Thailand. She has further improved the efficacy of the ALVAC-based vaccine modality by priming with DNA and removing epitopes (within the Variable region 1 -V1) that induce interfering antibodies. She uncovered that efferocytosis, mediated by CD14+ myeloid cells, are a primary novel correlate of the efficacy of these vaccine modalitis. Her recent work has led to the demonstration that SAMT-247, a zinc finger protein inhibitor, potently synergize with the DNA/ALVAC/gp120/alum vaccine regimen. The novel HIV vaccine candidates will be to be tested in Phase I human HIV vaccine Trial (CLEAR trial) in 2024/25. Plans include the formulation of SAMT-247 for slow release in vaginal rings, to be combined with vaccination in adolescent females at risk of HIV acquisition.



B-101

mRNA/LNP: a disruptive technology for infectious disease vaccines and beyond

Andrea Carfi, PhD, Chief Scientific Officer, Moderna Genomics

The mRNA technology has proven to be safe and highly efficacious in preventing COVID-19 disease. Moderna and Pfizer were able to get emergency use authorization (EUA) for their respective vaccines in less than a year. The success of the Moderna and Pfizer COVID-19 vaccines has resulted in a large number of companies and public institution to intensify and expand their effort on the mRNA technology and several new drugs are now in clinical studies with three new vaccines in late stage development (Cytomegalovirus (CMV) vaccine, Respiratory Syncytia Virus (RSV) vaccine for older adults and seasonal influenza vaccine). During my talk I will present data on the mRNA vaccines mode of action and some of the work that has led to the selection of the current Moderna mRNA and LNPs. Finally, to show the great potential of this technology I will present as well as examples of applications beyond infectious disease vaccines.



Andrea Carfi is the CSO for Infectious Disease at Moderna. Moderna Infectious Disease focuses on the discovery and development of vaccines as well as other therapeutic and prophylactic approaches against infectious disease targets using Moderna proprietary mRNA technology. Andrea joined Moderna 12017 as Head of Antigen Design and Selection and Project Leader. Since January 2019 he is leading Infectious Disease Research.

Andrea has almost 20 years of experience in drug discovery and vaccine development at Moderna, GSK, Novartis Vaccines and IRBM / Merck. Over the years he has held roles of increasing responsibility with a focus on structural biology, antigen design, small molecule antivirals discovery and vaccines

development. Prior to joining Moderna Andrea was at GSK and Novartis Vaccines for seven years. During this time he led the US based Protein Biochemistry team which was responsible for the design, selection, characterization and early development of novel vaccine targets against viral infectious disease. Some of these vaccine candidates are now in late stage clinical trials. Andrea was also leading the Novartis Vaccines Antigen Design platform across the research sites of Cambridge, US and Siena, Italy. During his time at Moderna Andrea has led the early development of the CMV mRNA vaccine, now in a Phase 3 efficacy study, and has built both a large portfolio of mRNA vaccines against Infectious Disease targets. Most recently Andrea was closely involved in the development of Spikevax, the Moderna mRNA vaccine against COVID-19.

Andrea holds a Master of Science in Physics for University of Canterbury in UK, a Master of Science in Chemistry from Pavia University, Italy, and a PhD in Biophysics from the Université Joseph Fourier in Grenoble, France. He also trained as postdoctoral fellow in the laboratories of Prof. Stephen Harrison and Prof. Don Wiley at Children's Hospital, Boston US. Andrea is co-author of more than 100 publication in peer-reviewed scientific journals.

Human coronaviruses induce diverse interferon signaling responses in primary nasal epithelial cells

B-102

Susan R Weiss, PhD, Perelman School of Medicine, University of Pennsylvania; Clayton Otter, AB, Perelman School of Medicine, University of Pennsylvania; David M Renner, BA, Perelman School of Medicine, University of Pennsylvania; David M Renner, BA, Perelman School of Medicine, University of Pennsylvania; Alejandra Fausto, BA, Perelman School of Medicine, University of Pennsylvania; Li Hui Tan, PhD, Otorhinolaryngology-Head and Neck Surgery, Perelman School of Medicine, University of Pennsylvania and Department of Surgery, Corporal Michael J. Crescenz VA Medical Center; Noam A. Cohen,MD, PhD, Otorhinolaryngology-Head and Neck Surgery, Perelman School of Medicine, University of Pennsylvania and Department of Surgery, Corporal Michael J. Crescenz VA Medical Center

All respiratory viruses establish a primary infection in the nasal epithelium, where efficient induction of antiviral innate immune responses may result in local control of viral replication, limited spread to the lower airway, and minimal pathogenesis. To study the role of antiviral interferon (IFN) signaling during infection, we utilize a primary epithelial culture system in which patient-derived sinonasal epithelial cells are grown at an air-liquid interface (ALI). Nasal ALI cultures recapitulate the polarized heterogeneous cellular population and mucociliary functions of the in vivo airway. We performed RNA seg analyses of nasal ALI cultures infected with 4 human coronaviruses (HCoVs) and found that these HCoVs diverged significantly in terms of antiviral IFN induction. MERS-CoV showed near complete shut-down of IFN signaling, SARS-CoV-2 showed moderate IFN induction, and the common cold-associated HCoVs (HCoV-229E and HCoV-NL63) showed the strongest IFN signature. Infections with MERS-CoV or SARS-CoV mutant recombinant viruses defective in IFN antagonists reverse its IFN-evasive phenotype, resulting in IFN induction similar to the seasonal HCoVs. We further carried out nasal cell infections with each of these HCoVs in the presence of ruxolitinib, a JAK (Janus kinase) inhibitor, which abrogates IFN signaling. While ruxolitinib treatment has minimal impact on viral titers at early time points, titers are increased significantly at later time points, with the most significant impact of ruxolitinib during seasonal HCoV infection (titers 2-3 log10 PFU/mL increased late in infection). These data indicate that induction of antiviral IFN signaling in the nasal epithelium may be pivotal in clearance or resolution of HCoV infection, especially during infections with HCoVs that replicate predominantly in the upper respiratory tract.



Susan Weiss obtained her PhD in Microbiology from Harvard University working on paramyxoviruses and did postdoctoral training in retroviruses at University of California, San Francisco. She came to the University of Pennsylvania (Penn) as an Assistant Professor in 1980, and is currently Professor and Vice Chair, Department of Microbiology and Co-director of the Penn Center for Research on Coronaviruses and Other Emerging Pathogens at the Perelman School of Medicine at Penn. She previously served as Associate Dean for Biomedical Postdoc Programs (2010-2019). She has worked on many aspects of coronavirus replication and pathogenesis over the last forty years, making contributions to understanding the basic biology as well as viral entry, organ tropism and virulence. This work focused for many years on the murine

coronavirus (MHV) mouse model of hepatitis. More recently she has work on SARS-CoV and MERS-CoV and since 2020 also on SARS-CoV-2, as well as the "common cold" coronaviruses. Her work for the last ten years has focused on coronavirus interaction with the host innate immune response, viral antagonists of double-stranded RNA induced antiviral pathways and interactions with the unfolded protein responses. Most recent work also focusses on coronavirus infection of the nasal epithelium, the earliest site of infection. Her other research interests include activation and antagonism of the double-stranded RNA induced antiviral responses, with a focus on the oligoadenylate-ribonuclease L (OAS-RNase L) pathway, flavivirus- primarily Zika-virus-host interactions and pathogenic effects of host endogenous dsRNA.



B-103 Challenges in Pan Betacoronavirus Countermeasure Design

Ralph S. Baric, PhD, Departments of Epidemiology, Microbiology and Immunology, University of North Carolina at Chapel Hill

The early 21st century has seen the emergence of several novel human and animal coronaviruses that have caused considerable economic losses and high morbidity and mortality rates across global populations. This accelerated pattern of emergence is highlighted to acknowledge the critical importance of developing broadly active countermeasures that can be rapidly implemented in outbreak, epidemic and pandemic settings across the globe. Focusing on pan betacoronavirus disease control from both historic and contemporary perspectives, challenges are highlighted and discussed in the context of the underlying mechanisms that regulate virus evolution and its downstream impact on strain diversification, antigenic variation, and countermeasure performance. The known correlates of protective or pathogenic immune outcomes and antigenic seniority are introduced in the context of pan betacoronavirus vaccine performance. while highlighting the critical importance of robust animal models of human disease. Then, a variety of novel vaccine platforms are designed, tested empirically to demonstrate superior immunogenic breadth and protective immunity across a diverse array of betacoronavirus challenge models. Gaps and future studies will acknowledge the critical need for genetically distant virologic strains and animal models designed to maximally probe the underlying immunologic and molecular mechanisms that will regulate protective and/or pathogenic outcomes in outbred populations.



Ralph S. Baric, PhD is the University of North Carolina Kenan Distinguished Professor of Epidemiology in the Gillings School of Global Public Health and Microbiology and Immunology in the School of Medicine. He earned a BS in Zoology and a PhD in Microbiology from North Carolina State University. He performed postdoctoral research in virology and immunology at the University of Southern California before joining the faculty at the University of North Carolina. Dr. Baric's research focuses on the pathogenesis and emergence mechanisms of RNA viruses, focusing on coronaviruses, flaviviruses and noroviruses. His group has made seminal contributions in virus genetics, identifying host susceptibility genes that regulate virus pathogenesis and emergencesis, and virulence. His laboratory participated in the development

of several antiviral drugs (remdesivir, molnupiravir), therapeutic antibodies and vaccines (Moderna, Jennsen) targeting the SARS-CoV2 virus which is responsible for the COVID19 pandemic. He is a member of the American Society for Microbiology (ASM) and American Society for Virology. He is a Harvey Weaver Scholar from the National Multiple Sclerosis Society and an Established Investigator from the American Heart Association. He served as chair-elect and subsequently the chair of ASM Division T, RNA viruses. He was a finalist for the World Technology Award, a senior editor for Plos Pathogens, and member of the Journal of Virology editorial board. He was a standing member of the NIH VirB study section from 2005-2009 and is a current member of NIH CMIA study section (2020-). He received the Innovation/Inspiration Award for UNC Faculty Research, the Lifetime achievement award from the Triangle Business Journal, Norma Berryhill Distinguished Lecturer, the UNC System's O. Max Gardner Award recipient and the North Carolina's Governor's Award recipient. He is a fellow of the American Academy for Microbiology and elected to the National Academy of Sciences and the American Academy of Arts and Sciences. At the Congressional Biomedical Research Congress in early 2020, Baric updated the House of Representative members and staffs regarding the dangers of the SARS-CoV2 pandemic, including research priorities and strategies to mitigate risk. B-104 Pandemic Preparedness and Response: Lessons from COVID-19

Anthony S. Fauci, MD, Georgetown University: School of Medicine and McCourt School of Public Policy

The global experience with COVID-19 holds important lessons for preparing for, and responding to, future emergences of pathogens with pandemic potential. Although dozens of lessons could be addressed 10 that are noteworthy will be addressed. The first lesson is inherent to any newly emergent infectious pathogen with pandemic potential: expect the unexpected. The second lesson is the importance of acting early, rapidly, and aggressively in implementing public health interventions and countermeasure development. The third lesson is that global informationsharing and collaborations are essential for a successful response to a pandemic. A fourth lesson is the importance of leveraging already existing capabilities such clinical trials networks to assess new countermeasures. The fifth, and arguably most important, lesson from the COVID-19 pandemic is that sustained investments in basic and clinical research are critical for the rapid development of effective countermeasures essential for an optimal pandemic response. The sixth lesson is the utility of the prototype pathogen approach to pandemic preparedness and response. The seventh lesson is the importance of attention to perturbations of the animal-human interface. The eighth lesson is that longstanding systemic health and social inequities drive pandemic-related disparities, and these must be addressed. The ninth lesson is that misinformation and disinformation are the enemy of public health and pandemic control. The tenth lesson is that emerging infections will be with us forever. Consideration of these 10 lessons will help us-and those who follow us-to achieve the goal of preventing future pandemics of the magnitude of COVID-19.



Anthony S. Fauci, MD is an American physician-scientist and a Distinguished University Professor in the Georgetown University School of Medicine's Department of Medicine. He also holds an additional appointment in the university's McCourt School of Public Policy. Previously, Dr. Fauci served as Director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, from 1984 to 2022. Dr. Fauci was a key advisor to seven Presidents on global HIV/AIDS issues, and on preparedness against emerging infectious disease threats. He also served as the Chief Medical Advisor to President's Emergency Plan for AIDS Relief (PEPFAR), which has helped save more than 25 million lives throughout the developing word.

Dr. Fauci is a member of the National Academy of Sciences, the National Academy of Medicine, the American Academy of Arts and Sciences, and many other professional societies. He has received numerous awards including the Presidential Medal of Freedom, the National Medal of Science, and the Mary Woodard Lasker Award for Public Service. He has been awarded 62 honorary doctoral degrees from universities in the United States and throughout the world, and is the author, coauthor, or editor of more than 1,400 scientific publications.



C-101 Monkeypox Infections, Therapeutics and Vaccines

Rachel Roper, PhD, East Caroline University, Brody Medical School

A worldwide monkeypox (mpox) outbreak was recognized in 2022 with more than 88,000 confirmed cases and 147 deaths as of June 2023. In addition cowpox continues to cause human infections in Europe, and smallpox continues to be a bioterrorism/biowarfare threat. Fortunately several drugs developed for smallpox also have efficacy against mpox and cowpox, which are all in the same genus, although human data on safety and efficacy are still being collected. Cases suggest that these drugs are not sufficient to end viral infection in all immunocompromised people. The currently available anti-poxvirus vaccines are generally protective, but the replication competent live vaccinia virus (ACAM2000) vaccine has serious side effects and is contraindicated for many people. Due to these safety concerns, routine smallpox vaccination stopped in most countries around 1970. The newer replication-deficient virus vaccine (Jynneos) has 6 large genome deletions yielding greatly improved safety, but it requires two doses, is missing immunogenic antigens, and is less protective. Numerous monkeypox infections have now been documented in people fully vaccinated with this vaccine.

A strategy for creating an improved anti-poxvirus vaccine with both better safety and efficacy than the current vaccines may be to remove targeted virulence genes to yield a vaccine that has the full complement of target antigens but which is missing the genes that block immune responses and increase virulence. My lab has worked on characterizing 2 such virulence genes, the A35R and the O1L genes. Removal of the A35 gene increases the safety of the vaccine strain ~1000 fold and induces significantly stronger antibody and T lymphocyte responses. The O1L gene is also a virulence factor. Each of these knock out viruses individually make very protective vaccines, protecting mice from a virulent challenge up to 700 LD50. The likelihood of continued spread or spillover of mpox and other poxviruses calls for continued research into therapeutics and vaccines.



Dr. Roper is a Professor of Microbiology and Immunology at East Carolina University (ECU) in the Brody School of Medicine. She received her B.S. from Texas A & M University and her M.S. and Ph.D. from the University of Rochester, School of Medicine and Dentistry where she received the M.A. Hare Research Excellence Award. During her post-doctoral training at the National Institutes of Health Lab of Viral Disease, she was awarded the NIH Fellows Award for Research Excellence. Dr. Roper has studied coronavirus and poxvirus virulence genes, genomics, and vaccines, including oncolytic viruses, and her publications have been cited over 7,000 times. She has been funded by NIH, the NSF, and Foundations and is a member of the National Academy of Inventors, and Co-Chair of the Global Virus Network Monkeypox Task Force. She serves on the American Society for Microbiology Inclusive

Diversity with Equity, Access, and Accountability (IDEAA) Committee of the Board and is an ECU Woman of Distinction. She has served on numerous national and international Grant Panels and Editorial Boards.

C-102 Adeno-associated virus 2 infection in children with non-A–E hepatitis

Emma Thomson, PhD, MRC, University of Glasgow Center for Virus Research

In April 2022, Scotland reported an unexplained outbreak of acute hepatitis primarily affecting children, which has since been identified in 35 countries. Initial research suggested a connection to human adenovirus, a virus not typically associated with hepatitis. This study presents a case-control examination, revealing a link between infection with the adeno-associated virus 2 (AAV2) and specific host genetic factors contributing to disease susceptibility.

Our use of next-generation sequencing, PCR with reverse transcription, serology, and in situ hybridization allowed us to identify recent AAV2 infection in plasma and liver samples. We also describe the presence of AAV2 within enlarged hepatocytes, accompanied by a significant T cell infiltrate in liver biopsy samples.

We also observed a high prevalence of the HLA class II HLA-DRB1*04:01 allele in hepatitis cases, suggesting a CD4+ T-cell-mediated immune pathology.

In conclusion, our findings reveal an association between a novel outbreak of pediatric acute hepatitis and AAV2 infection, likely co-acquired with the human adenovirus which acts as a 'helper virus' for AAV2 replication. Our study also underscores the role of HLA class II status in disease susceptibility.



Emma Thomson is Clinical Professor of Infectious Diseases at the MRC-University of Glasgow Centre for Virus Research and Professor of Emerging Viral Infections at the London School of Hygiene and Tropical Medicine in the United Kingdom. Her research group use next-generation sequencing (NGS) to detect new and emerging viruses in the UK and in East Africa (Uganda) and engage in improving local diagnostic capacity to allow for more rapid control interventions. Her team work on linking the genotype of viruses with the phenotype in the laboratory and in clinical settings. She worked with other centres across the UK on tracking the genotype and phenotype of SARS-CoV-2 as part of the COG-UK consortium (sequencing 2 million SARS-CoV-2 genomes

across the UK). Her team led a study outlining a change in entry mechanism, tropism and immune evasion of the Omicron variant (away from TMPRSS2 and towards cathepsinlinked entry), published in Nature Microbiology. She has also led studies that have contributed to genomic epidemiology by revealing multiple introductions of SARS-CoV-2 from mainland Europe into Scotland (Nature Microbiology). Her team recently identified the adeno-associated virus 2 (AAV2) to be associated with hepatitis in children in the UK, published in Nature this year.



C-103 Antibodies against Emerging Infections: A Global Collaboration

Erica Ollmann Saphire, PhD, MBA, La Jolla Institute for Immunology

Antibodies provide a critical line of defense against infectious diseases and are a primary goal of protective vaccines. Antibodies themselves can also serve as therapeutics or as design templates to develop or improve needed vaccines. Understanding the structure, reactivity, breadth, and protective activities of antibodies is key to both therapeutic and vaccine design. We have galvanized global consortia to understand which antibodies are most effective against viruses like Ebola, Lassa, and SARS-CoV-2. These consortia analyzed which antibodies

demonstrate potent neutralization, which inspire Fc-mediated effector functions, which exhibit breadth across strains, and which yield durable neutralization despite emergence of highly mutated variants, and why. Results from the Bill and Melinda Gates Foundation-, GHR- and NIAIDfunded Coronavirus Immunotherapeutics Consortium (CoVIC) that studied 400 candidate therapeutic antibodies against SARS-CoV-2 afforded fine epitope mapping on the spike protein; these distinctions forecast antibody activities. Structures of CoVIC IgGs in complex with the spike explain why some antibodies retain potency even though the footprint they target is highly

mutated, like in the Omicron Variants. The geometry of their IgG recognition allows bivalent binding that confers avidity to preserve neutralization activity. Results of another project, the Viral Immunotherapeutic Consortium (VIC), mapped first-in-class antibody therapies for Ebola Virus Disease (Inmazeb) and Lassa Fever (Arevirumab), explained their mechanism of action and why a cocktail approach that combines complementary functions endows resistance to escape and opens multiple avenues of in vivo protection. For Lassa virus in particular, these studies help explain why neutralizing antibodies against this virus are so rare and provide specific design strategies to develop antigens to find and elicit more potently neutralizing antibodies.



Erica Olimann Saphire, Ph.D. is the President, CEO and a Professor at the La Jolla Institute for Immunology. In her executive role, she is leading faculty in collaborative strategy, uncovering sex-based differences in the immune system and innovating vaccines. In her academic lab, Dr. Saphire is a structural biologist, virologist and immunologist. She galvanized and led NIH- and BMGFfunded global consortia uniting 40-60 competing investigators to compare competing antibody therapeutics, and learn which features forecast protection, and mitigate viral escape. Her research has led to the first ever structure of the entire human IgG antibody, the supramolecular complex by which IgG activates the complement cascade for immune protection, pioneering structures of the surface glycoproteins of Lassa, Ebola, Marburg, Rabies and other viruses,

and understanding how the viruses mediate entry and how human antibodies may defend against them. Her research has further revealed how viral matrix proteins hijack host lipids to polymerize conformational change and virus assembly and proved that certain viral proteins rearrange into different structures at different times for different functions. Dr. Saphire's work has been recognized at the White House with a PECASE, with young investigator awards from ICAR, ASM, ASBMB, and the MRC Centre for Virus Research. She has been recognized with awards from the Burroughs Wellcome Fund; a Fulbright for research in the United Kingdom, South Africa and Germany; and a Mercator Fellowship from Deutsche Forschungsgemeinschaft. In 2021, she was named Scientist of the Year by the ARCS Foundation San Diego. C-104 HIV Controllers as a model for therapeutic and prophylactic vaccines

Bruce Walker, MD, Ragon Institute of MGH, MIT and Harvard

Suppression of viremia to prevent disease progression and transmission without lifelong medication is the primary goal of functional HIV cure strategies. Remarkably, a subset of untreated persons living with HIV achieves durable control of viremia despite persistence of virus. These individuals, which include both elite and viremic controllers, are the best evidence that effective and durable immune control can be achieved. Moreover, new data suggest that some may have been cured by immunologically eliminating infectious virus. Overwhelming data indicate that HIV-specific CD8+ T cells are critical for this control, but the properties of these cells in the periphery and within lymph nodes that lead to durable control remain incompletely defined. By examination of HIV controllers with sudden aborted control we show that both specificity and function are critical properties of these cells. By evaluating inquinal lymph nodes and contemporaneous peripheral blood from spontaneous controllers and treatment-suppressed non-controllers, we show that cytotoxic effector molecule expression by lymphoid follicular CD8+ T cells in controllers is elevated proximate to infected cells the ability to generate lymphoid cytotoxic effectors upon antigen stimulation distinguishes spontaneous controllers from non-controllers. In addition, by studying exceptional elite controllers we show that CTL targeting of mutationally resistant amino acids defined by network analysis is associated with elimination of intact proviruses integrated in transcriptionally active sites in the host chromosome. Together these data provide not only additional evidence that HIV controllers are a key model for HIV cure but also provide critical insights to guide therapeutic and prophylactic vaccine development.



Dr. Bruce D. Walker, a 1980 graduate of Case Western Reserve University School of Medicine, is a physician-scientist and T cell immunologist, a Howard Hughes Medical Institute investigator, a Professor of Medicine at Harvard Medical School, and Professor of the Practice of Medicine at MIT. He is also the founding and current Director of the Ragon Institute of MGH, MIT and Harvard, whose mission is to harness the immune system to prevent and cure disease. Dr. Walker's laboratory studies T cell responses to chronic viral infections and are notable for the initial identification of HIV-specific T cell responses in infected persons, and subsequent characterization of mechanisms of T cell function, dysfunction and immune escape. He is active in Cambridge MA and in Durban, South Africa, where, as Adjunct Professor of Medicine at the University

of KwaZulu-Natal, he helped catalyze the creation of two research institutes dedicated to the study of HIV and TB. At the onset of the COVID-19 pandemic Dr. Walker helped to establish and co-lead the Massachusetts Consortium on Pathogen Readiness (MassCPR), a collaborative effort among over 800 scientists and clinicians united to address current and future pandemics. He is an elected member of the American Academy of Arts and Sciences, the National Academy of Medicine, the Association of American Physicians, and the American Society for Clinical Investigation. He is also the recipient of two MERIT Awards from the NIH and a Doris Duke Distinguished Clinical Scientist Award.



C-105 Discovery of New Agents of Disease

Gavin Cloherty, PhD, Head of Infectious Disease Research and the Abbott Pandemic Defense Coalition, Diagnostics



Gavin A. Cloherty, Ph.D., is Head of Infectious Disease Research and the Pandemic Defense Coalition for Abbott's diagnostics business. He provides scientific leadership in the area of infectious disease diagnostics by conducting groundbreaking clinical studies on SARS-CoV-2, hepatitis and HIV and developing new diagnostic tests. As one of the top experts in the field, his innovative research is changing the way infectious diseases are being diagnosed to help improve patient outcomes.

In 2021, Gavin led efforts to establish the Abbott Pandemic Defense Coalition, a first-of-its-kind, industry-led initiative that has brought together 15 academic and public health organizations located around the world to support early detection

and rapid response to pandemic threats. The Coalition is actively hunting, tracking, analyzing and researching numerous pathogens of public health concern in member countries.

Gavin has more than 20 years of experience with Abbott and leads a team of scientists in the study of the viral diversity of HIV and hepatitis. His expertise is sought after globally through his established partnerships with commercial organizations, ministries of health, government agencies and academic institutions, such as the Centers for Disease Control and Prevention (CDC) and National Institutes of Health's AIDS Clinical Trial Group (ACTG) and Hepatitis B Research Network (HBRN). He has worked with the Republic of Georgia to help eradicate hepatitis C in the country and is looking to expand these efforts to other regions of the world severely impacted by this disease.

Gavin graduated from the National University of Ireland, Galway, where he received his Ph.D. in molecular biology and a Bachelor of Science in microbiology and zoology.

Gavin is a member of numerous professional and scientific societies, including the International AIDS Society and the American Association for the Study of Liver Disease. He also is a contributor to multiple editorial boards, including the Journal of Clinical Microbiology and Journal of Clinical Virology.

D-101 Novel Antiviral Therapeutics for hepatits viruses

Shyamasundaran Kottilil, MBBS, PhD, Interim IHV Director; Director, Division of Clinical Care & Research;

Chief, Division of Infectious Diseases; Professor of Medicine, Institute of Human Virology, University of Maryland School of Medicine; Senior Advisor, Global Virus Network

Chronic viral hepatitis is a major public health problem that affects over 400 million people worldwide. Hepatitis B and C account for almost all of these chronic conditions which contribute to development of hepatocellular carcinoma, liver failure and transplantation. Hepatitis Delta coinfection can occur in patients with chronic hepatitis B and result in the most aggressive form of liver fibrosis progression. Recently, significant progress has been made in the development of direct acting agents that can either cure (HCV) or suppress viral replication (HBV and HDV) leading to better clinical outcomes. For HBV, stopping antiviral therapy will lead to rebound of HBV DNA. Presence of HBV cccDNA and lack of effective virus-specific immunity are key reasons for this phenomenon. Targeting HBV reservoir or covalently closed circular DNA is a unique and essential approach to achieve functional cure for HBV. This presentation will review novel approaches to target HBV reservoirs and therapeutics for HDV.





D-102

At the crossroads of viral infection of CD4+ T cells and mental health

Howard E. Gendelman, MD, University of Nebraska Medical Center

We will present recent studies focused on the interplay between aging, HIV-1 infection, and neurodegenerative diseases. The dynamic interplay between viral infection of CD4+ T cell subsets, immunity, antiretroviral therapy (ART), and neurodegenerative diseases was not previously possible. This problem was solved by the creation of a humanized Alzheimer's mouse. We showed that amyloid β (Aβ)-specific helper T cell type-1 and -17 effector T cell clones propel neurotoxic innate neuroinflammatory responses, proteinopathy, and neuronal dysfunction associated with cognitive impairments. Moreover, through parallel studies, we demonstrated that regulatory T cells (Treg) attenuate neuroinflammation and Alzheimer's disease (AD) neuropathology, then restore cognitive function. We now demonstrate that during HIV-1 infection of these mice we not simply see increases in neuroinflammation, but that viral immune response can facilitate proteinopathy. We show, in these mice. HIV-1 compartmentalization, virus-amyloid adaptive and innate immunity alterations, and immune-pathogenic and regulatory events. These can serve both to accelerate or ameliorate AD processes. Our research has enabled immune transformative medicines that directly interrogate how T cell immunity drives the tempo of HIV/AIDS in the setting of neurodegenerative disease. Tregs that are engineered to recognize AB by a transgenic T cell receptor or a chimeric antigen receptor are employed as therapeutic strategies to restore brain homeostasis, reduce plaque burden, and facilitate neuroprotective outcomes. Overall, we are, we present the influences of chronic HIV-1 infection in the setting of progressive AD and can study its relationship to immunity and antiretroviral therapy.



Dr. Howard E. Gendelman is the Margaret R. Larson Professor of Internal Medicine and Infectious Diseases, Chairman of the Department of Pharmacology and Experimental Neuroscience, and Director of the Center for Neurodegenerative Disorders at the University of Nebraska Medical Center. Dr. Gendelman is credited in unraveling how functional immune alterations induce metabolic changes and lead to cell damage in a range of chronic infectious and neurodegenerative disorders. The discoveries led to immune transformative therapeutics that prevent, slow, or reverse viral and neural maladies. He is credited for the demonstration that AIDS dementia is a reversible metabolic encephalopathy. His work has led to regulatory T cell-based immunotherapies for Parkinson's and Alzheimer's diseases are in clinical trials. He is a co-founder of Exavir Therapeutics, Inc., a biotechnology start-up focused on work he co-

of Exavir Therapeutics, Inc., a biotechnology start-up focused on work he copioneered in developing ultra-long acting nanotherapies for treatment and prevention of HIV infection.



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Direct infection of microglia in human brain organoids induces inflammation leading to bystander neuron dysfunction and death: Implications for HIV-associated neurocognitive disorder (HAND)

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While the introduction of antiviral therapy has strikingly altered the clinical course of HIV infection in humans, milder forms of HIV-associated neurocognitive disorder (HAND) remain common in the presence of ART. Microglia are believed to represent the principal cellular targets for HIV infection in the brain but it remains unknown how microglia infection ultimately induces the dysfunction and death of neurons—the characteristic finding in HAND.

Two iPSC-derived brain organoid systems (cerebral organoids and choroid plexus (ChP) organoids) were used as three-dimensional CNS models to study HAND pathogenesis. Based on immunostaining, productive HIV infection was strictly limited to microglia in both organoid systems. HIV infection was associated with marked increases in CCL2 and CXCL10 chemokine gene expression as well as the induction of multiple IFN responsive genes including MX1, ISG15, ISG20, IFI27 and IFITM3. Addition of ART greatly reduced HIV replication in the organoids. Of note, despite ART addition, low-level production of CCL2 and CXCL10 and the IFN responsive genes persisted. Single-cell RNA sequencing (scRNA-seq) revealed sharp increases in expression of the S100 family of inflammatory genes in HIV-infected microglia. The S100 family of gene products stimulates inflammation by binding to a variety of receptors including the Receptors for Advanced Glycation (RAGE), Toll-like receptor 4 (TLR4), CD147 /EMMPRIN (extracellular matrix metalloproteinase inducer), and specific G-protein coupled receptors leading to activation of master regulators of inflammation-NF-kappaB and AP1, S100 gene expression was not limited to microglia but instead was detected in several uninfected cell types including bystander neurons. Within these neurons, expression of neurotransmitter transporters sharply declined while genes involved in cellular senescence and death markedly increased. Changes in gene expression detected by scRNA-seq in microglia and other cell types following HIV infection detected in the scRNA-seq assays were confirmed RT-PCR assays.

Taken together, these studies in iPSC-derived brain organoid highlight how HIV infection of microglia triggers the expression of genes involved in IFN responsiveness, cellular activation and inflammation that fundamentally alter the cellular microenvironment in a manner that culminates in the dysfunction and death of uninfected bystander neurons. We suggest that HAND corresponds to the clinical manifestation of this cascade of neurotoxic effects that is lessened but not eliminated by antiviral therapy.



Warner C. Greene, M.D., Ph.D., is the Nick and Sue Hellmann Distinguished Professor of Translational Medicine at the Gladstone Institute of Virology and served as the founding director of the Gladstone Institute of Virology and Immunology from 1992–2018. Greene is past Director of The Michael Hulton Center for HIV Cure Research at Gladstone and is also a Professor of Medicine, and Microbiology and Immunology at the University of California, San Francisco. His Iaboratory explores the biology of HIV latency and new approaches to achieving an HIV cure. It is also engaged in studies of SARS-CoV-2 with a focus on understanding the role of clotting and inflammation in COVID-19 and the development of inhalable peptide inhibitors that block fusion of SARS-CoV-2 virions.

Greene received his B.A. with greatest distinction from Stanford University in 1971 and his M.D. and Ph.D. from Washington University School of Medicine in 1977. He then served as an intern and

resident in internal medicine at Harvard's Massachusetts General Hospital. In 1979, he became an investigator and later senior investigator National Cancer Institute. In 1987, Dr. Greene was named Professor of Medicine at Duke University School of Medicine and Investigator in the Howard Hughes Medical Institute. In 1992 he accepted his current appointments at Gladstone and the University of California. San Francisco.

From 2007–2016, Greene expanded his work to include global health in sub-Saharan Africa serving as president and executive chairman of the Accordia Global Health Foundation. Accordia's mission was to overcome the burden of infectious diseases in Africa by building centers of excellence and strengthening medical institutions. In 2016, Accordia merged with Africare.

The recipients of many scientific awards, Greene has been recognized by the Institute for Scientific Information as one of the 100 most-cited scientists in the world. He is also an elected member of the National Academy of Medicine, the American Academy of Arts and Sciences, and served as President of the Association of American Physicians in 2012. Dr. Greene is the also the 2019 IHV Lifetime Achievement Awardee for Scientific Contributions. He is most proud of having trained and mentored more than 120 students and fellows.

In 2022, after a 40-year career in academic research, Greene cofounded InvisiShield Technologies, a biotech company focused on developing nasal spray preventives for SARS-CoV-2, influenza, and RSV. Greene is now seconded from Gladstone serving as President and Chief Scientific Officer of InvisiShield Technologies.



D-104 HIV-1 Persistence in Myeloid Cell Reservoirs

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HIV-1 persists in cellular reservoirs that can re-ignite viremia if antiretroviral therapy (ART) is interrupted1. Therefore, insight into the nature of those reservoirs may be revealed from the composition of recrudescing viremia following treatment cessation. We have adopted an approach to identify the presence of rebound-competent viruses with a myeloid cell origin in plasma of individuals undergoing structured treatment interruptions. HIV-1 is an enveloped virus that acquires its membrane from that of the host cell. We have exploited this to enable immunoaffinity enrichment of virions with a myeloid cell origin. The envelope glycoproteins of affinity -purified virions were then assessed for myeloid cell tropism. Macrophage-tropic viruses were identified plasma of individuals undergoing analytic treatment interruption (ATI). Macrophage-tropic viruses could also be enriched from post-ATI plasma using macrophage-specific (CD14) but not CD4+ T cellspecific (CD3) antibodies, suggesting that macrophage-tropic viruses had a macrophage origin. Molecular clock analysis indicated that the establishment of macrophage-tropic HIV-1 variants predated ATI. Collectively, these data suggest that macrophages are a viral reservoir in HIV-1-infected individuals on effective ART and contribute to viral recrudescence when treatment is interrupted. These findings have implications for the design of curative strategies for HIV-1.



Dr. Mario Stevenson is the Raymond F. Schinazi and Family Endowed Chair in Biomedicine, Director of the University of Miami AIDS Institute and Co-Director of the Center for AIDS Research at the University of Miami Miller School of Medicine. Prior to 2011, Dr. Stevenson was the David Freelander Chair for AIDS Research at the University of Massachusetts Medical School and the Director of the Center for AIDS research at that Institution. Dr. Stevenson obtained his BSc. (1980) and PhD (1984) in Glasgow, Scotland.

Dr. Stevenson is a molecular virologist who has been working on the viral etiology of AIDS for over 30 years. Dr. Stevenson's has been investigating mechanisms regulating HIV replication, persistence and disease pathogenesis. Dr. Stevenson has served as Chair of the HIV AIDS Virology Study Section at the National Institutes of Health, Chair of the Scientific Advisory Board of the

National AIDS Conference (CROI), and has served on the NIH Office of AIDS Research that sets AIDS research directives. From 2006-2015, he served as Chair of the Scientific Advisory Board and is currently a member of the Board of Trustees of the American Foundation for AIDS Research (amfAR) and a scientific board member of the Elizabeth Glaser Pediatric AIDS Foundation. Dr. Stevenson is a recipient of Harvard Medical School's Shipley Lectureship, recipient of the Gertrude Elion award, Schally Research Award and Barcelona's IRSI-Caixa award.

D-105 Antibodies in HIV-1 Vaccine and Therapy

Michel Nussenzweig, MD, PhD, Rockefeller University



Michel Nussenzweig was born in Sao Paulo Brazil on February 10th 1955. He received a B.S. summa cum laude from New York University in 1976, a Ph.D. degree from the Rockefeller University in 1981 and an M.D. degree from New York University Medical School in 1982. During his PhD with Ralph Steinman he discovered that dendritic cells are antigen presenting cells. After completing a medical internship, and residency, and infectious fellowship at the Massachusetts General Hospital he joined Dr. Philip Leder in the department of genetics at Harvard Medical School for postdoctoral training. He returned to Rockefeller University in 1990 as an assistant professor and Howard Hughes Investigator to head an independent laboratory. He was promoted to professor in 1996 and holds the Zanvil A. Cohn and Ralph M. Steinman Chair of

Immunology. Nussenzweig's laboratory studies the molecular aspects of the immune system's innate and adaptive responses using a combination of biochemistry, molecular biology, and genetics. His work on adaptive immunity, he focuses on B lymphocytes and antibodies to HIV-1, while his studies of innate immunity focus on dendritic cells. His work led to the rapid development of new antibodybased therapies for infections by HIV and the novel SARS-CoV-2 coronavirus. He has received numerous awards and prizes including the Robert Koch Prize, and the Sanofi-Pasteur Award. He is a member of the American Academy of Arts and Sciences, the US National Academy of Medicine and the US National Academy of Sciences.