INTERNATIONAL WORKSHOP ON

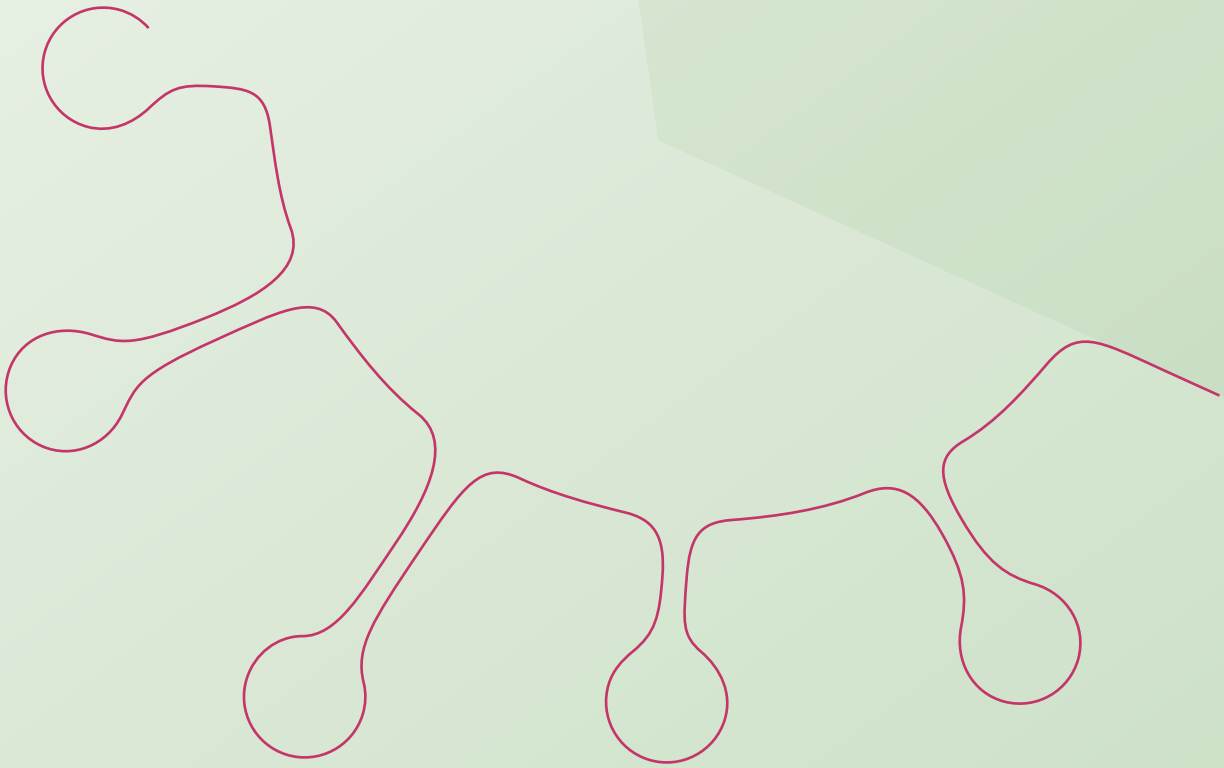
VIRAL INFECTIONS & INFLAMMATION

HYBRID MEETING | 2023 6-7 September **Rockville, MD, United States**

Program Book

virology education

AcademicMedicalEducation.com



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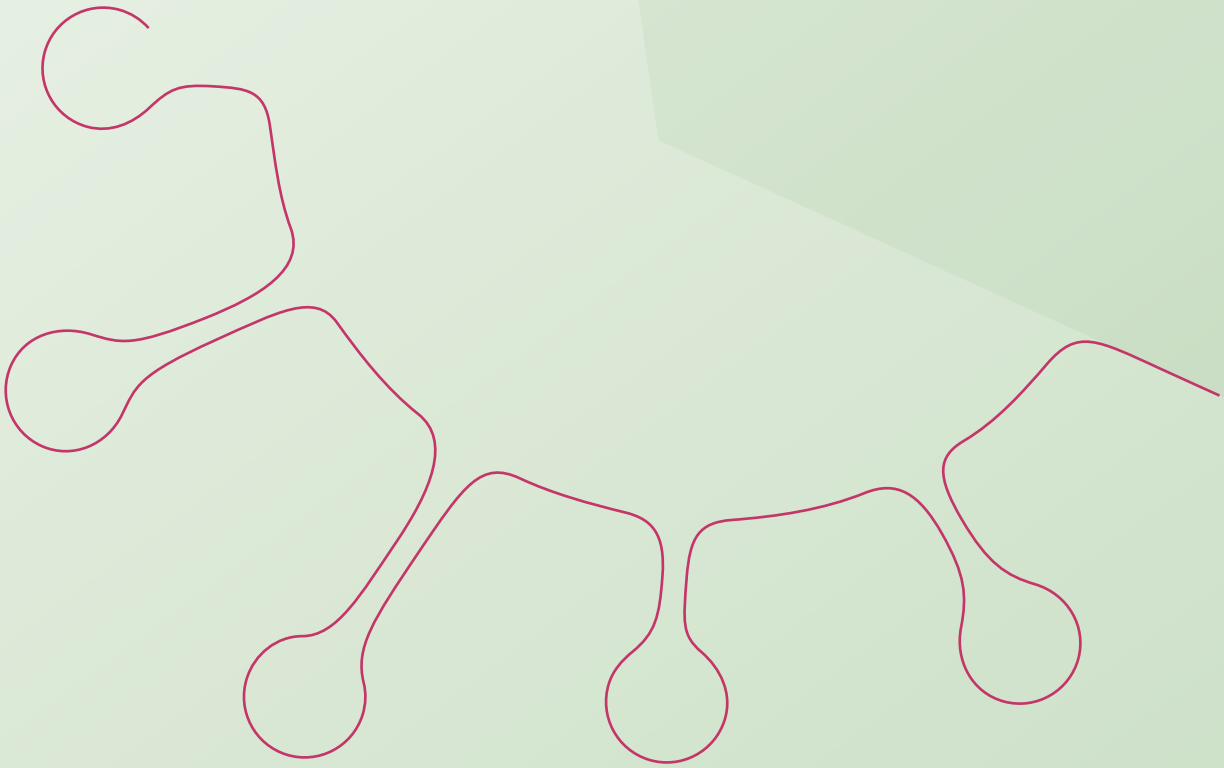

Welcome

Dear Colleagues,

We are delighted to welcome you to the second edition of the **International Workshop on Viral Infections & Inflammation Workshop 2023** in Rockville, MD, United States.

Inflammatory response and cytokine storm in severely ill COVID-19 patients have put a spotlight on the importance of inflammation in viral infections. Prevalence of long-term COVID is also a concern and potentially related to the suboptimal function of the immune system.

Yet, these concerns are not unique to COVID-19. In the case of HIV for instance, despite remarkable improvements in antiretroviral therapy, immune reconstitution remains limited in some patients even a long time after treatment initiation. Exhaustion of primary immune resources due to persistent activation and inflammation drives premature immune aging and impacts life expectancy.

Although HIV and SARS-CoV-2 are fundamentally different infections with distinct long-term consequences, underlying mechanisms that drive those complications might be common.

Common underlying mechanisms imply the possibility to employ similar therapeutic interventions. For instance, neutralizing antibodies, antiviral drugs, and therapeutic vaccines to eliminate the persistent virus or anti-inflammatory drugs to ameliorate chronic inflammation.

We hope you enjoy your time in Rockville and we wish you an enjoyable and educational workshop!

The Organinzing Committee

Organizing Committee

Roger Paredes MD, PhD
IrsiCaixa AIDS Research Institute,
Spain

Steven Deeks, MD
University of California, San Francisco,
United States

Steven Grinspoon, MD
Harvard Medical School /
Massachusetts General Hospital,
United States

Anthony Kelleher, MBBS, PhD, FRACP, FRCPA
The Kirby Institute,
Australia

Daniel Kuritzkes, MD
Brigham and Women's Hospital /
Harvard Medical School, United States

Michaela Müller-Trutwin, PhD
Institut Pasteur,
France

Avindra Nath, MD
NIH,
United States

Jonathan Schapiro, MD
National Hemophilia Center, Sheba
Medical Center, Israel

Irini Sereti, MD
NIAID/NIH,
United States

Serena Spudich, MD
Yale University,
United States

Badge Policy
All registered delegates are provided with an personal workshop badge. Admission to all events is restricted to registered delegates and official guests wearing their name badges. Please wear your badge at all times to ensure admission to the workshop sessions.

Certificate of Attendance
Certificates of attendance will be sent by e-mail in the week following the workshop (after completion of the post-workshop survey.)

Code of Conduct
All individuals are required to observe our Code of Conduct. We cannot tolerate any form of discrimination, harassment, disrespect, or the marginalization of those involved in our programs. Please report any incidents to VE and AME via info@amededu.com or to one of our onsite personnel. Any participant who is found to have exhibited any inappropriate conduct or behavior against others may be removed from the program.
View in full: academicmedicaleducation.com/our-commitment-diversity-and-inclusion

Workshop Secretariat
The workshop secretariat is located at the registration desk in the pre-function area of the meeting room (Grand Hall 1D13).
It is open throughout the workshop to address all your questions concerning logistics.

Feedback
Your feedback is very valuable to us as it allows us to continue improving future Viral Infections & Inflammation workshops. Please complete the feedback forms that are distributed via email at the end of each workshop day. Your feedback is much appreciated – we will use it to improve the program in 2024.

Posters
Posters are displayed in the poster area (room 1D06) next to the meeting room (Grand Hall 1D13). Please seek out the posters during refreshment and lunch break. All poster presenters are asked to be at their posters at a specific time so that you can discuss their important work with them.

Presentations and Webcasts
The webcast and PDF presentations are available on the virtual platform where the meeting will be livestreamed for three weeks after the workshop. After this time, they will be made accessible on demand via the conference website.
www.AcademicMedicalEducation.com, provided the speakers have given consent.

Meals
Lunch on Thursday, 7 September will be NOT included.
Delegates can place the order for their meal via the recommended caterer in the morning. Lunch boxes will be provided on time for lunch and served in the Cafeteria.

Presenters
Presenters are requested to submit their presentation as early as possible, latest in the break prior to their session. Our technicians will be available for you at the technician table.

Social Media
We encourage you to post news about the Viral Infections & Inflammation workshop to your social media accounts and tweet about Viral Infections & Inflammation as often as you like during the workshop. You can post your own tweet to your followers using the hashtag #HIVInflammation

Virtual

Virtual Platform - Networking

The Meeting Hub allows you to connect and communicate with other attendees. Once you have located an attendee you want to connect with, click the Connect button. Once the other attendee accepts your request, you can choose to interact by starting a live chat or live video call. You can also schedule a meeting at a later time, send messages and take notes. Contact information for all attendees you have connected with will be included when you export contacts.

Virtual Platform - Notes

You will be able to take notes during the virtual workshop. Any notes that you take throughout the event can be exported by selecting the Export icon in the top right of the screen near your Profile image.

Our Team

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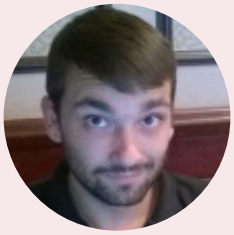
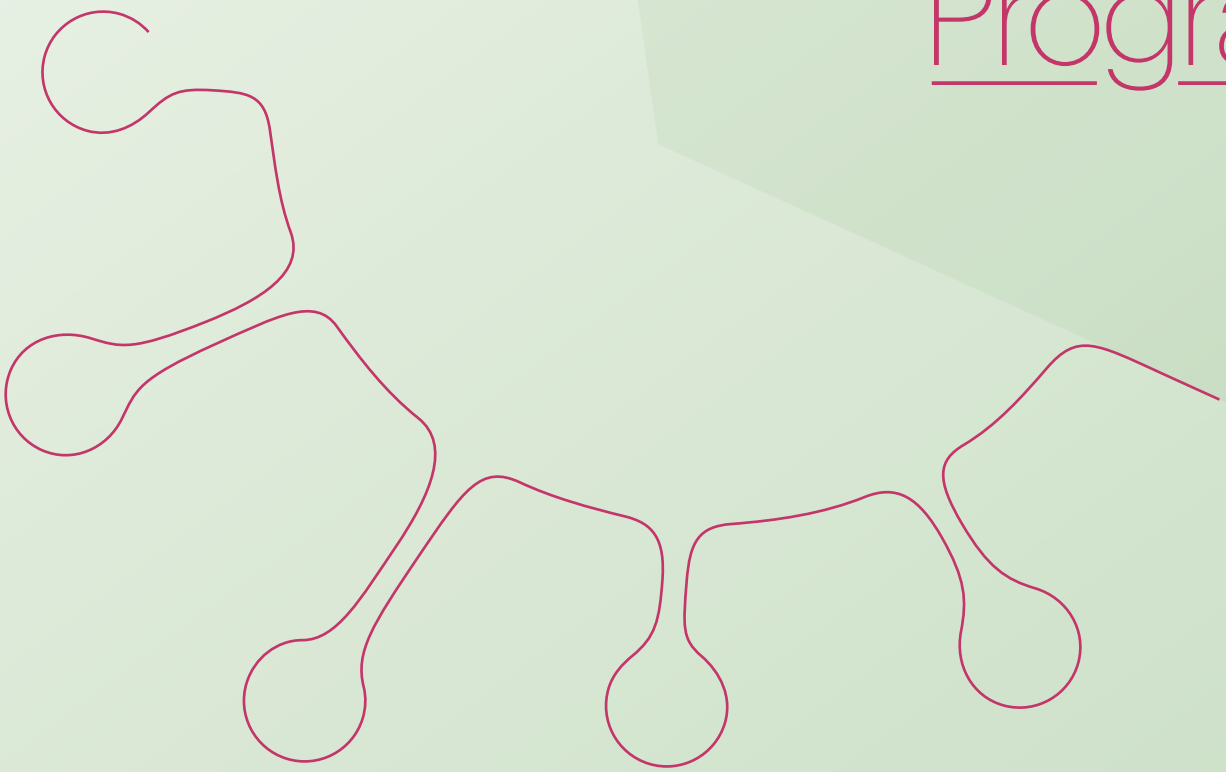


João Peixoto
AV Coordinator

Program



Wednesday, 6 September 2023

Times in Eastern Daylight Time (EDT)

Opening Session & Plenary Talk
Chair: Daniel Kuritzkes

1:00 PM **Opening of the Workshop**
Daniel Kuritzkes, MD
Brigham and Women's Hospital / Harvard Medical School, United States

1:05 PM **Update on the REPRIEVE Trial to Prevent Cardiovascular Events in People with HIV**
Steven Grinspoon, MD
Harvard Medical School, Massachusetts General Hospital, United States

Session 1 **Post-COVID Syndromes**
Chairs: Steven Grinspoon & Jason Baker

1:30 PM **Viruses, Immune Dysfunction, and ME/CFS**
Maureen Hanson, PhD
Cornell University, United States

1:55 PM **Underlying Mechanisms of Long COVID**
Michael Peluso, MD
University of California, San Francisco, United States

Oral Abstract-driven Presentations:

2:20 PM High Levels of Il-1, Tnf- and Mip-1 One Month after the Onset of the Acute SARS-CoV-2 Infection, Predictors of Post COVID-19 in Hospitalized Patients VIRTUAL #1
Jacobo Alonso-Domínguez

2:30 PM Determinants of the Onset and Prognosis of the Post-COVID-19 Condition: A 2-Year Prospective Cohort Study #2
Roger Paredes

2:40 PM **Discussion: How to Conduct Clinical Trials and Distinguish Long COVID from Fatigue**

3:00 PM Coffee Break & Poster Viewing

3:30 PM **Satellite Symposium** (program on page 14)

Session 2	**Post-infectious Syndromes** *Chairs: Roger Paredes & Maureen Hanson*	
4:30 PM	**Immune Signatures in Vaccine-associated Myocarditis** **Anis Barmada, MPhil** Yale University School of Medicine, United States	
4:55 PM	**What We Know Now about HIV and Long COVID** **Annie Antar, MD, PhD** Johns Hopkins University School of Medicine, United States	
5:20 PM	**Epstein–Barr Virus and Multiple Sclerosis: Which Mechanisms are at Play?** **Tobias Lanz, MD** Stanford University, United States	
	Oral Abstract- driven Presentation:	
5:45 PM	A Role for Inflammasome Activation and Oxidative Stress in SARS-CoV-2 Breakthrough Infection and Symptomatic Rebound **Silvia Lucena Lage**	#3
6:05 PM	**Live Q&A and Discussion**	
6:15 PM	End of Day 1	

Thursday, 7 September 2023

Times in Eastern Daylight Time (EDT)

Session 3 **Post-acute Sequalae Following Different Infections**
Chairs: Arun Venkatesan & Irini Sereti

8:35AM **Post-acute Sequelae following Ebola infection**
David Wohl, MD
UNC School of Medicine, United States

9:00 AM **Endogeneous Retroviruses and Inflammation**
Yasmine Belkaid, PhD
NIH/NIAID, United States

Oral Abstract-driven Presentations:

9:25 AM HIV Exposed Uninfected (Heu) Infants Have Pro-inflammatory Bioprofiles That Correlate with Their Mothers' Bioprofiles Independent of Viral Levels and Persist for at Least Six Months #4
Li Yin

9:35 AM Possible Role of Intestinal Damage and Endotoxemia in the Development of Endotholial Dysfunction, Thrombosis and Secondary Lung Damage in Patients with COVID-19 VIRTUAL #5
Liudmyla Shostakovych-Koretskaya

9:45 AM **Live Q&A and Discussion**

10:05 AM Coffe Break & Poster Viewing

Session 4 **Chronic Viral Infections and Inflammation-related Comorbidities**
Chairs: Avindra Nath & Lisa Henderson

10:35 AM **HIV, Inflammation, and Macrophages**
Maureen M. Goodenow, PhD
NIH, United States

11:00 AM **Inflammation in People with Low Nadir CD4 Counts**
Irini Sereti, MD
NIAID, NIH, United States

11:25 AM **Acute Disseminated Encephalomyelitis**
Arun Venkatesan, MD PhD
Johns Hopkins University School of Medicine, United States

Oral Abstract-driven Presentation:

11:50 AM The Plasma Microbiome Contributes to Immune Reconstitution in HIV Infected Individuals on Suppressive ART VIRTUAL #6
Wei Jiang

12:00 PM **Live Q&A and Discussion**

12:20 AM Lunch Break

Session 5	**Interventations Targeting Inflammation and Post-viral Syndromes** *Chairs Anthony Kelleher & Priscilla Hsue*	
1:20 PM	**Inflammasome Activation in Severe Cases of COVID-19** **Dario Zamboni, PhD** University of São Paulo, Brazil	
1:44 PM	**Developing CAR T Cells for Use in Chronic HIV Infection** **Martin Tolstrup, MSc, PhD** Aarhus University Hospital, Denmark	
	Oral Abstract-driven Presentation:	
2:10 PM	Impact of Glatiramer Acetate Treatment in SIVmac-Infected Macaques **Beatrice Jacqulin**	#7
2:20 PM	**Live Q&A and Discussion**	
2:45 PM	**Take Home Message** **Irini Sereti, MD** NIAID, NIH, United States	
2:50 PM	End of the Workshop	

Wednesday, 6 September 2023

Times in Eastern Daylight Time (EDT)

Satellite Symposium:
The Impact of Viral Glycoproteins on Inflammation and Immunity
Chairs: Irini Sereti & Avindra Nath

3:30 PM **Opening of the Symposium**
Irini Sereti, MD & Avindra Nath, MD
NIAID, NIH, United States; NIAID, United States

3:35 PM **Immunopathology of viral encephalitis**
Avindra Nath, MD
NIH, United States

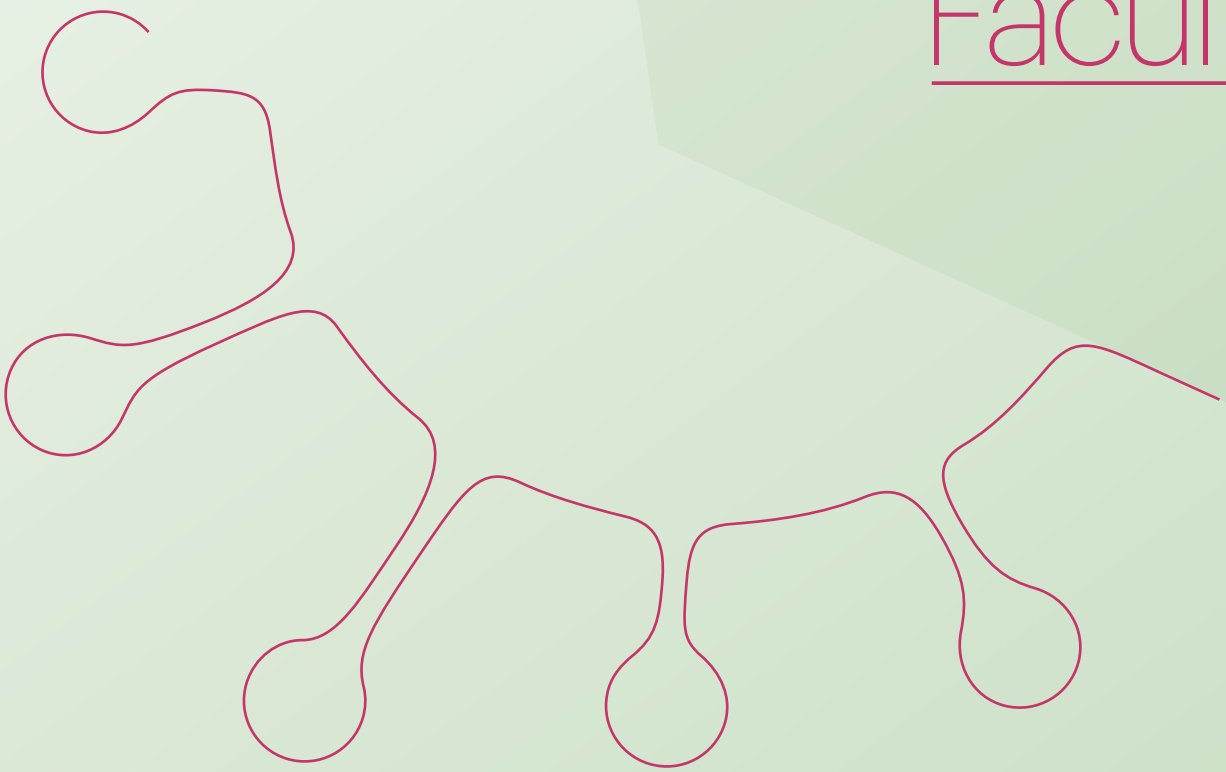
3:50 PM **Immune Responses to AAV in the Context of Gene Therapy**
Carsten Bonnemann, MD
NINDS, NIH, United States

4:05 PM **Host and Viral Glycoproteins in HIV Neuropathogenesis**
Lishomwa Ndhlovu, MD, PhD
Weill Cornell Medicine, United States

4:20 PM **Live Q&A and Discussion**

4:30 PM **Closure of the Symposium**

Faculty



Invited Speaker

Annie Antar

MD, PhD

Johns Hopkins University School of Medicine, United States

Dr. Annie Antar is an assistant professor of medicine at the Johns Hopkins University School of Medicine in the Division of Infectious Diseases. She is a physician-scientist focused on viral pathogenesis. Dr. Antar earned her undergraduate degree from Harvard University and her MD and PhD degrees from Vanderbilt University School of Medicine.

She completed internal medicine residency and a fellowship in infectious diseases at the Johns Hopkins Hospital, where her post-doctoral work with Drs. Robert and Janet Siliciano focused on the HIV latent reservoir. Her current work focuses on understanding the persistence of the HIV latent reservoir and, since 2020, on the long COVID. She has led or co-led two prospective cohort studies focused on long COVID, one of which is a national cohort focused on the intersection of HIV and long COVID.

No potential conflict of interest to report

Invited Speaker

Anis Barmada

MPhil

Yale University School of Medicine, United States

Anis Barmada is an M.D./Ph.D. student and P.D. Soros Fellow in the Department of Immunobiology at the Yale University School of Medicine in New Haven, Connecticut. He completed his B.S. at the University of Illinois at Chicago in the United States in biology, chemistry, and mathematics.

He then completed an M.Phil. in Genomic Medicine with distinction at the University of Cambridge and Wellcome Sanger Institute in the United Kingdom as a Gates Cambridge Scholar, where he worked in the laboratory of Dr. Roser Vento-Tormo on elucidating immune signatures in COVID-19 using single-cell approaches. He most recently led the investigation into immune signatures and drivers of SARS-CoV-2 mRNA vaccine-associated myocarditis in the laboratory of Dr. Carrie Lucas at the Yale School of Medicine. Anis currently serves as the Editor-in-Chief of the Yale Journal of Biology and Medicine, and he has contributed many science communication pieces in media outlets such as Scientific American and The Scholar.

No potential conflict of interest to report

Invited Speaker

Yasmine Belkaid,

PhD

NIH/NIAID,
United States

Dr. Yasmine Belkaid is a Distinguished Investigator at the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) in Bethesda, Maryland. She obtained her Master in Biochemistry at the University of Science and Technology Houari Boumediene in Algiers, Algeria, and her Ph.D. from Pasteur Institute in Paris, France. Following a postdoctoral fellowship at the NIH on immune regulation during infection, she started her research program at the Children's Hospital Research Foundation in Cincinnati, Ohio. In 2005, she joined the NIH and NIAID and was appointed senior scientist in 2008.

Her laboratory explores fundamental mechanisms that regulate tissue homeostasis and host immune responses and uncovered key roles for the microbiota and dietary factors in the control of immunity and protection to pathogens. Dr Belkaid is the Chief of the Laboratory of Host Immunity and Microbiome, the Director of the trans NIH Center for Human Immunology, and is the Founder and Director of the NIAID Microbiome Program. Dr Belkaid is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the National Academy of Medicine, and the recipient of numerous awards including the Lurie Prize in Biomedical Sciences, the Emil von Behring Prize, the Sanofi-Institut Pasteur Award, the Robert Koch Award, and the AAI Excellence in Mentoring Award.

No potential conflict of interest to report

Invited Speaker

Carsten Bönnemann,

MD

NINDS/ NIH,
United States

Carsten Bönnemann graduated from Medical School at the University of Freiburg in Germany. He trained in pediatrics in Hamburg and Göttingen (where he was awarded the Habilitation in pediatrics), and in neurology/ child neurology at Massachusetts General Hospital/Harvard Medical School in Boston. He did postdoctoral research in genetics and neuromuscular specialty training at Boston Children's Hospital/Harvard Medical School. From 2002 he was Co-Director of the Neuromuscular Program and Director of the Pediatric Neurogenetics Clinic at Children's Hospital of Philadelphia/University of Pennsylvania School of Medicine, where he continues to be on faculty as Adjunct Full Professor of Neurology. In 2010 he joined the NIH as a tenured Senior Investigator and Chief of the Neuromuscular and Neurogenetic Disorders of Childhood Section in the Neurogenetics Branch of the National Institute of Neurological Disorders and Stroke. Clinical, genomic and translational work in the Section centers in particular around early onset neuromuscular disorders such as the congenital myopathies and congenital muscular dystrophies and on the development of molecular and gene directed treatment approaches to these conditions, including first-in-human intrathecal and intravenous AAV mediated gene transfer trials. Dr. Bönnemann was a Pew Fellow in the Biomedical Sciences, he received the 2010 Derek Denny-Brown Neurological Scholar Award and the 2023 Jacoby Award from the American Neurological Association, and in 2022 the Legacy Award of the Muscular Dystrophy Association USA. He is Co-Editor-in-Chief of the Journal of Neuromuscular Diseases (JND).

No potential conflict of interest to report

Organizing Committee

Steven Deeks,
MD

University of California San Francisco,
United States

Steven G. Deeks, MD, is a Professor of Medicine in Residence at the University of California, San Francisco (UCSF) and a faculty member in the Division of HIV, Infectious Diseases and Global Medicine at Zuckerberg San Francisco General Hospital. Dr. Deeks has been engaged in HIV research and clinical care since 1993. He is a recognized expert on HIV-associated immune dysfunction and its impact on HIV persistence (the "reservoir") and health during antiretroviral therapy. Dr. Deeks has published over 600 peer-review articles, editorials and invited reviews on these and related topics. He has been the recipient of several NIH grants and is the contact principal investigator of DARE (the Delaney AIDS Research Enterprise), an NIH-funded international collaboratory aimed at developing therapeutic interventions to cure HIV infection. He recently directed the amfAR Institute for HIV Cure Research.

Dr. Deeks is the co-chair of the "Towards an HIV Cure" International Working Group and a former co-chair of the NIH Office of AIDS Research Toward a Cure Planning Group. He was elected to the American Society for Clinical Investigation (ASCI) and Association of American Physicians (AAP), is the editor-in-chief of Current Opinion in HIV and AIDS and serves on the scientific advisory board for Science Translational Medicine. In early 2020, he leveraged his HIV research program to construct the "Long-term Impact of Infection with Novel Coronavirus (LIINC)" cohort, which is now supporting dozens of studies addressing the impact of SARS-CoV-2 on health. He is a former member of the Office of AIDS Research Advisory Council (ORAC) and of the Department on Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents. In 2022, he received the Lifetime Achievement in Mentoring Award from UCSF. In addition to his clinical and translational investigation, Dr. Deeks maintains a primary care clinic for people living with HIV.

Potential conflict of interest

Gilead, Merck, BryoLogyx, Enochian Biosciences, Tendel, AbbVie, Eli Lilly, GSK, Hoopika, and Immunocore.

Invited Speaker

Maureen Goodenow,
PhD

NIH,
United States

Dr. Goodenow is Senior Advisor to the Director of the National Institutes of Health (NIH) and Chief and Senior Investigator of the Molecular HIV and Host Interactions Section in the NIH intramural research program within the National Institute of Allergy and Infectious Diseases. From 2016 to 2023, she was the NIH Associate Director for AIDS Research and Director of the Office of AIDS Research (OAR). From 2015 to 2016, she was the Acting Director of the Office for Research and Science within the U.S. Department of State, Office of the U.S. Global AIDS Coordinator and Global Health Diplomacy, where her portfolio included combination HIV prevention trials funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

Previously, Dr. Goodenow was Professor of Pathology, Immunology, and Laboratory Medicine at the University of Florida, Gainesville where she was awarded the Stephany W. Holloway University Endowed Chair for AIDS Research. She also was the Director of the Center for Research in Pediatric Immune Deficiency. Her research focuses on HIV molecular epidemiology, immune pathogenesis, inflammation, and vaccines for treatment and cure in pediatric and youth populations. Dr. Goodenow has published over 125 articles and book chapters and trained more than 30 doctoral and postdoctoral fellows. She received her Ph.D. in molecular genetics from the Albert Einstein College of Medicine in New York. Following a postdoctoral fellowship in molecular oncology at the Sloan Kettering Institute in New York, she was a visiting scientist at the Pasteur Institute in Paris, where she began her studies of HIV.

No potential conflict of interest to report

Organizing Committee

Steven Grinspoon,

MD

Harvard Medical School / Massachusetts General Hospital, United States

Dr. Steven Grinspoon is a Professor of Medicine, Harvard Medical School, Chief of the MGH Metabolism Unit, and Director of the Nutrition Obesity Research Center at Harvard. He has had a long-standing interest in the metabolic and immune complications of HIV disease. He chaired the American Heart Association State of the Science Conference on Cardiovascular Disease in HIV-infected patients.

His work has suggested significant cardiovascular disease in people with HIV (PWH) and highlighted the relative contributions of traditional risk factors, including diabetes and excess visceral fat accumulation, and of nontraditional risk factors, including inflammation and immune activation, using novel PET and CT techniques linking arterial inflammation to high risk vulnerable plaque. In this regard, he is a co-leader of the 7700 participant, global NIH-funded REPRIEVE study to prevent cardiovascular disease in HIV.

In addition, he has shown efficacy of strategies to improve ectopic adipose tissue, leading the development of an FDA approved strategy for visceral fat reduction. For his work, Dr. Grinspoon was awarded the 2016 Aurbach Laureate award in translational research from the Endocrine Society. Dr. Grinspoon is a member of the American Society of Clinical Investigation and the Association of American Physicians, honoring his achievements.

Potential conflict of interest

NIH, Kowa, ViiV, Gilead, Theratechnologies, and Marathon Asset Management.

Invited Speaker

Maureen Hanson

PhD

Cornell University, United States

Maureen Hanson is a molecular/cell biologist at Cornell University in Ithaca, New York. She has a B.S. from Duke University and a Ph.D. from Harvard University, where she also held an NIH postdoctoral fellowship. Her first faculty position was at the University of Virginia. Then she moved to Cornell, where she is Liberty Hyde Bailey Professor in the Department of Molecular Biology and Genetics. She has served as Associate Director of the Cornell Biotechnology Program and Director of the Cornell NSF Plant Science Center, Until 2009 her research was in molecular biology of plants, especially organelle genetics and cell biology, and for this work she received her college's Award for Outstanding Basic Research, the SUNY Chancellor's Award for Faculty Service, and was elected to the American Academy of Arts and Sciences and the National Academy of Sciences. In 2009 she began an additional research program on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.

Her initial research concerned the gut microbiome and mitochondrial genetics in Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS). In 2017 she became Director of the Center for Enervating Neuroimmune Disease, which is supported by an NIH U54 Center grant. In addition to leading her own research group, using metabolomic, proteomic, and immunological methods to identify the molecular basis of the disease, and overseeing the ME/CFS Center, she advocates for societal awareness and more research funding for the neglected post-viral illness ME/CFS.

No potential conflict of interest to report

Organizing Committee

Anthony Kelleher,

MBBS, PhD, FRACP, FRCPA

The Kirby Institute, Australia

Professor Anthony (Tony) Kelleher is a clinician scientist. He graduated from Medicine at UNSW in 1986. He trained in internal medicine and pathology at St Vincent's Hospital, Sydney at the height of the HIV epidemic, qualifying as a Clinical Immunologist and Immunopathologist in 1995.

Professor Kelleher completed his PhD in 1997, describing the modulation of the HIV infected immune system by a range of interventions including therapeutic vaccines and IL-2. He made the first observations describing the reconstitution of antigen specific CD4+ T cell responses in patients receiving potent anti-retroviral therapy in the context of an early phase trial of the HIV protease inhibitor, Ritonavir.

Professor Kelleher was appointed Director of the Kirby Institute at UNSW Sydney in early 2019. He is also Head of the Kirby Institute's Immunovirology and Pathogenesis Program, and Principal of the Infection Immunology and Inflammation Theme at UNSW Medicine. As a clinical academic at St Vincent's Hospital Sydney, Professor Kelleher is responsible for clinical care of patients with HIV infection and autoimmune diseases as well as oversight of the NSW State HIV Reference laboratory.

Potential conflict of interest

ViiV, Merck Australia, Cepheid, CSL and Merck

Program Chair

Daniel Kuritzkes,

MD

Brigham and Women's Hospital / Harvard Medical School, United States

Daniel Kuritzkes is the Harriet Ryan Albee Professor of Medicine at Harvard Medical School and Chief of the Division of Infectious Diseases at Brigham and Women's Hospital in Boston, Massachusetts. He received his B.S. and M.S. degrees from Yale University and his M.D. from Harvard Medical School.

Dr. Kuritzkes has published extensively on antiretroviral therapy and drug resistance in HIV-1 infection. He has chaired several multicenter studies of HIV therapy and previously chaired the AIDS Clinical Trials Group. He served as a member of the NIH Office of AIDS Research Advisory Council and as a member of the U.S. Department of Health and Human Services panel on guidelines for antiretroviral therapy.

He has been a member of several editorial boards and serves an Associate Editor of the Journal of Infectious Diseases. His research interests focus on HIV therapeutics, antiretroviral drug resistance, and HIV eradication.

Potential conflict of interest

Gilead, Merck, ViiV, AbbVie, Atea, Decoy, GSK, Janssen, Moderna, Pfizer, Roche, and Shionogi.

Invited Speaker

Tobias Lanz,

MD

Stanford University,
United States

Tobias Lanz, MD is an assistant professor at the Institute for Immunity, Transplantation, and Infection and the Division of Immunology and Rheumatology at Stanford. His research focuses on B cell biology in autoimmune and neuroimmunological diseases. He uses high-throughput screening technologies, and methods from structural and cell biology to identify new autoantigens and to understand how certain self-reactive B cells escape tolerance mechanisms. He is particularly interested in molecular mechanisms that explain the association between Epstein Barr Virus (EBV) and autoimmunity. Tobias went to medical school at the Eberhard Karls University in Tübingen, Germany and at the University College of London. He wrote his MD thesis at Dr. Michael Platten's laboratory at the Hertie Institute for Clinical Brain Research in Tübingen, Germany before joining Dr. Lawrence Steinman's neuroimmunological laboratory at Stanford as a research scholar. After medical school he pursued his scientific and clinical training at the German Cancer Research Center (DKFZ) and the Department of Neurology at the University Hospital in Heidelberg, Germany. In 2015 he joined Dr. William Robinson's lab at Stanford, where he investigated environmental triggers of autoimmunity, including viruses and milk consumption.

In his most recent work, he characterized the B cell repertoire in the spinal fluid of patients with multiple sclerosis (MS) and identified molecular mimicry between EBV EBNA1 and the glial cellular adhesion molecule GlialCAM as a driver of neuroinflammation (Lanz et al., Nature, 2022). His long term objective is to leverage these newly discovered mechanistic insights to develop next-generation biomarkers and therapeutics for autoimmune diseases

No otential conflict of interest to report

Organizing Committee

Michaela Müller-Trutwin,

PhD

Institut Pasteur,
France

Michaela Müller-Trutwin is Professor at Institut Pasteur and head of the "HIV, Inflammation and Persistence" Unit. She studied Biology at the University in Bonn and Frankfurt. She obtained her PhD from Paris-University, France (Barré-Sinoussi lab). She worked at Research institutes in West- and Central-Africa.

She served as chair of the "Nonhuman primate models working group" and within the "innate immunity coordinated action" at the ANRS. Among other duties, she serves as the chair of the coordinated action on HIV basic research at the ANRS-MIE, the Vice-president of the Scientific Council at Institut Pasteur and member of the Steering Committee at IDMIT (French NHP research center). She has co-organized multiple meetings (Keystone, HIV dynamics, EACS HIV Cure symposia etc). The lab is focused on deciphering the early host immune responses to identify factors involved in viral reservoir control and tissue damage protection with the aim to translate the findings into clinical research. Her team made key contributions on the role of inflammation in HIV pathogenesis.

More recently, they uncovered an important role of NK cells in the control of SIV replication in tissues. Her work has been honored by awards, such as by the French Medical Research Foundation.

Potential conflict of interest to report
Gilead

Organizing Committee

Avindra Nath,

MD

National Institutes of Health, United States

Dr. Nath is the Clinical Director of the National Institute of Neurological Disorders and Stroke (NINDS) at NIH, where he is also Chief of the Section of Infections of the Nervous System, Director of the Translational Center for Neurological Sciences.

He is a physician–scientist who specializes in neuro-immunology and neurovirology. His research is focused on the clinical manifestations, pathophysiology and treatment of emerging neurological infections with a focus on HIV infection. In recent years, he has studied the neurological complications of endogenous retroviruses, Ebola, Zika virus and SARS-CoV-2 and conducts research on patients with undiagnosed neuroinflammatory disorders. He has served on advisory committees to the NIH, CDC, FDA and WHO. The International Society of NeuroVirology gave him the Pioneer in NeuroVirology Award for his contributions to HIV neuropathogenesis and elected him as the President of the Society. He received the Wybran award from the Society of Neuroimmune Pharmacology for contributions to Neurovirology. He also received the NIH Director's award for his work on SARS-CoV-2 and the HHS Secretary's award for his work on Ebola infection.

No potential conflict of interest to report

Invited Speaker

Lishomwa Ndhlovu,

MD, PhD

Weill Cornell Medicine, United States

Lishomwa (Lish) Ndhlovu MD, PhD is a Professor of Immunology in Medicine in the Division of Infectious Diseases at Weill Cornell Medicine. The thrust of his research program is confronting the challenges of HIV and aging and is developing specific strategies to prevent, slow or eliminate complications associated with HIV. His team combines immunology, virology and epigenetic methods exploring molecular mechanism of HIV pathogenesis and persistence through pre-clinical and clinical investigations and has expanded towards finding an HIV cure.

He has also become increasingly involved in bringing the same urgency and focus to the COVID-19 pandemic and exploits immuno-epigenetic approaches to resolve molecular mechanisms regulating SARS-CoV-2 infection across tissues and cell types in people with and without HIV. His lab is largely supported by individual and consortia grants from the NIH.

He is a member of the International Neuro-HIV Cure Consortium and Co-leader of the $26.5 million NIH - funded Martin Delaney Collaboratory for HIV Cure "HOPE" and NIDA funded U01-SCORCH program documenting single cell opioid responses in the brain in the setting of HIV. Heis an elected Fellow of the American Academy of Microbiology and serves as Co-Editor in Chief of the journal, AIDS Research and Human Retroviruses.

Potential conflict of interest

NIH, ViiV Healthcare, Cytodyn, and Ledidi AS

Organizing Committee

Roger Parades

MD, PhD

IrsiCaixa AIDS Research Institute, Spain

Roger Paredes, MD, PhD, is Head of the Infectious Diseases Department, Hospital Germans Trias i Pujol and Principal Investigator of the Microbial Genomics Group at the IrsiCaixa AIDS Research Institute, Badalona, Catalonia, Spain. He obtained an MD, PhD degree in Medicine and Surgery from the Autonomous University of Barcelona (UAB) and specialised in HIV research at the Brigham & Women's Hospital, Harvard Medical School, through a La Caixa grant for postgraduate studies.

His team at irsiCaixa has demonstrated the clinical utility of HIV-1 deep sequencing in both high- and low-income countries, and is now leading pioneering research into the role of the gut microbiome in the pathogenesis of HIV infection and chronic inflammation.
During the COVID-19 pandemic, Dr Paredes has been the Spanish National Coordinator of seminal NIH/NIAID-funded randomized clinical trials, including ACTT-1 and 2 and the ACTIV-3/TICO platform, which have defined the current standard of care for this disease in hospitalized patients as well as in outpatients. Dr. Paredes is member of the COVID-19 treatment guidelines of the Spanish ID Society and the Catalan Institute of Health.

He is also member of the WHO Global Clinical Platform for COVID-19 Clinical Advisory Group and serves in the WHO's HIV Drug Resistance Strategy Steering Committee, the HIV treatment guidelines group and the European Laboratory Initiative.

Potential conflict of interest to report

Gilead, ViiV, MSD, Pfizer, GSK, Lilly, Roche, AstraZeneca, Atea and Theracthnologies

Invited Speakers

Micheal Peluso,

MD

Harvard Medical School / Massachusetts General Hospital, United States

Dr. Peluso is an infectious disease physician at the University of California, San Francisco. Prior to COVID, his research focus was on the chronic sequelae of HIV infection. When the SARS-CoV-2 pandemic emerged, Dr. Peluso led the efforts to implement the Long-term Impact of Infection with Novel Coronavirus (LIINC, pronounced "link") study at San Francisco General Hospital, based on the hypothesis that COVID could have a long-term impact on health and well-being. LIINC was one of the first post-COVID cohorts in the U.S. and now includes hundreds of individuals with and without Long COVID, many of whom have been followed for more than 2 years. He leads projects within LIINC aimed at understanding the biological mechanisms that drive Long COVID and is also responsible for implementation of the UCSF enrolling sites for the NIH's RECOVER initiative.

Potential conflict of interest

Gilead and AstraZeneca

Organizing Committee

Jonathan Schapiro,

MD

National Hemophilia Center,
Sheba Medical Center,
Israel

Jonathan M Schapiro, MD has devoted his career to HIV clinical care, research and education since completing his Fellowship in Infectious Diseases and Geographic Medicine at the Stanford University School of Medicine Center For AIDS Research, Stanford CA. Dr. Schapiro Graduated from the Ben Gurion University School of Medicine and completed his Medicine Residency at the Rabin Medical Center in Israel.

Dr. Schapiro's research has focused on the causes of antiretroviral drug failure, interventions to optimize clinical care, and new drug development. His interests have include resistance and cross-resistance between drugs, associations between resistance and pharmacology, development of new antiretroviral agents with improved resistance and pharmacological profiles, the clinical utility of resistance and drug level testing, and integrating resistance assays and other diagnostics into clinical care. He has been involved in the development of advanced interpretation systems for these assays, and has worked to highlight the importance of interactions between drug exposure and resistance. Dr. Schapiro currently runs the HIV/AIDS clinic at the National Hemophilia Center in Tel Aviv, Israel.

Potential conflict of interest

Pfizer, Moderna, Merck, Gilead Sciences, GlaxoSmithKline, Tibotec-Janssen, Teva, ViiV Healthcare, and WHO.

Organizing Committee

Irini Sereti

MD

NIAID, NIH
United States

Dr Sereti is the Chief of the HIV Pathogenesis Section in the Laboratory of Immunoregulation at NIAID. After her Internal Medicine training and Chief residency at Northwestern University in Chicago, she completed an infectious disease fellowship at NIAID/NIH and joined the Laboratory of Immunoregulation, initially as a staff clinician, and starting in 2009 as a tenure track investigator. She received tenure in 2015. Her group studies the acute (IRIS) and long-term inflammatory complications of treated HIV and the etiology, prognosis and management of idiopathic CD4 lymphopenia, a rare disorder of low CD4 counts in the absence of HIV.

Her previous work on inflammation and lymphopenia has aspired new projects on COVID-19 to address both the pathogenic mechanisms of inflammation and lymphopenia and to study immune interventions. Dr Sereti is a physician-scientist with a strong commitment to diversity, excellence in clinical care and mentorship.

No potential conflict of interest to report

Organzing Committee

Serena Spudich,

MD

Yale University,
United States

Serena is Gilbert H. Glaser Professor of Neurology and Chief, Division of Neurological Infections and Global Neurology at Yale University.

Her clinical and translational research explores effects of HIV and other viral infections in the nervous system, focusing on effects of acute infection, antiviral and immune treatments, and cure strategies on viral pathogenesis and persistence in the central nervous system (CNS). She collaborates with colleagues of multiple disciplines in studies in the United States and in international settings, exploring questions of inflammation, injury, and viral reservoirs within the central nervous system. She has been active in the AIDS Clinical Trials Group (ACTG) Neurology and HIV Reservoirs and Eradication committees, co-leads the International NeuroHIV Cure Consortium, serves on the US DHHS Antiretroviral Treatment Guidelines Committee, CROI Program Committee, and leads multidisciplinary projects addressing the pathobiology of HIV and SARS-CoV-2 in the CNS. She also is a neurology physician who cares for patients with viral infections and neurological disorders in clinics at Yale.

No potential conflict of interest to report

Invited Speaker

Martin Tolstrup,

MSc, PhD

Aarhus University Hospital,
Denmark

Martin Tolstrup is a professor in immunology of viral infections at Department of Clinical Medicine, Aarhus University and Head of the research laboratory at the Department of Infectious Diseases, Aarhus University Hospital, Denmark. Dr Tolstrup received his MSc and PhD from Aarhus University.

He has worked extensively on studies of HIV persistence and how to manipulate the chronic HIV infection. Dr Tolstrup have been involved in numerous clinical trials testing both latency reversing agent for HIV reservoir purging as well as immunotherapy interventions. Recently, the use of broadly neutralizing antibodies has become a focus as agents to specifically target viral infected cells.

No potential conflict of interest to report

Invited Speaker

Arun Venkatesen,

MD, PhD

Johns Hopkins University School of Medicine, United States

Arun Venkatesan, M.D., Ph.D. is a Professor at the Johns Hopkins University School of Medicine, in the Department of Neurology, Division of Neuroimmunology and Neurological Infections. He received his B.S. in Bioengineering at the University of California, Berkeley, followed by an M.D. and Ph.D. degree at the University of California, Los Angeles, where he studied viral pathogenesis. F
ollowing residency in Neurology and a fellowship in Neuroinfectious Diseases at Johns Hopkins, he joined the faculty, where he currently serves as Director of the Johns Hopkins Encephalitis Center, a multidisciplinary clinical and research program devoted to delineating pathogenesis and optimizing diagnosis and management of patients with infectious and immune-mediated encephalitis. His laboratory studies mechanisms of central nervous system injury in the setting of infection and neuroinflammation. He has received funding from the National Institutes of Health, Howard Hughes Medical Institute, National Multiple Sclerosis Society, and Maryland Stem Cell Research Fund.

No potential conflict of interest to report

Invited Speakers

David Wohl

MD

UNC School of Medicine, United States

Dr. Wohl is a Professor of Medicine in the Division of Infectious Diseases at the University of North Carolina (UNC). He is co-Principal Investigator of the Global UNC Infectious Diseases Clinical Research Unit and Site Leader of its Chapel Hill research site.

Dr. Wohl is a clinical scientist with a focus on emergent infectious diseases. He has spent over 20 years leading research into the prevention and treatment of HIV and served two terms as a member of the US Department of Health and Human Services (DHHS) Antiretroviral Guidelines Panel.

Since 2014, he has been working continuously in Liberia, West Africa, conducting research with Ebola survivors to learn about chronic complications and sexual transmission of this infection and establishing the UNC Project Liberia research platform at two locations in the country. He and his team have extended this work to examine Lassa fever, a viral hemorrhagic fever endemic in West Africa.

In 2020, he contributed to the UNC clinical and research response to COVID-19. He is medical director of the UNC Chapel Hill drive through testing site as well as two COVID-19 vaccination clinics and the Chapel Hill COVID-19 monoclonal antibody infusion center. He serves as Vice Chair of ACTIV-2, an international trial of promising SARS-CoV-2 therapeutics.

He has an active clinical practice at the UNC Infectious Diseases Clinic.

Potential conflict of interest to report

NIH, Gilead, ViiV, and Janssen.

Invited Speaker

Dario Zamboni,

PhD

University of São Paulo, Brazil

Dario Zamboni is a full professor at Ribeirao Preto School of Medicine of the University of Sao Paulo (FMRP/USP) and head of the Innate Immunity and Microbial Pathogenesis Laboratory at FMRP/USP. He received his Ph.D. from the Federal University of São Paulo and a PEW fellowship to perform his postdoctoral training at Yale University, School of Medicine.

Dr. Zamboni has published extensively on the recognition of microbes by intracellular pattern recognition receptors and the interaction of host cells with intracellular pathogens, such as Leishmania, Legionella, Coxiella, and inflammatory viruses. He is chair of the Department of Cellular and Molecular Biology of FMRP/USP and has chaired several institutional boards and committees for funding awards, including PEW and FAPESP. He has been a member of several editorial boards and serves as Editor of the journals such as eLife, Plos Pathogens, Plos Neglected Tropical Disease, among others. His research interests focus on Innate Immunity, Microbial Pathogenesis, and the Interaction of Host Cells with Intracellular Pathogens.

No potential conflict of interest to report

Abstracts

O_#1 High Levels of Il-1, Tnf- and Mip-1 One Month after the Onset of the Acute Sars-Cov-2 Infection, Predictors of Post COVID-19 in Hospitalized Patients

Alonso-Domínguez J[1], Gallego-Rodríguez M[1], Martínez-Barros I[1], Calderón-Cruz B[2], Leiro V[3,4], Pérez-González A[1], Poveda E[1]
[1]Group of Virology and Pathogenesis, Galicia Sur Health Research Institute (IIS Galicia Sur)-Complexo Hospitalario Universitario de Vigo, SERGAS-UVigo, Vigo, Spain, [2]Statistics and Methodology Unit, Galicia Sur Health Research Institute (ISS Galicia Sur)-Complexo Hospitalario Universitario de Vigo, SERGAS-Uvigo, Vigo, Spain, [3]Servicio de Neumología, Complexo Hospitalario Universitario de Vigo (CHUVI), Sergas, Vigo, Spain, [4]NeumoVigo I+i Research Group, Galicia Sur Health Research Institute (IIS Galicia Sur). SERGAS-UVIGO, Vigo, Spain

Background: According to WHO "post COVID-19" is defined as the continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months that cannot be explained by an alternative diagnosis. The pathophysiological mechanisms remain controversial; however, a link between a persistent inflammatory environment and these long-term sequelae has been suggested. Herein, we assessed the dynamic of up- and downstream molecules of the NLRP3 inflammasome's pathway, among other inflammatory cytokines.

Material and Methods: A longitudinal study with individuals belonging to the Galicia Sur Health Research Institute COVID-19 Cohort was performed defining three groups: healthy blood donors (HC) and donors with a confirmed SARS-CoV-2 infection who had been hospitalized. The latter was divided into 2 groups: post COVID-19 (PC) and non-post COVID-19 (nPC) patients based on the presence or absence of symptomatology at month 6, respectively. Multiplex bead-based immunoassay was used to quantify the levels of plasma cytokines (IL-1β, IL-3, IL-6, IL-8, IL-18, IP-10, MIG, TNF-α, IFN-γ, MIP-1α, and MIP-1β). Reactive Oxygen Species (ROS) levels were quantified by measuring total peroxide (TPX) with a commercial colorimetric assay. Both quantifications were performed at baseline-time of SARS-CoV-2 diagnosis (M0), month 1 (M1) and 6 (M6) after the onset of the SARS-CoV-2 infection. Statistical analysis including Friedman's test, Mann-Whitney U test and Kruskal-Wallis' test were performed to identify differences between different time points and the study groups.

Results: A total of 68 individuals were included: 27 nPC, 27 PC and 14 healthy controls. Within COVID-19 patients, 37.0% met obesity criteria (BMI ≥ 30), with a median hospitalization time of 7 days [IQR: 4-9.75] from March to December 2020, 20.4 % were admitted to the ICU and 29.6 % required invasive mechanical ventilation. The most frequent symptoms among people with post COVID-19 condition were thoracic 59.3 % (dyspnea, chest pain, cough), general 44.4 % (asthenia, hair loss), nervous 25.9 % (behavioral disorder, headache) and 25.9 % musculoskeletal (arthralgias, myalgias). No significant differences between nPC and PC groups were observed based on clinical data (age, gender, comorbidities, SARS-CoV-2 severity). At baseline, significant higher values of ROS and cytokines were recognized for nPC and PC compared with HC that subsequently decrease during the follow-up. Of note, only IL-1β (PC: 8.94 [5.63-12.81] vs nPC: 6.27 [2.21-8.80], p = 0.024), MIP-1α (PC: 25.45 [15.65-38.85] vs nPC: 18.99 [9.18-23.82], p = 0.020) and TNF-α (PC: 22.45 [15.65-31.69] vs nPC: 15.85 [12.35-22.34], p = 0.026) levels (in pg/ml) were significantly higher among PC than nPC at month 1 after the onset of SARS-CoV-2 infection. A ROC analysis established the best cut-offs for distinguishing PC and nPC at month 1 and to design a model which correctly identified all patients who experienced post COVID-19 symptomatology when the levels of IL-1β, MIP-1α, and TNF-α were above of these 3 cut-offs.

Conclusions: These findings suggest that a persistent inflammatory state one month after the onset of SARS-CoV-2 infection related to specific cytokines (IL-1β, MIP-1α, and TNF-α) may be useful to predict post COVID-19 symptomatology.

O_#2 Determinants of the Onset and Prognosis of the Post-COVID-19 Condition: A 2-Year Prospective Cohort Study

Paredes R[1,2,3,4,5,10,11], Mateu L[2,3,4,5,6], Tebe C[7], Loste C[2,3,5,6], Santos J[2,3], Lladós G[2,3,4,6], López C[2,3], España-Cueto S[2,3], Toledo R[2,3], Font M[2,3], Chamorro A[2,3], Muñoz-Lopez F1, Nevot M1, Vallejo N8, Teis A8, Puig J2,3, Fumaz C2,3,6, Muñoz-Moreno J[2,3], Prats A[2,3,6], Estany C[2,3], Coll-Fernandez R[9], Herrero C[3], Casares P[3], Garcia A[3], Clotet B[1,2,3,4,5,10], Massanella M[1,6,10]
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Background: At least 5-10% of subjects surviving COVID-19 develop the post-COVID-19 condition (PCC) or "Long COVID". The clinical presentation of PCC is heterogeneous, its pathogenesis is being deciphered, and objective, validated biomarkers are lacking. It is unknown if PCC is a single entity or a heterogeneous syndrome with overlapping pathophysiological basis. In a large crossectional evaluation, the RECOVER study in the US identified four clusters of subjects with PCC according to their presenting symptoms. The long-term clinical implications of PCC remain unknown.

Methods: We conducted a 2-year prospective cohort study of subjects surviving COVID-19, including individuals fulfilling the WHO PCC definition and subjects with full clinical recovery. We systematically collected post-COVID-19 symptoms using prespecified questionnaires and performed additional diagnostic imaging tests when needed. Factors associated with PCC were identified and modelled using logistic regression. Unsupervised clustering analysis was used to group subjects with PCC according to their presenting symptoms. Factors associated with PCC recovery were modelled using a direct acyclic graph approach.

Findings: The study included 548 individuals, 341 with PCC, followed for a median of 23 months (IQR 16.5 – 23.5) and 207 subjects fully recovered. In the model with best fit subjects who were male and had tertiary studies were less likely to develop PCC, whereas history of headache, or presence of tachycardia, fatigue, neurocognitive and neurosensitive complaints and dyspnea at COVID-19 diagnosis predicted the development of PCC. The cluster analysis revealed the presence of three symptom clusters with additive number of symptoms. Only 26 subjects (7.6%) recovered from PCC during follow-up; almost all of them (n=24) belonged to the less symptomatic cluster A, dominated mainly by fatigue. Recovery from PCC was more likely in subjects who were male, required ICU admission, or had cardiovascular comorbidities, hyporexia and/or smell/taste alterations during acute COVID-19. Subjects presenting with muscle pain, impaired attention, dyspnea or tachycardia, conversely, were less likely to recover from PCC.

Interpretation: Preexisting medical and socioeconomic factors, as well as acute COVID-19 symptoms predict the development of and recovery from the PCC. Recovery is extremely rare during the first 2 years, posing a major challenge to healthcare systems.

O_#3 A Role for Inflammasome Activation and Oxidative Stress in Sars-CoV-2 Breakthrough Infection and Symptomatic Rebound

Lucena Lage S[1], Rocco J[1], Epling B[1], Laidlaw E[1], Pinheiro Amaral E[1], Rupert A[2], Galindo F[1], Lisco A[1], Manion M[1], Sereti I[1]
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Despite the efficacy of mRNA vaccines in reducing risk of severe COVID-19, the disease caused by the SARS-CoV-2 virus, breakthrough infections still occur. In addition, a clinical and/or virological rebound 2-8 days after improvement or recovery from COVID-19 has been reported following nirmatrelvir/ritonavir treatment or even in untreated individuals. The pathogenesis of this rebound phenomenon remains unknown. We have previously reported that COVID-19 hyperinflammation and clinical severity is associated with a robust and persistent oxidative stress-related inflammasome activation in circulating blood monocytes and hypothesized a role for these innate immune pathways in omicron variant COVID-19 acute and rebound-related symptoms.

Herein, we evaluated seven healthy volunteers (HV), seven patients with acute omicron infection (acute) and seven individuals with rebounding symptoms (rebound), by incubating their circulating blood monocytes with a probe to assess active caspase-1/4/5 (FLICA) followed by the apoptosis-associated speck-like protein (ASC) staining for canonical inflammasome complex detection (also known as 'ASC-speck'). Oxidative stress was evaluated by measuring intracellular levels of mitochondrial superoxide (MitoSOX) and lipid peroxidation (LAA), both hallmarks of the oxidative stress response, as well as the antioxidant glutathione peptide, which is required to detoxify cells from oxidized lipids. Biomarkers, nucleocapsid antigen, and anti-SARS-CoV-2 antibodies and T cell responses were also evaluated.
We found an enrichment of circulating monocytes displaying elevated levels of FLICA and ASC-speck formation, in both the acute and rebound patients when compared to HV, thus suggesting systemic inflammasome activation. The rebound group differed from HVs for a significantly increased levels of MitoSOX and LAA along with lower intracellular levels of glutathione, further highlighting the inability of those monocytes to control the oxidative stress responses. Also, a positive correlation of MitoSOX with FLICA and the inflammasome-triggered cytokine IL-18 was found.

When compared to rebound COVID-19 patients, acutely infected individuals presented higher levels of serum SARS-CoV-2 nucleocapsid antigen (Serum Nuc Ag) which positively correlated with inflammatory markers, including FLICA and plasma IL-18. On the other hand, rebound patients were characterized by robust anti-SARS-CoV-2 T-cell and antibody responses, which inversely correlated with Serum Nuc Ag and inflammasome and oxidative stress markers, consistent with less antigen and inflammation levels when adaptive immune responses are present. Collectively, our findings suggest that antigen-driven and stress-related innate immune inflammatory responses contribute to both SARS-CoV-2 breakthrough infections and symptomatic COVID-19 rebounds.

O_#4 HIV Exposed Uninfected (HEU) Infants Have Pro-inflammatory Bioprofiles That Correlate with Their Mothers' Bioprofiles Independent of Viral Levels and Persist for at Least Six Months

Yin L[1], Fischer B[2], Venturi G[2], Nepal U[1], Choudhary S[2], Shen J[1], Chang K[1], Raplee I[1], Borkar S[1], Kim-Chang J[2], D Paris K[3], Goodenow M[1], Sleasman J[2]
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Introduction: Compared to HIV unexposed infants (HUU), HEU infants have a higher risk for adverse metabolic, infectious, and neurodevelopmental outcomes. However, the relationships between immunity in pregnant women with HIV (PWH) and their HEU infants are largely unexplored. Proinflammatory immune pathways from PWH and their HEU infants were examined in comparison to pregnant women without HIV (PWOH) and their HUU infants.

Methods: The study included 23 mother/baby pairs of PWH on antiretroviral therapy (ART) with HIV suppressed (VS) during pregnancy and an equal number of PWH on ART whose HIV was not suppressed (VNS). PWOH and their neonates served as a reference group (N=18). HEU infants were evaluated at birth and 6 months along with a longitudinal cohort of 32 HUU infants. Cryopreserved plasma samples were obtained from HEU study participants enrolled in PACTG 316, a study examining Nevirapine for the prevention of maternal-fetal HIV transmission. Twenty-one immune biomarkers associated with germinal center (GC) formation, macrophage or lymphocyte activation, and inflammation were measured using Mesoscale Diagnostics multiplex assays. Mann-Whiney U test compared individual biomarkers between two groups. One-way ANOVA/Kruskal-Wallis test compared multiple groups. Spearman's rank test assessed biomarker correlations between mothers and their babies.

Results: Compared to PWOH, bioprofiles related to B cell development (sCD40L), immune activation (sCD27), and inflammation (CXCL9, CCL5) were significantly elevated in both VS and VNS PWH. In contrast, APRIL, a marker of GC development, was lower in PWH. Among newborns, HEU compared to HUU neonates showed significantly higher concentrations of biomarkers associated with B cell GC development (APRIL, BAFF, sCD40L, IL-21), macrophage (sCD14) and lymphocyte (sCD27, IFN-γ, IL-22) activation, as well as pro-inflammation (CXCL9, CCL4, CCL5, CXCL8, TNF-α, IL-1β, IL-6) and anti-inflammation (IL-10, IL-1RA). Among these elevated biomarkers in HEU newborn, most (APRIL, BAFF, sCD40L, IL-21, sCD14, sCD27, CCL4, CCL5, TNF-α, IL-1β, IL-6, IL-1RA) remained elevated compared with HUU infants at 6 months of age. In contrast, sCD163, IL-17A, and CXCL10 were similar in HEU and HUU infants. A correlation study was performed to investigate relationships of biomarker profiles between mother/newborn dyads. Among PWOH and PWH mother/baby pairs there was a positive correlation in BAFF, IL-21, sCD14, IL-17A, and CXCL9. In addition, HEU-PWH displayed positive correlations in APRIL, sCD163, IFN-γ, CXCL10, CCL4, CCL5, TNF-α, IL-1β, IL-6, and IL-1RA. UMAP combined all biomarkers to reveal similar patterns independent of viral suppression or non-suppression (PWH-VS and PWH-VNS) that were distinct from PWOH. Similarly, HEU born to PWH-VS or PWH-VNS displayed similar patterns that were distinct from HUU and their respective mothers.

Conclusions: HEU infants, even though uninfected, displayed bioprofiles of immune activation and inflammation, which persisted to 6 months of life when compared to HUU infants. Many pro-inflammatory biomarkers

elevated in PWH are reflected in their HEU infants and in general are independent of detectable viral replication. Biomarkers most perturbed in HEU infants are involved in macrophage activation and GC formation. These results suggest that early immune priming is likely impaired in HEU infants and may contribute to the increased morbidity observed in HEU infants.

O_#5 Possible Role of Intestinal Damage and Endotoxemia in the Development of Endotholial Dysfunction, Thrombosis and Secondary Lung Damage in Patients with COVID-19

Shostakovych-Koretskaya L[1,2], Tsihankov K[3], Logvinenko V[2]
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Introduction: The role of endotoxicosis, as a major pathogenic component in the development of severe forms of SARS-CoV-2, with numerous manifestations not only on the side of the lungs, but also in other organs, more and more scientific evidence.
Objectives. Based on a clinical and morphological study of the characteristics of intestinal lesions at different stages of Covid-19, substantiate the hypothesis of endotoxicosis as a key activator of systemic endothelial dysfunction and secondary lung damage in COVID-19.

Materials and methods. The study is based on a clinical and pathomorphological study of autopsy material from 18 deaths from COVID-19 . In some cases, the method of immersion microscopy was used, an immunohistochemical study was performed.

Results: Among the 18 dead 10 were men and 8 women. In all the deceased, the diagnosis of COVID-19 was verified by the PCR. The median age of the deceased was 69 years, the average day of illness upon admission to the hospital was 9 ± 5 days, the average length of stay in the hospital was 16 ± 6 days. The main manifestation of the action of an alternative factor in the development of diffuse alveolar damage (DAD) was microthrombosis against the background of leukocyte traps, which were formed by netosis of hyperactivated polymorphonuclear leukocytes (PMNs). The absence of a pre-existing inflammatory process and signs of migration of leukocytes through the walls of the capillaries into the lumen of the alveoli was noted. At the same time, the histological picture of changes in the small intestine corresponded to viral enteritis with the presence of phagocytic macrophages and PMNs with signs of hyperactivation in the inflammatory infiltrate, as well as cells expressing the CD14 lipopolysaccharide receptor. In the proliferative stage of DAP, there was persistence of exudation, the formation of an inflammatory infiltrate with an immunodeficient character, a large number of macrophages. At the same time, the formation of erosive-necrotic autoimmune jejunoileitis was observed in the distal parts of the small intestine.In the vessels of the mucous membrane and submucosa, which were well visualized during the IHC reaction with CD31, swelling and pronounced desquamation of the endothelium were noted.
A hypothesis of the pathogenesis of COVID-19 has been proposed, according to which lung damage can occur secondarily, according to the mechanism of hepatopulmonary syndrome.

Conclusions: There is reason to believe that the mucosa of the distal small intestine, along with the respiratory system, is the gateway of infection in severe COVID-19. The identified morphological manifestations of severe endothelial dysfunction with endothelial damage in COVID-19 indicate more endotoxin damage by the mechanism of a paraallergic reaction, rather than direct viral damage.

O_#6 The Plasma Microbiome Contributes to Immune Reconstitution in HIV Infected Individuals on Suppressive ART

Jiang W[1],
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Background: In HIV infection, even under long-term antiretroviral therapy (ART), up to 20% of HIV-infected individuals fail to restore CD4+ T cell counts to levels similar to those of healthy controls. The mechanisms of poor CD4+ T cell reconstitution on suppressive ART are not fully understood.

Methods: Here, we tested the hypothesis that lipopolysaccharide (LPS) from bacteria enriched in the plasma from immune non-responders (INRs) contributes to blunted CD4+ T cell recovery on suppressive ART in HIV. We characterized plasma microbiome in HIV INRs (aviremic, CD4+ T cell ––––+counts < 350 cells/ml), immune responders (IRs, CD4+ T cell counts > 500 cells/ml), and healthy controls. Next, we analyzed the structure of the lipid A domain of three bacterial species identified by mass spectrometry (MS) and evaluated the LPS function through LPS-induced proinflammatory responses and CD4+ T cell apoptosis in PBMCs. In comparison, we also evaluated plasma levels of proinflammatory cytokine and chemokine patterns in these three groups. At last, to study the causality of microbiome-blunted CD4+ T cell recovery in HIV, B6 mice were intraperitoneally (i.p.) injected with heat-killed Burkholderia fungorum, Serratia marcescens, or Phyllobacterium myrsinacearum, twice per week for total of eight weeks.

Results: INRs exhibited elevated plasma levels of total microbial translocation compared to the IRs and healthy controls ($P<0.05$, non-parametic MannWhiteney U tests). The most enriched bacteria were Burkholderia and Serratia in INRs and were Phyllobacterium in IRs ($P<0.05$, MannWhiteney U tests). Further, unlike P. myrsinacearum LPS, B. fungorum and S. marcescens LPS induced proinflammatory responses and CD4+ T cell apoptosis in PBMCs ($P<0.05$, MannWhiteney U tests), and gene profiles of bacteria-mediated cell activation pathways in THP-1 cells in vitro. Notably, LPS structural analysis by mass spectrometry revealed that lipid A from P. myrsinacearum exhibited a divergent structure consistent with weak toll-like receptor (TLR) 4 agonism, similar to the biological profile of probiotic bacteria.

In contrast, lipid A from B. fungorum and S. marcescens showed structures more consistent with canonical TLR4 agonists stemming from proinflammatory bacterial strains.
Finally, intraperitoneal (i.p.) injection of inactivated B. fungorum and S. marcescens but not P. myrsinacearum resulted in cell apoptosis in mesenteric lymph nodes of C57BL/6 mice in vivo ($P<0.05$, MannWhiteney U tests).

Conclusions: These results suggest that the microbial products are causally associated with INR phenotype. In summary, variation in blood microbial LPS immunogenicity may contribute to immune reconstitution in response to suppressive ART. Collectively, this work is consistent with immunologically silencing microbiome being causal and targetable with therapy in HIV.

O_#7 Impact of Glatiramer Acetate Treatment in SIVmac-Infected Macaques

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A residual chronic inflammation often persists in people living with HIV despite efficient anti-retroviral treatment (ART). The causes might be multifactorial, with microbial translocation being a potential major contributor. The increased risk of non-AIDS comorbidities and mortality associated with chronic inflammation represents an unmet need for new therapeutics targeting HIV-induced inflammation. Glatiramer acetate (GA) is used for treatment of a human autoimmune disease and has also shown regulatory effects in murine models of intestinal inflammatory diseases. The underlying mechanisms of GA action remain elusive.

We aimed to investigate whether GA reduces inflammation in a nonhuman primate model of HIV infection (SIV-infected cynomolgus macaques). We conducted a study in 30 animals with group 1 (Gr1) corresponding to SIV-infected, non-treated animals (N=9), group 2 (Gr2) and group 3 (Gr3) to animals in which treatment with GA (4 months) was initiated in the chronic (N=6) or acute phase (N=6) of SIV infection, and group 4 (Gr4, N=6) and group 5 (Gr5, N=3) corresponding to SIV-infected animals in which ART was initiated in the acute phase, with Gr4 receiving GA with the same timing as Gr2. Blood and tissue samples were analyzed for canonical markers of disease progression, systemic and intestinal immune activation, stress, and cytotoxic activity (flow cytometry, ELISA, imaging). Gr2 (chronic GA) showed higher CD4 T cell levels and T4/T8 ratios in blood, higher CD4+ T cell frequencies in lymph nodes (LN) and rectal biopsies, and lower systemic inflammation (sCD163, HSP60) than controls (Gr1). Tfh cells in LN, known to increase in viremic macaques, had a different dynamic from total CD4+T cells since they were lower in Gr2 than in Gr1. Gr4 (cART+GA) also had higher CD4 T cell levels in rectal biopsies than the control Gr5 (cART alone). A transient decrease of inflammation was observed in all groups treated with GA compared with the control group (Gr1, no treatment). Twenty animals were euthanized 1 year post-infection to further analyze the impact in tissues. In all GA treated animals, we observed maintenance of CD4 T cells and limited T cell activation in LN, spleen, colon and jejunum, compared to controls. Systemic T4/T8 ratios were higher and inflammation levels were lower (IP-10 and HSP60). No major effects on viremia or viral reservoirs were observed, except in LN.

These results indicate that GA treatment has the potential to improve CD4 T cell preservation in lymphoid tissues and reduce inflammation during SIV infection. Thus, GA treatment represents an interesting strategy that should be further investigated.

P_#1

Abstract P_#1 was withdrawn

P_#2 Distinct Gene Expression Signatures are Associated with Viral Suppression in Youth with HIV on ART: Implications for Novel Diagnostic or Therapeutic Targets

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Background: Human immunodeficiency virus (HIV) replication is regulated by complex interactions between host and viral factors to promote or inhibit HIV replication. While antiretroviral therapy (ART) can suppress HIV replication, viral infection persists. In the current study, we examined differential host peripheral blood cell gene expression among youth with HIV on ART with or without sustained viral suppression and youth without HIV. The goal was to identify host cellular factors and pathways unique to youth with suppressed virus infection and provide insights into molecular interactions associated with control or persistence of viral replication.

Methods: Peripheral blood cell mRNA was profiled using Affymetrix HG-U133 Plus 2.0 Arrays (~54,675 probes) for 27 youth with HIV (predominantly African American males ages 18-23 years with no HIV-associated comorbidities who initiated ART prior to CD4 T cell decline) and 25 youth without HIV balanced for age, gender, and race. Over three years of ART, 19/27 youth with HIV achieved sustained viral suppression (VS) (< 50 RNA copies per ml plasma), while 8/27 had detectable viral replication (VNS) while on ART [median (QR) 6959 (127, 19655) RNA copies per ml plasma]. Principal component and hierarchical clustering analyses were applied to distinguish gene expression profiles. Differentially expressed genes (DEGs) were identified using Significance Analysis of Microarrays (FC ≥ 1.3 and FDR ≤ 0.05). DEG functions were inferred using the Database for Annotation, Visualization, and Integrated Discovery (DAVID) and Gene Ontology (GO). Protein-Protein Interaction (PPI) network analyses were performed using STRING database and Cytoscape. Cytoscape plugin cytohubba was applied to identify important nodes (hub genes) in PPI network ranked by high connectivity or correlation.

Results: When compared with participants without HIV, VNS had 1003 DEGs with perturbations of 47 pathways related to interferon signaling and defense against viruses. In contrast, VS showed perturbations of 14 pathways with 367 DEGs, including platelet activation and regulation of serine/threonine protein kinase. Some perturbed pathways, such as positive regulation of RNA polymerase II transcription or apoptotic signaling, were similar between VS or VNS youth compared to youth without HIV, while hub genes regulating chronic inflammation (HSP90AB1, RhoA, PDGFA, and STK4) were unique among youth with VS compared to youth without HIV. Direct comparison between youth with VS or VNS identified 131 DEGs involved in DNA repair, RNA processing, and negative regulation of RNA polymerase II transcription pathways, while YY1, Dicer1, and XRCC2 were hub genes associated with viral suppression in youth.

Conclusions: Youth on ART with VS display a unique gene expression profile distinct from youth without HIV infection or youth on ART with VNS. Comparing youth who are virally suppressed to those non-suppressed on ART can identify sentinel biomarkers for early indications of viral resurgence and the development of personalized treatment regimens for people with HIV. Comparisons between youth with viral suppression and those without HIV can guide the design of expression-based diagnostic classifiers and identify inflammatory pathways that serve as sensitive indicators for viral or comorbid conditions.

P_#3 Cytomegalovirus Serostatus Alters the Transcriptomic Response to RhCMV/SIV Vaccination

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Rhesus cytomegalovirus (RhCMV) -vectored vaccines against simian immunodeficiency virus (SIV) have been shown to provide impressive protection against repeated low-dose challenges. Because 83% of the global population are CMV infected, the protective mechanisms used by CMV-vectored vaccines developed for people may be complicated by the immunologic impact of prior wild-type CMV infection. We and others previously showed that RhCMV infections cause transformative immunologic change in the host.

Such changes, including changes in NK-cell subsets and expansion of innate-memory CD8+ T cells, could cooperate with adaptive immune responses to protect against HIV/SIV. With respect to conventional non-vectored vaccine, wild-type CMV infection has been associated with weaker antibody responses against influenza A vaccination. To uncover effects of pre-existing CMV infection on vaccine efficacy, we performed transcriptomic analysis of PBMCs from RhCMV-seronegative and -seropositive animals before and after RhCMV/SIV vaccination.

We found that RhCMV seropositivity was associated with downregulated matrisome pathways and upregulated T cell response pathways. Vaccination with RhCMV/SIV similarly induced downregulation in matrisome pathways. Interestingly, pathways related to the cell cycle were upregulated only in RhCMV-seronegative animals during vaccination, while metabolism pathways were downregulated only in RhCMV-seropositive animals during vaccination. Similar changes were observed in the transcriptomics of gut tissue from these animals, which additionally correlated with microbiome constituents, suggesting systematic changes in the host response to environmental stimuli. Thus, prior wild-type RhCMV infection qualitatively alters the host's immune response to RhCMV-vectored vaccination.

P_#4 Pre-exposure Neurocognitive Biomarkers Are Associated with Susceptibility to Severe Respiratory Viral Infection

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Cognitive function and other psychological factors (e.g. stress) have long been associated with physiological health. In particular, reaction time, vigilance and processing speed are central to the human ability to perform optimally. Accumulating evidence suggests that intra-individual variability in reaction time (and other cognitive domains) may reflect neurobiological disturbance and have valuable prognostic significance \cite{salthouseImplications2007}. Higher variability of reaction time has been associated with greater mortality over 19-years of follow up in both younger and older adults as well as risk for falls and neurodegenerative disorders (Shipley 2006, Haynes 2017).

Cognitive function is also closely linked to immune health and there is increasing recognition that immune cells play a physiological role in cognition and stress response (Kipnis 2012). For example, T-cells were reported to have a pro-cognitive effect and neurotransmitters involved in the immune response, such as acetylcholine, dopamine and noradrenaline, also play a key role in cognition. In healthy aging adults, elevated concentrations of pro-inflammatory cytokines has been linked to worse cognition (Serre 2020). This relationship is further reflected by the fact that many of the same factors that impair immune response (e.g. sleep deprivation, stress, alcohol consumption, depression, infections) also impair cognitive performance. Furthermore, observational studies suggest that brain health, and its behavioral consequences, could be antecedent risk factors for infection, e.g., a retrospective study of electronic health network data found that people with history of psychiatric illness have a higher risk of being diagnosed with COVID-19.

In this presentation, we will provide data that suggests that pre-exposure neurocognitive biomarkers may have prognostic value in predicting severity of infection of an individual after exposure to a respiratory virus. This data was collected from a longitudinal viral challenge study where human participants were challenged with the common cold midway through the study. We find that the post-exposure viral shedding and symptom severity are highly associated with a novel measure of pre-exposure cognitive performance variability (CPV), defined before viral exposure occurs. Each individual's CPV score is computed from data collected from a repeated NeuroCognitive Performance Test (NCPT) over a 3 day pre-exposure period.

Of the 18 NCPT measures reported by the tests, 6 contribute materially to the CPV score, prospectively differentiating the high from the low shedders. Among these 6 are the 4 clinical measures digSym-time, digSym-correct, trail-time, and reaction-time, commonly used for assessing cognitive executive functioning. CPV is found to be correlated with stress and also with several genes previously reported to be associated with cognitive development and dysfunction.
A perturbation study over the number and timing of NCPT sessions indicates that as few as 5 sessions is sufficient to maintain high association between the pre-exposure CPV score and post-exposure viral shedding, as long as the timing of these sessions is balanced over the three pre-exposure days. Our results suggest that variations in cognitive function are closely related to immunity and susceptibility to severe infection. Further studying these relationships may help us better understand the links between neurocognitive and neuroimmune systems which is timely in this COVID-19 pandemic era.

P_#5 The Relationship between Inflammatory Cytokines and COVID-19 Associated Coagulopathy

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Introduction: Cytokine storm and coagulopathy are two main complications of COVID-19 and are more profound in severe cases. Hyperinflammation and hypercoagulability are two common features, accompanied by a higher rate of morbidity and mortality. This study evaluated the role of inflammatory cytokines in COVID-19 associated Coagulopathy among COVID-19 infected patients at Mulago National Specialized Hospital in Kampala, Uganda.

Methodology: This was an analytical cross-sectional study design. One hundred hospitalized patients diagnosed with a positive SARS-CoV-2 polymerase chain reaction (PCR), were selected for this study. Invitro quantitative determination of inflammatory cytokines and assessment of the coagulation cascade was done.

Results: There was a significant difference of IL-6 concentration between cases (4.7) and controls (0.0), ($p<0.001$). The concentration levels of IL-10 were significantly different between the cases (31.9) and the controls (0.2), ($p<0.001$). There was a significant difference of IFN-γ concentration levels between cases (119.3) and controls (2.7), ($p<0.001$). There was a significant difference in concentration levels of TNF-α between cases (26.3) and controls (0.6), ($p<0.001$). There was a significant difference in prothrombin time for cases (15.2) and controls (13.6), ($p<0.001$). The PT-INR results were significantly different between the cases (1.4) and the control (1.0), ($p<0.001$). There were 87% of the patients with an abnormal result of PT-INR as compared to 2% of those in the control group ($p<0.001$). 85% of cases had a prolonged PT-INR and shortened in 2%. There was no significant difference between aPTT results of COVID-19 patients (31.0) and that of the healthy individuals (29.5), ($p= 0.127$). Furthermore, there was no significant difference between the number of patients with abnormal results of aPTT for COVID-19 patients (12%) and that of the control group (7%), ($p= 0.446$). There was a significant difference in D-dimer results between cases (3.5) and the control group (0.2), ($p<0.001$). There were high concentrations of D-dimers in 71% of the cases and non in the control group ($p<0.001$). There was an association between elevated levels of IL-6 and COVID-19 associated coagulopathy (binary Logistic model: OR =10.76, CI 95% 1.3, 93.0, p-value 0.031) Furthermore, high levels of IL-10 were also associated with coagulopathies in COVID-19 Patients (binary Logistic model: OR =25.5, CI 95% 7.7, 85.2, $p<0.001$). COVID-19 patients with elevated levels of IL-10 were at a higher risk of developing coagulopathies.

Conclusion: There was an association between inflammatory cytokines and COVID-19 associated coagulopathy. Patients with elevated levels of IL-6 and IL-10 had the highest odds of leading to coagulopathies among COVID-19 patients. The prevalence of coagulopathies among COVID-19 patients was 98%.

The most common coagulopathy among COVID-19 patients was the abnormal result of PT-INR. The most affected pathways in the coagulation cascade were the extrinsic and common pathways. Abnormal results of PT/INR indicate that a clotting factor may be missing or defective in the extrinsic and common pathways.

P_#6 Plasma TILRR Protein, Inflammation Cytokines, Risk of HIV Seroconversion and Severe COVID-19 Disease

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TILRR, identified as a co-receptor of IL-1R1 in 2010 and is a variant of FREM1 protein, plays an important role in enhancing IL-1/IL-1R1/TLR-NFκB inflammation responses through its association with IL-1R1. Our studies showed that TILRR is an important modulator of many genes involved in inflammatory responses and promotes inflammatory cytokine secretion by epithelial cells. It promotes immune cell migration through the induction of soluble inflammatory mediators. More recently we discovered that TILRR protein is not only expressed in PBMCs and tissues but also circulates in blood. The levels of plasma TILRR protein among individuals vary greatly, ranging from less than 2.38ng/ml to >5μg/ml, and the levels of plasma TILRR protein were positively correlated with the levels of plasma interleukin-1β (rho: 0.2593, $p<0.0001$), MCP-1 (rho:0.2377, $p<0.0001$), and IL-17A(rho:0.1225, $p=0.0216$). The presence of TILRR protein, an inflammatory response modulator, in blood and its correlation with levels of several proinflammatory cytokines suggest that TILRR not only modulates inflammatory responses in cells and tissues but may also modulate systemic inflammation.

Inflammation is a double-edged sword and underlies a wide variety of physiological and pathophysiological processes. Chronic and persistent inflammation is pathologic and associated with a number of human infectious and chronic diseases, such as HIV, SARS-CoV-2, H1N1, obesity, type 2 diabetes, atherosclerosis, asthma and neurodegenerative diseases. The great variations in the levels of plasma TILRR protein among individuals and its positive correlations with several pro-inflammatory cytokines suggest that individuals with a high level of plasma TILRR protein could be at a higher risk of infection or have more severe responses to some infectious diseases.

Our studies showed that this is indeed the case for HIV-1 infection. We analyzed TILRR protein and proinflammatory cytokines of 941 archived HIV negative plasma samples from 390 women who were HIV negative when they were enrolled in the Pumwani cohort. We find that women with median plasma TILRR protein levels ≥100 ng/ml seroconverted significantly faster than women with plasma TILRR protein levels <100 ng/ml (log-rank=100.124, $p<0.0001$; relative risk=3.72 and odds ratio=15.29). Our pilot study with SARS-CoV-2 infected patients also showed that plasma TILRR protein levels are significantly higher in the COVID-19 ICU patients than its level in the COVID-19 patients with mild symptoms ($P<0.00001$).
Further studies on the influence of high plasma TILRR protein level as a high-risk factor for infectious and chronic diseases would help to develop better diagnostics and better treatment.

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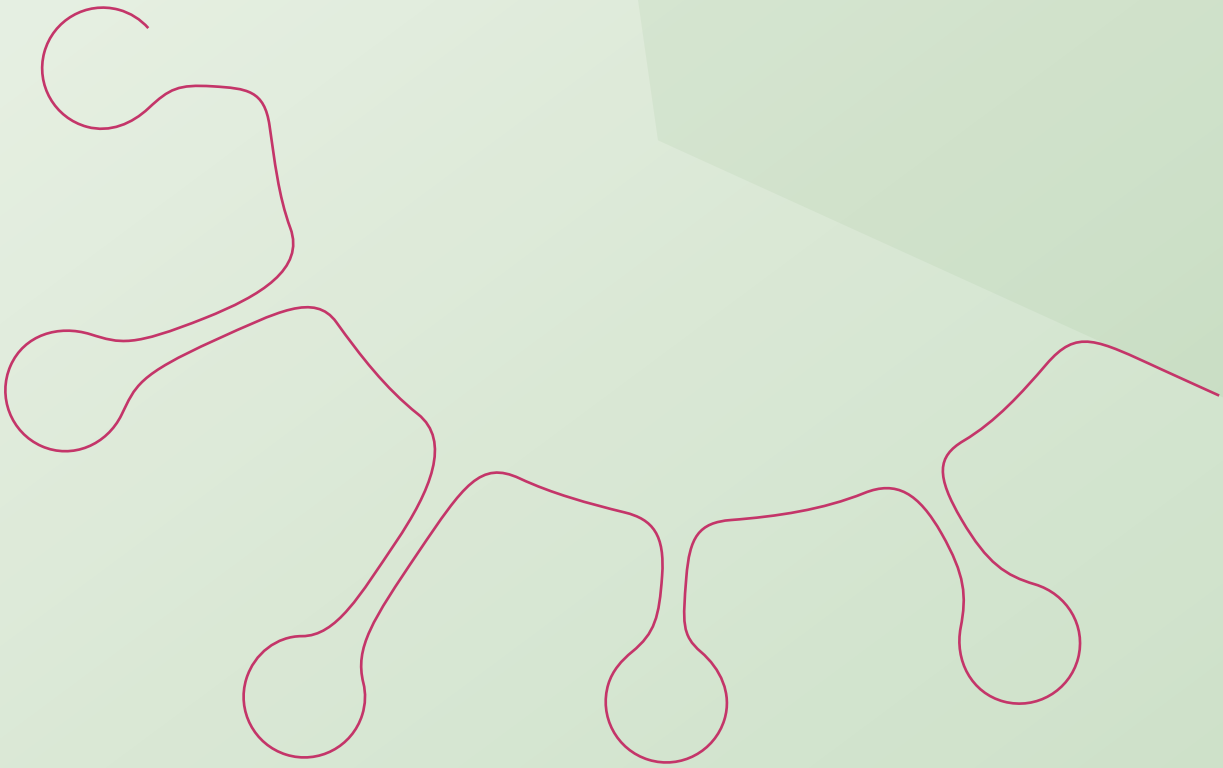

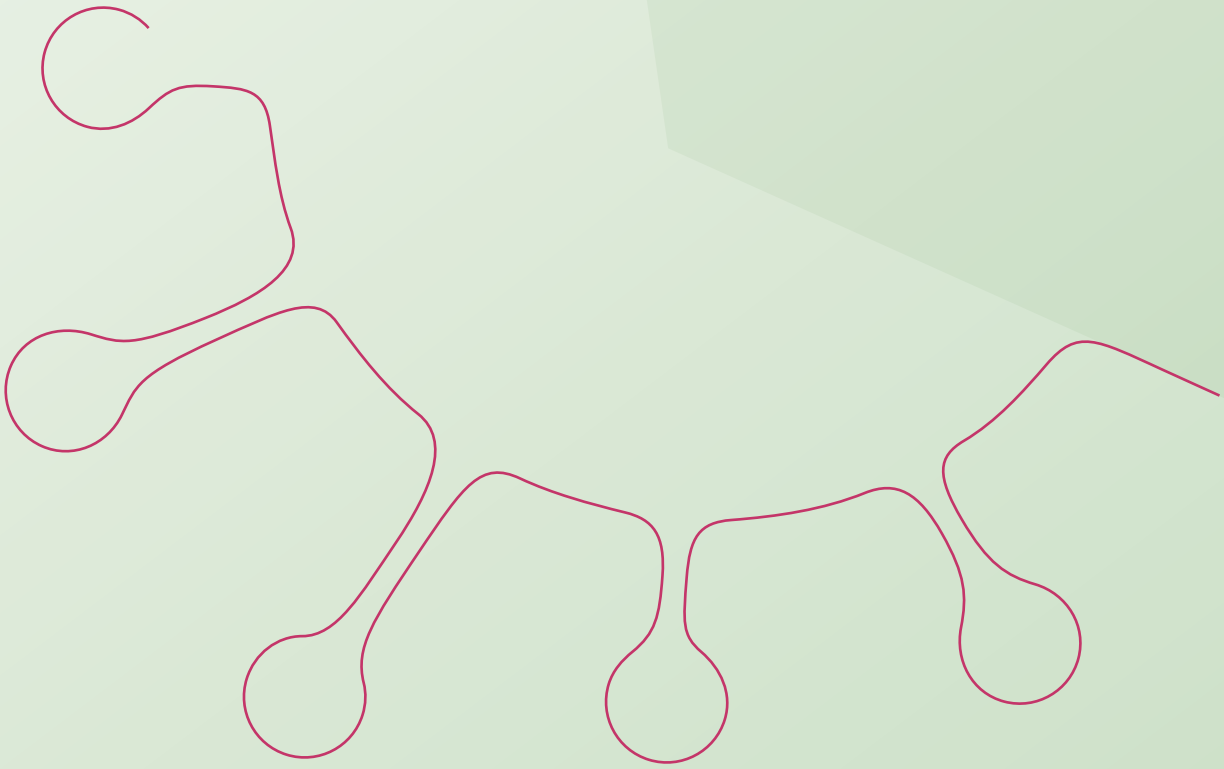

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