Center for Childhood Infections & Vaccines

7th Annual Symposium

December 4th, 2023

1:00 PM – 6:00 PM

Health Sciences Research Building (HSRB-II)

EMORY UNIVERSITY · Children's Healthcare of Atlanta · MOREHOUSE SCHOOL OF MEDICINE · Georgia Institute of Technology

Table of Contents

Welcome

Dear Colleagues,

We welcome you to the 7th Annual Center for Childhood Infections and Vaccines (CCIV) Symposium. We are so excited to have you here with us, and we look forward to an informative and engaging day.

This year's symposium features 27 abstracts from our talented faculty, staff, trainees, and students. We have a packed agenda of presentations exploring infectious diseases and vaccine research happening at Emory University and Children's Healthcare of Atlanta.

We are delighted to have Dr. Theresa Alenghat and Dr. Paul Thomas as our keynote speakers this year. Dr. Alenghat is an Associate Professor of Pediatrics at the University of Cincinnati and Cincinnati Children's Hospital. Her research focus is on epithelial and immune cell homeostasis in the context of intestinal health and disease. Dr. Paul Thomas joins us from St. Jude Children's Research Hospital where he is a faculty member in the Department of Immunology.

Two renowned Rollins School of Public Health investigators also join us, Dr. Cynthia Whitney a physician-scientist and Executive Director of the Child Health and Mortality Prevention Surveillance Network (CHAMPS) , and Dr. Natalie Dean, an Assistant Professor of Biostatistics, Bioinformatics, and Epidemiology. Dr. Dean also serves as Co-Director of the Emory Alliance for Vaccine Epidemiology.

We appreciate you taking the time to attend the symposium.

Sincerely,

Ann Chahroudi, MD, PhD
Symposium Co-Chair
Associate Division Chief for Research, Pediatric Infectious Diseases
Professor of Pediatrics
Director, Emory + Children's Center for Childhood Infections & Vaccines
Emory University School of Medicine

Jens Wrammert, PhD
Symposium Co-Chair
Associate Professor,
Emory Vaccine Center
Associate Professor, Department of Microbiology and Immunology,
Emory University School of Medicine
Investigator, Emory Center for AIDS Research
Emory University

Cassie Grimsley Ackerley, MD
Symposium Co-Chair
Assistant Professor of Medicine and Pediatrics, Division of Infectious Diseases and Pediatric Infectious Diseases
Emory University School of Medicine

Our Keynote Speakers

Theresa Alenghat, VMD, PhD
Associate Professor of Pediatrics
Cincinnati Children's Hospital
University of Cincinnati

Dr. Theresa Alenghat investigates epithelial and immune cell homeostasis in the context of intestinal health and disease. The goals of her lab are to provide insight into molecular mechanisms, including epigenomic pathways, that mediate the host-microbiota relationship.

Dr. Alenghat aims to determine how this level of regulation affects innate immunity, enteric infections in neonates and children, and chronic conditions such as inflammatory bowel disease.

Paul G. Thomas, PhD
Faculty, Department of Immunology
St. Jude Children's Research Hospital

Following his postdoctoral training with Nobel laureate Dr. Peter Doherty, Dr. Paul G. Thomas joined the faculty of the Department of Immunology at St. Jude Children's Research Hospital in 2009. His work has been instrumental in generating a new understanding of T cell receptor specificity and defining key elements of innate and adaptive immune responses that determine clinical outcomes of viral infections.

Dr. Thomas leads several complex institutional programs including human influenza surveillance efforts and virtual repository development, and currently serves as PI for the 7-year, 12-institution DIVINCI consortium. In addition to his scientific achievements, Dr. Thomas is widely regarded for his mentorship and empowerment of junior scientists.

Our Internal Guest Speakers

Natalie Dean, PhD

Assistant Professor, Biostatistics, Bioinformatics, and Epidemiology
Rollins School of Public Health
Co-Director, Emory Alliance for Vaccine Epidemiology (EAVE)
Emory University

Dr. Natalie Dean is an Assistant Professor in the Department of Biostatistics and Bioinformatics at Emory's Rollins School of Public Health. She received her PhD in Biostatistics from Harvard University and previously worked as a consultant for the WHO's HIV Department and as a faculty at the University of Florida. Her primary research area is infectious disease epidemiology, with a focus on innovative study designs for evaluating vaccines during public health emergencies. She is co-director of the Emory Alliance for Vaccine Epidemiology and a PI of Emory's CDC-funded Center for Innovation in Outbreak Analytics. During the COVID-19 pandemic, she was active in public engagement, with authored pieces in the Washington Post, New York Times, and other outlets. She received the 2024 Communications Award from the Joint Policy Board for Mathematics.

Cynthia Whitney, MD, MPH

Professor, Global Health, Rollins School of Public Health
Executive Director and Principal Investigator, Child Health and Mortality Prevention Surveillance (CHAMPS)
Emory University

Dr. Whitney became the Principal Investigator and Executive Director of the Child Health and Mortality Prevention Surveillance (CHAMPS) program in 2020. CHAMPS is a large multicounty program operating in 7 countries that generates accurate information on causes of child mortality using cutting-edge diagnostic techniques; CHAMPS is based in the Emory Global Health Institute. Dr. Whitney became a Professor at Emory University in the Rollins School of Public Health, Hubert Department of Global Health in 2019. Before that, she was Chief of the Respiratory Diseases Branch in the Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, and had worked for 25 years at the U.S. Centers for Disease Control and Prevention in Atlanta, Georgia, USA.

Schedule

Time/Room	Presentation
1:00 – 1:50 PM	**Keynote Presentation**
N100	*"Regulation of the Host-Microbiota Relationship"*

Theresa Alenghat, VMD, PhD
Associate Professor
Department of Pediatrics
University of Cincinnati
Cincinnati Children's Hospital

1:50 – 2:10 PM	**Internal Speaker**
N100	*"What infectious diseases cause stillbirths and child deaths in high-mortality settings? Results from Child Health and Mortality Prevention Surveillance (CHAMPS)"*

Cynthia Whitney, MD, MPH
Professor, Global Health, Rollins School of Public Health
Executive Director and Principal Investigator, Child Health and Mortality Prevention Surveillance (CHAMPS)
Emory University

2:10 – 2:20 PM	**Break**
2:20 – 3:10 PM	**Breakout Sessions**
N100	*Session 1: Inclusive Leadership and Conflict Management*

Moderators:

Andi Shane, MD, MPH, MSc
Professor of Pediatrics,
Division of Infectious Diseases
Adjunct Professor of Global Health, Hubert Department of Global Health
Marcus Professor of Hospital Epidemiology and Infection Prevention
Emory University

Andres Camacho-Gonzalez, MD, MSc
Associate Professor of Pediatrics,
Division of Infectious Diseases
Director, Pediatric HIV Clinical Trials Unit
Emory University

Paul G. Thomas, PhD
Faculty, Department of Immunology
St. Jude Children's Research Hospital

N147	*Session 2: Research in the Virtual Environment: Delivering Engaging Presentations and Building Collaborations*

Moderators:

Mehul Suthar, PhD
Associate Professor, Emory Vaccine Center
Associate Professor, Department of Pediatrics
Emory University

Christina Rostad, MD
Associate Professor of Pediatrics,
Division of Infectious Diseases
Emory University

Theresa Alenghat, VMD, PhD
Associate Professor
Department of Pediatrics
University of Cincinnati
Cincinnati Children's Hospital

N257 *Session 3: Sustainability in Bench Science and Clinical Research*

Moderators:

Preeti Jaggi, MD
Professor of Pediatrics, Division of Infectious Diseases
Emory University

Justin Bright
Sustainability & Social Justice Fellow, Office of Sustainability Initiatives
Emory University

3:10 – 3:20 PM **Break**

3:20 – 3:40 PM **Internal Speaker**

N100 *"Considerations for the Test Negative Design for Evaluating Vaccine Effectiveness"*

Natalie Dean, PhD
Assistant Professor, Biostatistics, Bioinformatics, and Epidemiology
Rollins School of Public Health
Co-Director, Emory Alliance for Vaccine Epidemiology (EAVE)
Emory University

3:40 – 3:55 PM **Oral Abstract Presentation #1**

N100 *"Durable Antibody Responses After SARS-CoV-2 Infection in Infants/Young Children"*

Devyani Joshi, PhD
Postdoctoral Fellow, Wrammert Lab
Emory University

3:55 – 4:10 PM **Oral Abstract Presentation #2**

N100 *"The Impact of Implementing Opt-Out HIV Screening in Adolescents Presenting in the Pediatric Emergency Department in Metro Atlanta"*

Mark Griffiths, MD
Associate Professor of Pediatrics and Emergency Medicine
Emory University

4:10 – 4:25 PM **Oral Abstract Presentation #3**

N100 *"Cyclosporines Promote Virus Entry by Modulating Cellular Trafficking of IFITM Proteins"*

David Prikryl, PhD
Postdoctoral Fellow, Melikian Lab
Emory University

4:25 – 4:30 PM **Break**

4:30 – 5:20 PM	Keynote Presentation

N100

"Predicting Influenza Protection and Pathology from Baseline Immune Profiles"

Paul G. Thomas, PhD
Member, St. Jude Faculty
St. Jude Children's Research Hospital

5:20 PM	Poster Session / Reception

Atrium

1. *Correlate of protection from a longitudinal cohort of Chilean people with COVID-19.*
   Maria Avendano, MS, PhD(c)
2. *Investigating the correlation between plasma cytokines and levels of virus rebound post-ATI in SIVmac251-infected infant rhesus macaques.*
   Tehillah Chinunga, BS, PhD(c)
3. *Association of SARS-CoV-2 variants with COVID-19 clinical features and outcomes in adults hospitalized with acute respiratory infection.*
   Jong-Ha Choi, BS
4. *Durability of antibody responses to RSV in older adults following hospitalization for acute respiratory infection.*
   Caroline Ciric, BS
5. *Imaging of Single SARS-COV-2 Pseudovirus Entry in Living Cells.*
   Monica Cortez, BS, PhD(c)
6. *Impact of IFNα on hepatocyte proteome in chronically HBV infected primary human hepatocytes.*
   Georgios Dangas, BS
7. *Determining how release of surface-anchored M protein induces pathological inflammation in Streptococcal infections.*
   Ananya Dash, MS, PhD(c)
8. *Social Risk Factors for RSV-related Hospitalizations in Adults ≥50 years of age.*
   Khalel De Castro, BS
9. *Single cell RNA-Sequencing reveals neurological perturbations in postnatally ZIKV-infected infant rhesus macaques.*
   Venkata Edara, PhD
10. *Epidemiology, Clinical Features, and Outcomes of Rhinovirus/Enterovirus in Older Adults Hospitalized with Acute Respiratory Infections and those with CHF and COPD Exacerbations.*
    Gabby Ess
11. *Targeting SIV viral reservoir with early ART in combination with immune interventions in infant rhesus macaques.*
    Omotayo Farinre, PhD
12. *Th2 Immune Responses Modulates the Anti-viral and Anti-inflammatory Activity During Mild COVID-19 Disease.*
    Tamara Garcia, PhD

13. *Virus-like particles as an RSV vaccine.*
    Binh Ha, PhD

14. *SARS-CoV-2 IgG Antibodies in Vaccinated and Non-vaccinated Pediatric Healthcare Workers: A Longitudinal Surveillance Study.*
    Dunia Hatabah, MD

15. *A long-term 3D cell culture model utilizing murine and de novo HBV infection approaches.*
    Christopher Jones, PhD

16. *AAV9-Delivered eCD4 as Part of a "Shock and Kill" Cure Strategy in SIV-Infected Infant Macaques.*
    Alexis King, BS

17. *Clinical Features and Outcomes of Children vs. Adults Hospitalized with Coronavirus Disease 2019 (COVID-19).*
    Grace Li, BS

18. *Microbiota-derived Metabolites modulate COVID-19 Vaccine-induced Humoral immune responses in Down syndrome individuals.*
    Manini Majithia

19. *Delayed Viral Rebound Following Antibody Administration in Infant Macaques.*
    Jenna Powers, BS, MD(c)

20. *Novel Immunomodulator to Address Immune Dysregulation and Viral Comorbidities in Children with Kawasaki Disease.*
    Guadalupe Quinones, BS

21. *Jak Inhibitors for Treatment, Prevention or Reversal of Sepsis and Related Comorbidities.*
    Sebastian Roa, BA

22. *Disrupting SIV Reservoir Seeding by Targeting Stemness Pathways in Rhesus Macaques.*
    Inna Ruiz-Salinas, PhD

23. *Characterizing spatio-temporal interactions of HIV-1 capsid with host factors.*
    Sara Sagadiev, BS, PhD(c)

24. *Clinical features, risk factors, and outcomes of COVID-19 in Immunocompromised adults hospitalized with acute respiratory infection.*
    Elizabeth Grace Taylor, BS

Durable Antibody Responses after SARS-CoV-2 Infection in Infants/Young Children

Authors: Joshi, Devyani; Nyhoff, Lindsay; Zarnitsyna, Veronika; Moreno, Alberto; Manning, Kelly; Linderman, Susanne; Burrell, Allison; Stephens, Kathy; Norwood, Carson; Mantus, Grace; Ahmed, Rafi; Anderson, Evan; Staat, Mary; Suthar, Mehul; Wrammert, Jens

Presenting Author: Devyani Joshi, PhD

Background: As SARS-CoV-2 establishes as an endemic infection, exposure in early childhood may become routine. Therefore, it is critical to evaluate the magnitude and durability of immunity following early life infection, which may help to predict whether early immunity is sufficient to prevent severe disease later. Additionally, comparison of immune response to infection in infants/young children and adults provides essential context for effective scheduling of vaccinations in view of continuously emerging variants. Infants/young children in the study were followed with weekly nasal swabs and timely blood collections beginning soon after birth, allowing to identify symptomatic and asymptomatic respiratory infections and evaluation of the immune response both prior to and longitudinally after first SARS-CoV-2 infection. Additionally, our cohort of mild/moderately infected adult COVID-19 patients enables a direct comparison of the infection-induced immune response in these age groups.

Methods: The IgG, IgG subclasses, IgA, and IgM binding antibody responses to different coronaviruses and SARS-CoV-2 variants were measured using multiplex electrochemiluminescence (ECLIA) immunoassay by Mesoscale Discovery (MSD). The neutralizing antibody responses to SARS-CoV-2 variants were evaluated using Focus reduction neutralization (FRNT) assay.

Results: Antibody responses to SARS-CoV-2 spike antigens in infants/young children peaked approximately 30 days after infection and were maintained up to 500 days with little apparent decay. While the magnitude of humoral responses was similar to adults, both binding and neutralization titers to WT SARS-CoV-2 were significantly more durable in infants/young children, with spike and RBD IgG antibody half-life nearly 4X as long as in adults. IgG subclass analysis revealed that while IgG1 dominated the response in both groups, IgG3 was more common in adults and IgG2 in infants/young children. SARS-CoV-2 infection resulted in increased antibody responses to previous epidemic coronaviruses, SARS-CoV and MERS-CoV, representing cross-reactive antibodies directed to spike epitopes which are largely conserved between these coronaviruses.

Conclusion: Infants/young children produce more durable antibody responses after SARS-CoV-2 infection than adults. While mechanistic explanation of our findings is currently under investigation, it could be attributed to different immunological milieus during induction of responses or that the previous microbial exposure might affect the ability of bone marrow to support long lived plasma cells.

The Impact of Implementing Opt-Out HIV Screening in Adolescents Presenting in the Pediatric Emergency Department in Metro Atlanta

Authors: François, Sandy; Griffiths, Mark A.; Cameron, Melissa N.; Daniel, Jordan E.; Wynn, Bridget A.; Brown, Sara P.; Thompson, Sarah; Carter, Rebeka G.; DeNaples, Kelly; Kandaswamy, Swaminathan; Orenstein, Evan; Camacho-González, Andrés; Morris, Claudia R. and Middlebrooks, Lauren.

Presenting Author: Mark A. Griffiths, MD

The Centers for Disease Control and Prevention recommends HIV screening for all patients ≥13 years. Parts of Metro Atlanta have HIV positive rates at 8-times the national average. Adolescents are the least likely group to know their HIV status, have the lowest rate of linkage to care, and viral suppression. Children's Healthcare of Atlanta (Children's) implemented an opt-out HIV testing program in its emergency departments (ED) for patients ≥13 years undergoing venipuncture in 2 of their 3 sites. The objective is to increase testing in adolescents leading to earlier HIV diagnosis and linkage-to-care.

Children's electronic medical record EPIC and its population discovery tool were used to compare testing volumes of 13–24-year-olds, 15 weeks pre and post the July 6th, 2023, clinical implementation. Data for all 3 sites was reviewed but only 2 sites received educational promotion. Results were cross-referenced to determine newly diagnosed adolescents living with HIV (ALHIV) from known positives. The data was compared using descriptive statistics.

A total of 461 patients were tested pre-implementation, 311(67%) girls and 150(33%) boys. Two new ALHIV; 1 coinfected with syphilis, median age was 17, both assigned male at birth. After 15 weeks of implementation, 654 patients were tested: 457(70%) girls and 197(30%) boys. Five new ALHIV; the median age was 16, assignment at birth was (4) male, 2 coinfected with syphilis, and (1) female. This demonstrates an overall positivity rate of nearly 1% and 1 in 49 boys tested positive. At sites receiving education for 1 and 3 months, testing increased by 25% and 68% respectively vs 20% at our site with no education. The initiative showed a 150% increase in newly diagnosed cases; all were linked to care within 1-48 days.

Atlanta remains a hotspot for new HIV cases. Five new cases in 15 weeks highlights the importance of universal HIV testing of adolescents and reflects a public health crisis. The new initiative significantly increased HIV screening and will likely identify ALHIV at an earlier stage of infection, facilitating timely access to medical care. This can lead to improved clinical and immunological outcomes and a reduced risk of secondary transmission.

Cyclosporines Promote Virus Entry by Modulating Cellular Trafficking of IFITM Proteins

Authors: Prikryl, David; Marin, Mariana; Desai, Tanay M.; Du, Yuhong; Fu, Haian; and Melikyan, Gregory B.

Presenting Author: David Prikryl, PhD

Interferon-induced transmembrane proteins (IFITMs) are host factors that block entry of diverse enveloped viruses. The range of restricted viruses depends on the IFITMs' subcellular localization. IFITM1 located at the plasma membrane prevents entry of viruses that are thought to fuse with the plasma membrane, while IFITM2 and IFITM3 concentrate in late endosomes and block infection of viruses entering from intracellular compartments. Through high-throughput screening of small-molecule compounds, we found that cyclosporine A (CsA) rescues the Influenza A virus fusion with cells overexpressing IFITM3. Importantly, CsA induces rapid relocalization of IFITM3 to the perinuclear area, without causing significant degradation of this protein. Immunostaining experiments revealed that CsA mediates a nearly complete IFITM1 and IFITM3 redistribution to the Golgi apparatus. In line with previous reports, prolonged CsA treatment induced IFITM1 and IFITM3 degradation in cells expressing low endogenous levels of these proteins, whereas degradation was not detected in cells overexpressing IFITM3. Moreover, CsA pretreatment led to a marked redistribution of IFITMs to the Golgi within an hour, without causing notable degradation in cells expressing low levels of these proteins. These results highlight the importance of regulation of IFITM trafficking and reveal a novel mechanism of cyclosporine-mediated modulation of antiviral activity of these proteins. This work was supported by the NIH R01 AI135806 grant to GBM.

Poster Number: 1

Correlate of protection from a longitudinal cohort of Chilean people with COVID-19

Authors: M. J. Avendaño. X.Tong. R. P. McNamara. E. F. Serrano T. García-Salum. C. Pardo-Roa. J. Levican, E. Poblete E. Salinas, G. Valenzuela, A. Riquelme, G. Alterm, and R. A. Medina.

Presenting Author: Maria Avendaño, MS, PhD(c)

Current COVID-19 vaccines employ a traditional approach, focusing on inducing neutralizing antibodies against the virus. However, neutralizing activity is not the sole function that can protect against infection. Various effector functions such as cytotoxicity, cellular phagocytosis, and complement-dependent antibody deposition have been associated with protection against viral infections. Despite progress in understanding the immune response to SARS-CoV-2, defining the functional characteristics necessary for antibody-mediated protection against infection or severe disease remains elusive. To analyze the functional humoral immune response in-depth, we conducted systemic serology analysis of the humoral immune response against SARS-CoV-2 in both, ambulatory and hospitalized COVID-19 patients during the first 4 weeks since symptom onset. We observed distinct humoral trajectories between groups, considering both antigen and antibody dynamics. Hospitalized COVID-19 patients exhibited a relatively robust humoral response starting from the second week after symptom onset. By the third week, elevated antibody levels were detected for all the viral antigens (Spike, RBD, N, NTD, S1, and S2) and isotypes (IgG1-4, IgM, and IgA), except for IgG2 and IgG4 subclasses targeting the NTD region. Hospitalized individuals exhibited a rapid and highly functional humoral evolution, showcasing elevated overall binding antibody levels, neutralizing activity, and ADCP. In contrast, ambulatory individuals demonstrated an increase in FcγR2a-specific antibody responses targeting RBD and S2. Collectively, this work emphasizes the development of a specific but moderate humoral response in ambulatory individuals compared to the robust but non-specific humoral response seen in hospitalized individuals, which might explain disease severity during the course of infection.

Poster Number: 2

Investigating the Correlation Between Plasma Cytokines and Levels of Virus Rebound Post-ATI in SIVmac251-infected Infant Rhesus Macaques

Authors: Chinunga, Tehillah; Coirada, Fernanda; Bruno, Fernanda; Del Rio Estrada, Perla; Bricker, Katherine; Chahroudi, Ann and Ribeiro, Susan.

Presenting Author: Tehillah Chinunga, BS, PhD(c)

Background: During HIV or if modeled in non-human primates (NHPs) SIV infection, in addition to viral replication and CD4+ T cell depletion, inflammation persists. Anti-retroviral therapy (ART) suppresses viral replication, however, upon analytical treatment interruption (ATI), virus rebound occurs. Despite known effects of ART in lowering inflammation, the role of cytokines that contribute to persisting inflammation and their correlation with viral rebound dynamics, is yet to be determined. Moreover, literature on the cytokine profile of children living with HIV (CLWH) lacks an understanding of a mechanism by which viral rebound dynamics occur between high vs low rebounders during ATI.

Methods: We determined the plasma cytokine levels in SIVmac251-infected infant rhesus macaques by using the Mesoscale discovery (MSD) assay. Twenty-nine 29 cytokines (IFN-γ, IL-10, IL-12p70, IL-17A, IL-1β, IL-2, IL-4, IL-6, IL-8, TNF-α, CTACK, Fractalkine, ITAC, IFN-α-2a, IL-15, IL-18, IL-7, IP-10, MCP-1, MIP-1α, TGF-β1, TGF-β2, TGF-β3, GRO-α, IL-22, IL-9, MCP-2, MIP-3α and MIP-3β) were measured in plasma from eight SIVmac251-infected infant macaques, infected at 4 weeks old, at five-time points; 1-6 weeks post infection (wpi) pre- and post-ART, 62wpi on ART, 67wpi post-ART and post-ATI and 82-83 wpi late ATI. First we determined the dynamics of these cytokines over time (One-Way ANOVA across time points); second we determined which cytokines, early upon infection were associated with the viremia levels post-ATI (82wpi – Spearman correlation cytokines vs viral load 82wpi); and lastly, we divided the animals in lower and higher rebounders based on the viremia, and compared the cytokine levels between these 2 groups over time (unpaired t.test). Low viremia (low rebound) was defined as plasma viral load below 2000copies/mL and high viremia (high rebound) as greater than 2000 copies/mL.

Results and Conclusions: Pro-inflammatory cytokines such as CTACK, MCP-1, IP-10 and MIP-3β were upregulated early upon infection and IL-12p70 later post-infection more prominently during ATI. The Spearman correlation identified 7 cytokines significantly correlated with plasma viral load. Among the cytokines associated with high rebounders were MCP-1, IL-6 and MIP-3β; while pre-ATI IL-8, GRO-α, IP-10 and CTACK were prevalent in lower rebounders. This data suggests a role of cell trafficking in viral replication post-ATI.

Poster Number: 3

Association of SARS-CoV-2 variants with COVID-19 clinical features and outcomes in adults hospitalized with acute respiratory infection

Authors: Perez, Maria; Tippett, Ashley; Registre, Ludy; Hussaini, Laila; Reese, Olivia; Ciric, Caroline; Choi, Chris; Taylor, Elizabeth; Li, Wensheng; Hsiao, Hui-Mien; Stephens, Kathy; Gibson, Theda; Hubler, Robin; Lopman, Ben; Rouphael, Nadine; Kamidani, Satoshi; Anderson, Evan; Rostad, Christina; Wagonner, Jesse; and Piantadosi, Anne.

Presenting Author: Jong-Ha Choi, BS

Background: Data is needed to describe the association of clinical features and outcomes with SARS-CoV-2 variants. We aimed to compare variants for differences in symptoms and outcomes among adults hospitalized with COVID-19 acute respiratory infection (ARI).

Methods: From May 2021 to August 2022, we enrolled adults ≥18 years of age hospitalized with ARI at two Emory University hospitals. Demographic and clinical information was obtained from participant interviews and medical chart abstractions. Enrolled patients provided nasopharyngeal and oropharyngeal swabs and standard-of-care specimens. Samples which tested positive for SARS-CoV-2 by molecular testing were subjected to SARS-CoV-2 targeted spike SNP PCR and viral genome sequencing to determine a variant. Statistical analysis was performed using SAS version 9.4. Bivariate analysis was conducted to compare characteristics, and stepwise and standardized adjusted odds ratios were calculated.

Results: Of 1676 enrolled participants, 850 tested positive for SARS-CoV-2, of whom 594 had a variant identified by either SNP PCR or full genome sequencing. The distribution of variants among these cases were as follows: 39 Alpha variant, 2 Beta variant, 307 Delta variant, 9 Gamma variant, 5 Mu variant, and 230 with Omicron variant. When analysis was limited to participants with Alpha, Delta, or Omicron, those with Omicron were significantly older, more commonly white, female, and more commonly had underlying comorbidities. Participants with Omicron more commonly had sore throat and abdominal pain, but less commonly had fever, diarrhea, anosmia, ageusia, or shortness of breath. They were more commonly partially or fully vaccinated, and the majority of Omicron infections were breakthrough infections after vaccination. Most clinical outcomes were better for those with Omicron infections, while participants with Delta had the highest proportion of radiographic pneumonia, mechanical ventilation, and death.

Conclusions: SARS-CoV-2 variants were associated with distinct clinical characteristics and outcomes, and the Delta variant was associated with the highest frequency of pneumonia, mechanical ventilation, and death.

Poster Number: 4

Durability of antibody responses to RSV in older adults following hospitalization for acute respiratory infection

Authors: Ciric, Caroline; Ha, Binh; Tippet, Ashley; Hussaini, Laila; Salazar, Luis; Reese, Olivia; Li, Wensheng; Hsiao, Hui-men; Gibson, Theda; Begier, Elizabeth; Hubler, Robin; Liu, Qing; Gessner, Brad; Lopman, Ben; Rouphael, Nadine; Kamidani, Satoshi; Anderson, Evan; Anderson, Larry; and Rostad, Christina.

Presenting Author: Caroline Ciric, BS

Introduction: Respiratory syncytial virus (RSV) is a common viral pathogen identified in older adults with acute respiratory infections (ARIs). Data describing the durability of immune responses to RSV are limited but suggest responses may be short-lived. In this study, we assessed longitudinal antibody responses following RSV-associated hospitalization for 3 years.

Methods: Between September 2018 and March 2020, adults ≥50 years of age hospitalized with ARI at two Emory University hospitals who had a positive RSV test via PCR were enrolled. A nasopharyngeal swab, oropharyngeal swab, and 10mL blood were collected at enrollment (V1), 30 days after enrollment (V2), and in the 4 weeks prior to the start of the influenza season(s) for three years after enrollment (1 yr 2 yr, 3 yr). Syndrome-positive, RSV-negative controls were also enrolled. Serum samples were analyzed for RSV A/B lysate antigen by enzyme-linked immunosorbent assay (ELISA) and end-point titers were interpolated to a standard curve. Geometric mean titers (GMTs) were calculated, and statistical comparisons of log-transformed titers were performed using a mixed effects model in GraphPad Prism v9.0.

Results: Of the 30 enrolled participants who completed follow-up, there were 20 RSV-positive cases and 10 controls (Table 1). Of these, 22 (73%) were female, 22 (73%) Black, and 30 (100%) non-Hispanic ethnicity. Baseline demographics were similar in cases and controls. However, being immunocompromised was more common in cases, and heart disease was more common in controls. Peak antibody titers were observed in cases at V2 (IgG GMT 642,685), and these declined non-significantly prior to the start of the next RSV season (IgG GMT 396,059, P=0.1306) (Figure 1). Titers then declined significantly 2 years (IgG GMT 134,836, P=0.0003) and 3 years (IgG GMT 117,729, P<0.0001) after infection. RSV IgG GMTs were not significantly different between cases and controls at any time point. Results were similar when immunocompromised participants were excluded from the analysis.

Conclusions: RSV antibody responses peaked in early convalescence and persisted for 3 years after RSV-associated hospitalization. Antibody titers were similarly elevated in cases and controls, indicating the durability of RSV antibodies in older adults.

Poster Number: 5

Imaging of Single SARS-COV-2 Pseudovirus Entry in Living Cells

Authors: Monica K. Cortez, You Zhang, Mariana Marin, and Gregory B. Melikyan.

Presenting Author: Monica Cortez, BS, PhD(c)

SARS-CoV-2 infection is initiated by fusion of the viral envelope with the cell membrane, which is mediated by the viral Spike (S) glycoprotein. After binding to the cell surface receptor, angiotensin converting enzyme 2 (ACE2), S must be cleaved by host proteases to trigger fusion of viral and host membranes for successful delivery of the viral genome into the host cytoplasm. This occurs either at the plasma membrane, by transmembrane serine protease 2 (TMPRSS2), or within endosomes, by cysteine protease cathepsins L/B (CatL/B). Since it has been shown that both entry pathways are used by SARS-CoV-2, we hypothesized that the availability of surface proteases, such as TMPRSS2, and the rate of virus uptake are the main determinants of the dominant entry pathway of this virus. We employed a bulk virus-cell fusion assay to assess sensitivity to inhibitors of requisite surface and endosomal proteases and live-cell imaging of dual- and triple-fluorescent labeled virus particles to pinpoint the entry sites of SARS-CoV-2. For visualizing single pseudovirus fusion in the live cell setting, viral particles were labeled with membrane and content markers, including pH-sensitive fluorescent proteins that report acidification of the virion interior; we show that S-pseudovirus entry occurs from both the plasma membrane and endosomal pathways. Our results imply that the preferred entry sites are determined by the presence of the surface protease TMPRSS2, which accelerates SARS-CoV-2 fusion, thereby favoring entry from the plasma membrane. This work was supported by the NIH R01 AI053668 grant to GBM.

Poster Number: 6

Impact of IFNα on hepatocyte proteome in chronically HBV infected primary human hepatocytes

Authors: Dangas, George; Ogata, Kosuke; Seifert, Leon; Athanasiadis, Antonis; Yu, Yingpu; Jones, Christopher; Shue, Taylor; Jiang, Alfred; Zou, Chenhui; Quirk, Corrine; Schneider, William; Rice, Charles; de Jong, Ype; and Michailidis, Lefteris.

Presenting Author: Georgios Dangas, BS

Background: HBV pre-core mutations arise during chronic HBV infection and impact HBV pathogenesis and treatment responses. Launching infectious HBV from DNA remains a bottleneck. Studies focusing on HBV pre-core mutations have largely relied on clinical isolates without isogenic controls or DNA transfection of hepatoma cells over primary human hepatocytes (PHH). Studying pre-core mutations is further limited by the need for very high inocula to establish in vitro infections, limited viral spread, and challenges maintaining PHH functions in culture. Therefore, these systems only partially recapitulate chronic HBV, including cccDNA copy numbers.

Methods: To model chronic HBV in vitro we developed a system based on culturing mouse-passaged (mp)PHH isolated from HBV-infected humanized mice. These HBV-mpPHH can be maintained in culture for several weeks. A major advantage is that nearly all hepatocytes are infected and contain high levels of cccDNA. In addition, we established an innovative method to generate HBV stocks of different sequences including HBV with pre-core mutations. This method relies on transplanting transfected/infected mpPHH in already humanized mice and passaging the virus-containing sera into new mice. We used the HBV-mpPHH as a tool to compare wild-type and isogenic pre-core mutant HBV in terms of the impact on hepatocyte proteome and response to IFNα treatment.

Results: To our surprise, we identified very distinct protein expression patterns with 2,860 differentially expressed proteins between wild-type and pre-core HBV-mpPHH. While these studies are ongoing, most of the differences were found to be relevant to lipid and mRNA metabolic processes. In addition, treatment with IFNα revealed both induced and suppressed proteins. Among these differentially expressed proteins, we highlight here 42 proteins that are downregulated in the presence of HBV.

Conclusions: Together, these data are expected to identify host factors that have a crucial role in the context of HBV pre-core mutations and response to IFNα treatment. Moreover, the in vitro systems we developed together with CRISPR-based applications and systems biology analyses can be extended in other hepatotropic viruses.

Poster Number: 7

Determining how release of surface-anchored M protein induces pathological inflammation in Streptococcal infections

Authors: Dash, Ananya; and LaRock, Christopher

Presenting Author: Ananya Dash, MS, PhD(c)

M protein is one of the most abundant surface virulence factors of group A Streptococcus (GAS). This surface-anchored M protein interacts with multiple host factors to mediate bacterial attachment and prevent clearance of GAS. However, M protein is observed free from GAS in patients with necrotizing fasciitis and streptococcal toxic shock syndrome. Injection of M protein into mice induces severe lung damage caused by dysregulated neutrophils that undergo degranulation and can be reversed by neutrophil depletion. These studies suggest that M protein can contribute to pathological inflammation in severe streptococcal infections. Our preliminary data shows that GAS protease, SpeB cleaves M1 allele of M protein into a nearly full-length fragment. Based on substrate specificity of SpeB and M1 protein structure, target sites for cleavage were identified. Since there are more than 220 distinct M proteins with specific clinical outcomes associated with them, whether M protein release across different GAS serotypes has a critical role in post-infection sequelae of GAS remains unknown. Our study currently focuses on the M1 serotype, historically known for its prevalence and association with severe infections. To study the effect of M protein in vivo, GAS will be engineered to have a surface-locked protein by introducing mutations into the SpeB target sites. By also designing a GAS strain to express an M protein that cannot be anchored to the cell wall, M protein will be constitutively released. In a mouse intraperitoneal infection model, I will examine bacterial survival, immune cell activation and inflammatory signaling to determine whether M protein release contributes to pathogenesis. Our study can provide insights into the design of novel host-directed therapeutic strategies to target complications of GAS infections.

Poster Number: 8

Social Risk Factors for RSV-related Hospitalizations in Adults ≥50 years of age

Authors: De Castro, Khalel; Tippett, Ashley; Hussaini, Laila; Salazar, Luis; Reese, Olivia; Ciric, Caroline; Li, Wensheng; Hsiao, Hui-Mien; Stephens, Kathy; Gibson, Theda; Begier, Beth; Liu, Qing; Hubler, Robin; Gessner, Bradford; Lopman, Ben; Rouphael; Kamidani, Satoshi; Anderson, Evan; and Rostad, Christina.

Presenting Author: Khalel De Castro, BS

Background: Although respiratory syncytial virus (RSV) is a significant pathogen in elderly adults, little is known about the social risk factors for RSV disease in this population. In this study, we sought to evaluate the social determinants of RSV-related hospitalizations in older adults.

Methods: From October 2018 to April 2021, we enrolled patients ≥50 years of age who were admitted with an acute respiratory infection (ARI) at 2 hospital sites associated with Emory University. Enrolled patients participated in an interview regarding their medical and social history and their medical chart was abstracted. Nasopharyngeal and oropharyngeal swabs and standard-of-care specimens were obtained for BioFire® Respiratory Panel analysis. Characteristics were compared with bivariate analysis (two-tailed p-value <0.05) and generated a stepwise logistic regression model with inclusion in the model set at 0.05. Statistical analysis was performed using SAS v.9.4.

Results: Of the 1429 enrolled participants, 78 (5.5%) were RSV-positive and 1351 (94.5%) were RSV-negative (Table). Compared to RSV-negative participants, those with RSV were more commonly female (66.7% vs. 55.3%, P=0.05), more commonly immunocompromised (43.6% vs. 31.5%, P=0.03), especially with HIV/AIDS (11.5% vs. 3.5%, P=0.003), and more commonly had traveled >100 miles in the preceding 2 weeks (12.8% vs. 6.7%, P=0.04). No significant differences were found between the groups by baseline health status or other comorbidities. Participants with RSV had higher frequency of low to moderate activity at baseline than those who were RSV-negative. No significant differences were found between RSV risk and living with children, childcare and daycare attendance.

Conclusion: Risk factors for RSV-associated hospitalization in older adults included female sex, immunocompromised status, and travel within the preceding two weeks. Understanding risk factors for RSV disease severity may inform prevention recommendations.

Poster Number: 9

Single cell RNA-Sequencing reveals neurological perturbations in postnatally ZIKV-infected infant rhesus macaques

Authors: Edara, Venkata-Viswanadh; Schoof, Nils; Burgess, Divine; Richardson, Rebecca; Freeman, Sienna; Sampson, Maureen; Moore, Kathryn; Suthar, Mehul; Bosinger, Steven; Sloan, Steven; Raper, Jessica; and Chahroudi, Ann.

Presenting Author: Venkata Viswanadh Edara, PhD

Background: Consequences of postnatal ZIKV infection in infants and children are not well understood. We have previously shown abnormal brain structure and function that is predictive of behavior in infant rhesus macaques infected with ZIKV postnatally. Here, we explored the brain regions, cells, and pathways impacted by postnatal ZIKV infection to suggest mechanisms of injury and neuropathogenesis.

Methods: Infant rhesus macaques (RMs) were infected with ZIKV at one month of age and euthanized 14 days after infection for single cell transcriptomic analyses of the hippocampus, amygdala, and striatum. ZIKV-infected infant RMs were compared to age and sex-matched uninfected controls. Bioinformatic approaches using R (V4) and Seurat (V4) were utilized and, after quality control, 105,421 cells from controls and 94,975 cells from ZIKV-infected animals were analyzed.

Results: We identified unique transcriptional phenotypes in the CNS between uninfected and ZIKV-infected RMs, including nervous system development, glial cell differentiation, neuron differentiation, activation of innate immune response and regulation of myelination. As expected, we found a signature of activated microglia along with upregulation of transcription factors involved in interferon signaling and downstream activation of interferon stimulated genes (ISGs) such as IFI6, IRF9 and MX1 in ZIKV-infected RMs. Furthermore, ZIKV infection significantly reduced the expression of several genes involved in myelination processes among mature oligodendrocytes.

Conclusions: Our results show that acute ZIKV infection in infant RMs leads to CNS immune activation and downregulation of critical genes involved in myelination, which may have long lasting neurodevelopmental consequences.

Poster Number: 10

Epidemiology, Clinical Features, and Outcomes of Rhinovirus/Enterovirus in Older Adults Hospitalized with Acute Respiratory Infections and those with CHF and COPD Exacerbations

Authors: Ess, Gabby; Tippett, Ashley; Salazar, Luis W.; Reese, Olivia; Ciric, Caroline R.; Hussaini, Laila; Begier, Elizabeth; Hubler, Robin; Liu, Qing; Gessner, Bradford D.; Lopman, Benjamin; Kamidani, Satoshi; Rouphael, Nadine G.; Anderson, Evan J.; and Rostad, Christina A.

Presenting Author: Gabby Ess

Background: While Rhinovirus/Enterovirus (RV/EV) infections are common, the clinical characteristics of infections in hospitalized adults are not fully understood.

Methods: Adults ≥ 50 years of age hospitalized for Acute Respiratory Infections (ARI) or exacerbations of CHF or COPD in two hospitals in Atlanta, GA during the 2018-2019 and 2019-2020 respiratory seasons were offered enrollment. Following informed consent, participants were tested via BioFire® FilmArray® respiratory panels of nasopharyngeal and oropharyngeal swabs (combined), and standard-of-care molecular testing results were also recorded. Subjects were considered positive for RV/EV if any method of testing resulted positive. Baseline characteristics and clinical features were gathered via subject interviews and medical record abstractions. Variables were compared between subjects with RV/EV and two control groups: those negative for all pathogens and those negative for only RV/EV. Participants with RV/EV who had co-infections were excluded from the analysis. Descriptive statistics were performed using SAS v9.4.

Results: Of 1429 enrolled participants, 123 (8.6%) were positive for RV/EV, of whom 111 had RV/EV alone. When compared to those negative for all tested pathogens (n=1034), participants with RV/EV more commonly had underlying COPD (45.0% vs. 35.5%, P=0.047) and less commonly had CHF (36.0% vs. 48.3%, P=0.014) or experienced acute myocardial dysfunction (29.7% vs. 41.2%, P=0.019). Participants with RV/EV also more commonly experienced fever (39.6% vs. 27.7%, P=0.008), cough (90.1% vs. 69.0%, P< 0.001), sore throat (54.1% vs. 39.5%, P=0.003), chest pain (48.6% vs. 37.8%, P=0.026), and dyspnea/respiratory distress (25.2% vs. 13.1%, P< 0.001) than those negative for all pathogens. Differences between RV/EV positive and negative groups were similar to the all pathogen negative group, with the exception of no significant differences in acute myocardial dysfunction, fever, and COPD in the RV/EV negative group.

Conclusions: Among older adults hospitalized with ARIs, CHF, and/or COPD exacerbations, RV/EV was associated with symptoms of both upper and lower respiratory tract infection and was more frequent identified among those with COPD.

Poster Number: 11

Targeting SIV viral reservoir with early ART in combination with immune interventions in infant rhesus macaques

Authors: Farinre, Omotayo; King, Alexis; Anaya. Tzoalli; Jean, Sherrie; Wood, S. Jennifer; Ehnert, Stephanie; Liang, Shan; Laird, Greg; Mason, Rosemary; Roederer, Mario, Safrit, Jeffrey; Mavigner, Maud; and Chahroudi, Ann.

Presenting Author: Omotayo Farinre, PhD

Background: Persistent reservoirs of HIV-infected CD4+ T-cells remain the major obstacle to cure. Broadly neutralizing antibodies control viral replication and may promote infected cell clearance. We tested SIV-Env-specific rhesus IgG1 monoclonal antibodies (RhmAbs), IL-15 superagonist N-803, and early ART in SIV-infected infant rhesus macaques (RMs) to assess impact on viral reservoirs and rebound dynamics upon ART interruption.

Methods: Twenty-two infant RMs were orally-infected with SIVmac251 at 4 weeks-of-life and started on ART 1-2 weeks post-infection, then divided into 3 groups: i) ART only, ii) ART+SIV-RhmAbs (20mg/kg s.c. of ITS09.01-LS, ITS102.01-LS, ITS103.01-LS, ITS113.01-LS, one dose), and iii) ART+SIV-RhmAbs+N-803 (100mg/kg, one dose). Plasma viral loads and total and intact SIV-DNA in CD4+ T-cells were measured longitudinally. ART was discontinued at week 50.

Results: Viral load decay with ART was similar across groups. Levels of CD4+ T-cell-associated SIV-DNA declined on ART across all groups with no significant difference across groups. Similarly, Intact proviral SIV-DNA in CD4+ T-cells from blood or lymph nodes did not differ between groups at week 26; the same was true of total SIV-DNA at week 48. All animals experienced viral rebound 1-4 weeks after ART interruption with no group differences in time to rebound.

Conclusions: Compared to treating with early ART alone, adding RhmAbs +/- one dose of N-803 did not impact the level of persistent SIV once viral loads were suppressed nor did this combination delay viral rebound after ART interruption. Future studies should explore additional doses of RhmAbs and N-803.

Keywords: HIV, SIV, cure, pediatric, nonhuman primates

Poster Number: 12

Th2 Immune Responses Modulates the Anti-viral and Anti-inflammatory Activity During Mild COVID-19 Disease.

Authors: Garcia-Salum, Tamara; Fourati, Slim; Valenzuela, Gonzalo; Pardo-Roa, Catalina; Serrano, Eileen F; Pacheco, Gabriela; Pereira, Susan; Schotsaert, Michael; White, Kris; Levican, Jorge; Avendaño, María José; González, Claudia; Suthar, Mehul; Krammer, Florian; Garcia-Sastre, Adolfo; Riquelme, Arnoldo; Sekaly, Rafick-Pierre; and Medina, Rafael A.

Presenting Author: Tamara Garcia-Salum, PhD

Individuals infected by SARS-CoV-2 frequently develop mild disease; however, the underlying molecular pathways leading to such better outcomes are unknown. We integrated early clinical and molecular parameters to elucidate signatures that discriminate mild from moderate and severe outcomes. Using a training cohort (N=41) we show that mild patients had higher antibody titers and lower viral loads, which were associated with allergic diseases and increased expression of the Th2 cytokines IL-4 and IL-13. In contrast, moderate or severe individuals had higher viral loads and the bacterial translocation marker sCD14, and were associated with lower antibody responses, and increased IL-8, IP10 and IL-10. We built an integrative network model and tested these signatures with a test cohort (N=64), which predicted mild disease with over 98% accuracy at week one after disease onset and suggested a mechanistic role for Th2 responses in the reduction of disease severity. In vitro incubation of human tracheobronchial epithelial cells (HTBE) with IL-4 or IL-13 increased levels of the antiviral cytokine IFNg and decreased viral replication, and induced lower levels of IL-6, a proinflammatory cytokine associated to severe disease. Importantly, treated HTBE cells showed a specific gene signature, which was not significantly altered by SARS-CoV-2 infection. A subset of these genes highlighted potential novel antiviral pathways, which do not include antiviral interferon-stimulated genes. Overall, our results suggest that Th2 responses modulate viral load and inflammatory response during disease progression in mild COVID-19 patients.

Poster Number: 13

Virus-like particles as an RSV vaccine

Authors: Ha, Binh; Sun, HeYing; Sankaranarayanan, Ranjini; Tiwari, Pooja; and Anderson, Larry J.

Presenting Author: Binh Ha, PhD

RSV is the leading cause of lower respiratory tract infection inducing bronchiolitis and pneumonia in infants. Recently, RSV vaccines based on prefusion F protein have been approved for older adults and pregnant women. However, studies from our lab and others suggest G protein contributes to inflammation and disease; and G in a vaccine can dampen G-associated disease. Thus, an RSV vaccine including G protein might enhance the efficacy of RSV vaccines. Here, we report the use of virus-like particles (VLPs) as a platform to express F and G proteins, with RSV M, P, F and G protein stably transfected 293F cells. Studies in a mouse model show that VLPs expressing pre-fusion stabilized F (pre-F) and a G construct with subgroup A (Ga) and subgroup B (Gb) sequences and AddaS03 or alum adjuvant induced F, Ga and Gb binding antibodies and neutralizing antibodies. The AddaSO3 adjuvant induced the highest antibody titers. This RSV VLP platform expressing pre-F and Ga and Gb sequences potentially offers an improved RSV vaccine by reducing G-mediated inflammation and disease.

Poster Number: 14

SARS-CoV-2 IgG Antibodies in Vaccinated and Non-vaccinated Pediatric Healthcare Workers: A Longitudinal Surveillance Study

Authors: Hatabah, Dunia; Lata Gupta, Sneh; Heilman, Stacy; Korman, Rawan; Camacho-Gonzalez, Andres; Leake, Deb; Le, Mimi; Griffiths, Mark; Norwood, Carson; Shih, Samuel; Rees, Chris A.; Benedit, Laura; Suthar, Mehul; Miriam B.; Wrammert, Jens; and Morris, Claudia R.

Presenting Author: Dunia Hatabah, MD

Background: Vaccines against SARS-CoV-2 (SARS) target the spike protein. There is minimal information on longitudinal immune profiling of different subgroups including SARS recovered vs. naïve (never infected with SARS) and vaccinated vs. non-vaccinated in HCW.

Objective: Explore the impact of SARS vaccination on IgG antibody titers over time and cross-reactivity with other corona viruses in a longitudinal cohort of pediatric HCW

Methods: Prospective longitudinal cohort conducted from April 2020 to May 2022 in 642 pediatric healthcare workers (pHCW) working at Children's Healthcare of Atlanta in Atlanta, Georgia.

Results: 642 HCW were enrolled with a 4% prevalence of SARS-IgG & 8% incidence of new infection from Sept-Jan 2021. 341 participants had repeat IgG titers measured at different time intervals for post Covid-19 vaccine titers. None of the HCW enrolled in this study required emergency department visits or hospitalizations. A robust antibody response occurred against RBD (receptor-binding domain), spike and NTD (N-terminal domain) in all vaccinated individuals vs. non-vaccinated ($p<0.0001$). COVID-19 recovered-vaccinated participants had higher titers of spike, RBD and NTD compared to naïve individuals after vaccination ($p<0.0001$). Recovered participants showed higher IgG titers for other beta-corona variants irrespective of vaccination status. Single dose of vaccine was sufficient to attain maximum titer in Covid-19 recovered participants compared to naïve who required both doses of vaccine. RBD and Spike antibody titers were higher and more durable after booster as compared to primary series of vaccination. Individuals receiving Moderna and Pfizer showed comparable levels of IgG antibodies at one month post vaccination with a slower immune decay in the Moderna arm. Breakthrough infection rates were higher in the Pfizer arm.

Conclusions: All vaccinated HCW developed SARS-IgG to spike. Both SARS infection and vaccination yield antibodies that cross react to other beta-corona viruses, likely imparting additional immunity against different strains. RBD and Spike antibody titers were higher and more durable after booster as compared to primary series of vaccination. Longitudinal profiling of the immune response to vaccination may be useful for counseling future vaccination booster requirements.

Poster Number: 15

A long-term 3D cell culture model utilizing murine and de novo HBV infection approaches.

Authors: Jones, Christopher E; Dangas, George; Athanasiadis, Antonis; Shue, Taylor; Koenig, Maddy; Sanders, Madeleine; Levenson, Kenny; Barbosa, Luana; Zhou, Chenhui; de Jong, Ype; Michailidis, Lefteris.

Presenting Author: Christopher E. Jones, PhD

Background: In vitro investigation of HBV infection typically relies upon 2D culture of primary human hepatocytes (PHH) or cell lines. However, 2D cultures are limited as they do not necessarily accurately represent the 3D environment of hepatocytes, and alternate 3D cell culture models have therefore been developed and have become increasingly widely used. Various successful applications of 3D culture models in the study of HBV infection have been reported, including drug toxicity, screening and metabolism studies. Existing 3D models however are themselves limited as they are composed of hepatic cell lines or of PHH, which each have inherent limitations. Further, they rely solely upon de novo HBV infection, a strategy which does not necessarily result in high infection rates nor necessarily fully recapitulate in vivo infection. More rigorous and malleable 3D culture models are therefore desirable for the study of HBV infection.

Method: Mouse-passaged primary human hepatocytes (mpPHH) were infected with HBV (HBV-infected) or were treated with mock infection conditions (mock) and subsequently formed into 3D spheroids utilizing ultra-low adhesion (ULA) plates and a centrifugation protocol. Various outputs were subsequently measured - including viral antigen and human albumin (hAlb) - to monitor infection and hepatocyte health. Additionally, the efficacy of an antiviral capsid-assembly modulator (CpAM) (GLP-26) in the context of the model was investigated. Further, mpPHH infected by HBV in a murine model prior to isolation (HBV-mpPHH) were used to produce spheroids, which were subsequently analysed for ability to maintain infection.

Results: 3D mpPHH spheroids of various sizes were reliably produced and validated. Spheroids maintained measurable HBV infection for more than two months. Spheroid health was maintained for most of this duration, as determined by hAlb. Infection was controllable using an antiviral compound with known efficacy against HBV infection in vitro, and infection was observed to rebound after drug removal. Further, 3D HBV-mpPHH spheroids of various sizes were reliably produced and determined to be highly infected.

Conclusions: We here report a 3D mpPHH and HBV-mpPHH model as a novel and advantageous alternative to current systems, that shows promise for use in a range of studies including anti-HBV drug screens.

Poster Number: 16

AAV9-Delivered eCD4 as Part of a "Shock and Kill" Cure Strategy in SIV-Infected Infant Macaques

Authors: King, Alexis C.; Fonseca, Jairo A.; Farinre, Omotayo; Liang, Shan; da Costa, Lucas A.B.; Ehnert, Stephanie; Wood, Jennifer; Gardner, Matthew; Van Rompay, Koen A.; Martins, Mauricio A.; and Chahroudi, Ann.

Presenting Author: Alexis C. King, BS

Background: Latency reversal and clearance (Shock and Kill) is an HIV cure strategy that aims to reactivate and subsequently eliminate latently infected CD4+ T cells, including through antibody-mediated cellular cytotoxicity (ADCC). eCD4-Ig is a fusion protein comprised of the ectodomain of CD4, an IgG Fc portion, and a short tyrosine-sulfated peptide at its carboxy terminus resembling the tyrosine-sulfated regions of lentivirus coreceptors (e.g., CCR5 and CXCR4). eCD4-Ig can boost the ADCC activity of endogenous anti-HIV IgG antibodies in serum, making it a promising clearance agent.

Methods: For this study, seventy-two infant rhesus macaques were screened for neutralizing antibodies against AAV9, and twenty were selected: 17 of which had < 25% and 3 with ≤ 35% AAV9 neutralization at a 1:10 dilution of serum. These twenty macaques were orally infected with SIVmac251 at 4 weeks of life and started on antiretroviral therapy (ART) at 3 weeks post infection. On the same day (7 weeks of life), half of the animals were also dosed intramuscularly with 2.0x1012 genome copies/kg of an AAV9 vector expressing rhesus eCD4-IgG1. An IgG1 version of eCD4-Ig was specifically chosen for enhanced antibody effector functions.

Results: All our animals experienced peak SIV RNA levels of ≥ 107 copies/ml in plasma, and ART initiation resulted in at least a 3-log reduction of viral loads in the first two weeks of therapy. AAV-driven expression of eCD4-IgG1 was measured by ELISA, and peak serum concentrations exceeding 10 µg/ml were observed in 10/10-treated macaques. Eight of nine infant macaques (followed for at least 12 weeks after the AAV9-eCD4-IgG1 administration) experienced persistent levels of eCD4-IgG1 expression and only one displayed transient expression of eCD4-IgG1.

Conclusions: AAV9 is a promising delivery mechanism for eCD4Ig in infant NHP, achieving consistent expression in 8 out of 9 animals. Future plans for this study include administration of the latency reversal agent AZD5582 and investigation of its ability to 1) to induce SIV antigen expression, reversing latency and 2) induce the clearance of reactivated SIV-infected cells by eCD4-IgG1-mediated ADCC, therefore potentially reducing the size of the SIV viral reservoir.

Poster Number: 17

Clinical Features and Outcomes of Children vs. Adults Hospitalized with Coronavirus Disease 2019 (COVID-19)

Authors: Li, Grace; Gopchandani, Komal; Perez, Maria A.; Choi, Chris; Hsiao, Hui-Mien; Tippett, Ashley; Oseguera, Miriam; Foresythe, Abiodun; Brazer, Noah; Bhattacharya, Sanchita; Servellita, Venice; Gonzalez, Alice Sotomayor; Gulick, Dalia; Kraft, Colleen; Kasinathan, Vyjayanti; Wang, Yun F (Wayne); Bard, Jennifer Dien; Chen, Pei Ying; Flores-Vasquez, Jessica; Planet, Paul J; Devaraj, Sridevi; Annapragada, Ananth V.; Luna, Ruth Ann; Rostad, Christina A.; Chui, Charles.

Presenting Author: Grace Li, BS

Background: The purpose of this study was to compare clinical features and outcomes of children vs. adults who were hospitalized with coronavirus disease 2019 (COVID-19).

Methods: We performed a retrospective analysis of enrollments that were positive for SARS-CoV-2 by nasopharyngeal PCR from March 2020 to January 2023 whose respiratory specimens and clinical metadata were collected at 5 sites. We compared the clinical features and outcomes of children vs. adults using Chi-squared tests and determined the odds ratios of severe outcomes adjusting for sex, race, ethnicity, comorbidities, Omicron infection, vaccination, co-infections, and enrollment site. Statistical analyses were performed using SAS v9.4.

Results: Of 9101 enrollments, 2229 (24.5%) were hospitalized and 1560 (17.1%) were hospitalized for COVID-19 as the primary reason, of which 809 (51.9%) were children. The median age of hospitalized children was 4.0 years (IQR 0.6-12.4), 362 (44.8%) were female, and the majority were Latinx (393, 51.9%). Compared to adults, children had less comorbidities ($p<0.05$ for all comparisons), less commonly received any COVID-19 vaccination (10.4% vs. 35.8%, $p<0.0001$), and more commonly were infected with the Omicron variant (50.4% vs. 27.5%, $p<0.0001$). Children more commonly had fever, nasal congestion/rhinorrhea, conjunctivitis, and nausea/vomiting; but they less commonly had headache, chills, fatigue, cough, shortness of breath, anosmia/dysgeusia ($p<0.05$ for all comparisons). Children less commonly experienced coinfections (25.2% vs. 32.0%, $p=0.0151$), and these were most often respiratory viral coinfections (42.8%). Although children less commonly required supplemental oxygen (45.7% vs. 76.2%, $p<0.0001$) and mechanical ventilation (13.8% vs. 19.2%, $p<0.0001$), they more often were diagnosed with multisystem inflammatory syndrome (2.7% vs. 0.3%, $p<0.0001$) and required ICU admission at a similar frequency as adults (26.6% vs. 29.9%, $p=0.1537$). After adjusting for confounding variables, children had significantly increased odds of requiring high-flow oxygen (aOR 1.81, 95%CI 1.15, 2.87) and being diagnosed with MIS (aOR 9.19, 95%CI 1.07, 78.84), but decreased odds of death (aOR 0.07, 95%CI 0.01, 0.44) compared to adults.

Conclusion: Children are at risk for severe COVID-19 and MIS-C. COVID-19 vaccination is an important intervention to protect children's health, and vaccine uptake among hospitalized children in our cohort could be improved.

Poster Number: 18

Microbiota-derived Metabolites modulate COVID-19 Vaccine-induced Humoral immune responses in Down syndrome individuals.

Authors: Majithia, Manini; ten-Caten, Felipe; Coirada, Fernanda; Silveira,Cassia; Malheiros, Jackeline; Covolan, Luciene; and Ribeiro, Susan Pereira

Presenting Author: Manini Majithia

Background: Emergency COVID-19 vaccination was implemented for Down Syndrome (DS) individuals due to their higher mortality upon SARS-CoV-2 infection. These individuals present hyperinflammation and metabolic disorders. Previously, we have shown that pre-vaccination inflammatory levels modulate the induction of humoral responses. Metabolites also play major roles in immune-modulation. We hypothesized that the hyper-inflamed environment in DS individuals could contribute to poor immune responses to COVID-19 vaccination.

Method: To address this hypothesis, a cohort of DS and non-DS people was recruited in Brazil in 2021 (n=120). Plasma was collected for the evaluation of IgG SARS-CoV-2 antibodies (Wuhan and variants: P.1, B.1.1.7, B.1.351) and metabolites. Uninfected and vaccinated individuals (AstraZeneca) were selected based on similar vaccine doses and follow ups (3- and 6-months post-boost, n=42: 36 DS and 6 non-DS).

Results: While both groups presented SARS-CoV-2 antibodies post-vaccination, DS presented significantly lower Ab-titers than non-DS individuals at both time points for all proteins. Of note, 3β-hydroxy-5-cholenoate (a secondary bile acid) was increased in participants with higher antibody titers. Conversely, Trimethylamine N-oxide (TMAO), another gut microbiota derived metabolite, was inversely correlated. 3β-hydroxy-5-cholenoate is known to bind Ahr and Farnesoid X Receptor, respectively, have anti-inflammatory properties.

Conclusions: TMAO, generated from trimethylamine produced by the gut microbiota, is linked to diabetes and obesity, which are comorbidities associated with poor vaccine responses, similar to DS individuals. Interventions aiming at modulating this inflammatory milieu in DS individuals might be able to improve the magnitude and breadth of the vaccine responses in this population.

Keywords: 3β-hydroxy-5-cholenoate, Trimethylamine N-oxide, microbiota-derived metabolites

Poster Number: 19

Delayed Viral Rebound Following Antibody Administration in Infant Macaques

Authors: Powers, Jenna; Bricker, Katherine M.; Williams, Brianna; Oliver, Danielle; Obregon-Perko, Veronica; Rivera Rodriguez, Dormarie E.; Sukkestad, Sophia; Dashti, Amir; Mason, Rosemarie; Roederer, Mario; and Chahroudi, Ann.

Presenting Author: Jenna Powers, BS, MD(c)

Background: Interventions to prevent viral rebound in the absence of ART would be highly beneficial for the 1.7 million children living with HIV. Treatment with bNAbs has demonstrated a delay in time to rebound in both adult and pediatric clinical trials indicating the need for further investigation as a possible cure strategy.

Methods: Env-specific mAbs were isolated from SIV-infected RMs and expressed as full-length rhesus IgG1 modified to contain the LS-encoding mutation (M428L/N434S) to maximize circulation half-life. We evaluated the impact of 4 anti-SIV Env RhmAbs: ITS09.01-LS, ITS102.01-LS, ITS103.01-LS, ITS113.01-LS (anti-V2, CD4BS, CD4BS proximal, and MPER, respectively), selected for ability to neutralize SIVmac251. Fourteen rhesus macaque (RM) infants were orally challenged with SIVmac251 at 4 wks of age and treated with a triple ART regimen (TDF+FTC+DTG) for ~16 months beginning 4 wks post infection. Eight RMs received a s.c. injection at 20 mg/kg of each anti-SIV Env RhmAb one wk prior to ATI and six RMs remained on ART alone until ATI. Time to viral rebound and post rebound set point were monitored by quantitative PCR for SIVgag RNA in plasma. Serum RhmAb concentrations were measured by ELISA.

Results: All infant RMs were infected with peak viral loads of 106-108. ART was successful in suppressing viremia to <60 copies/ml in all RMs. All infant RMs rebounded after ART interruption; however, RhmAb-treated RMs experienced a significant delay in time to rebound compared to ART only controls ($p = 0.0007$; mean = 51d vs 10d, respectively). A positive correlation was observed between the time to rebound following ATI and the duration of detectable ITS113.01-LS in serum ($r=0.78$, $p=0.04$) and a positive trend for the time to rebound and mAb concentration during ATI. Of the 8 RhmAb-treated RMs, the two that exhibited the shortest time to rebound following ATI had the most rapid decline in serum RhmAb concentration.

Conclusions: We have demonstrated that administration of an anti-SIV Env RhmAb cocktail prior to ATI leads to delayed time to rebound in infant RMs. This research provides preclinical support for the use of polyfunctional mAbs to delay viral rebound in pediatric HIV-1 cure clinical trials.

Poster Number: 20

Novel Immunomodulator to Address Immune Dysregulation and Viral Comorbidities in Children with Kawasaki Disease

Authors: Quinones, Guadalupe; Roa Sebastian; Reece D, Monica; and Gavegnano Christina.

Presenting Author: Guadalupe Quinones, BS

Background: Kawasaki disease (KD), is a pediatric acute, self-limited medium vessel vasculitis that has a predilection for the coronary arteries and unknown etiology. It is the leading cause of acquired heart disease in developed nations. The underlying immune activation and dysfunction of KD confers decreased immune function and greater susceptibility to a wide range of infectious diseases, which in turn confers a markedly elevated risk of virus-induced comorbidities in children with KD. When diagnosed with KD, children have a greater risk of developing coronary artery aneurysms (CAA). Large CAA may lead to complications, including heart failure, myocardial infarctions, and death, underscoring the major unmet clinical need for safe, specific and potent agents for this indication.

Methods: Human Umbilical Vein Endothelial Cells (HUVEC), which mimic the pediatric endothelial milieu, were optimized for density and passage frequency. To mimic the in vivo immune dysregulatory profile observed in KD, our in vitro model of KD contained a cocktail of proinflammatory cytokines at physiologic concentrations CD40 Ligand (1ng/mL), TNF-alpha (2.5 ng/mL), IL-1 alpha (10 ng/mL), IL-1 beta (10 ng/mL), and IL-18 (50 ng/mL). Four conditions were established: HUVEC media with no cocktail, cocktail with 0.1 uM concentration of novel therapeutic, cocktail with 1.0 uM concentration of novel therapeutic, and cocktail with no novel therapeutic. The cells were stained with activation marker CD31 and subjected to flow cytometry. A one-way ANOVA for multiple comparisons against the cytokine cocktail control assessed for significance.

Results: Flow cytometry data demonstrated statistically significant reduction in percent positive cells in the treated cells versus the untreated HUVECs. This resulted in significant p-values of 0.042 for the cells with cytokine cocktail and 1 uM of the novel therapeutic and p-value of 0.028 for the cytokine cocktail and 0.1 uM of the novel therapeutic.

Conclusions: This novel therapeutic significantly reduces cellular immune activation in an in vitro model of KD at physiological concentrations in HUVEC. These data provide a foundation for further examination of this agent for restoration of immune function in KD patients; a long-term goal is to decrease susceptibility and comorbidities from viral infections via restored immune function.

Poster Number: 21

Jak Inhibitors for Treatment, Prevention or Reversal of Sepsis and Related Comorbidities

Authors: Roa, Sebastian; and Gavegnano, Christina

Presenting Author: Sebastian Roa, BA

Background: Septicemia is a life-threatening medical condition which is defined as a systemic inflammatory response to infection. Sepsis is driven by the binding of pathogen associated molecular patterns (PAMPs) and damage associated molecular patterns (DAMPs), which are recognized by myeloid cells which active signal cascades resulting in transcription and release of proinflammatory cytokines. The annual incidence of sepsis and septic shock in the United States is 300 per 100,000 people (CDC). Current treatments seek only to impact the microbes causing the infection, not the immune dysregulation and/or inflammation caused through the sepsis specific pathway. Direct-acting treatments represents major unmet clinical need.

Methods: Monocyte derived human primary macrophages harvested from whole blood were plated in a 24-well plate in RPMI media. The cells were stimulated with LPS from sepsis causing bacteria's: E. Coli, K. Pneumoniae, S. Marcescens, and P. Aeruginosa to simulate a sepsis event. The treatment group received 0.1 μM baricitinib. The cells were incubated for 24-hours before harvesting the cells for flow cytometry. The cells were stained with surface activation markers HLA-DR and CD-163 and subjected to flow cytometry to quantify impact of baricitinib upon reversal of in vitro sepsis-induced activation markers associated with disease severity and death in vivo.

Results: Flow cytometry data demonstrated statistically significant reduction in Mean Fluorescence Index (MFI) and percent positive cells in the treated cells versus the untreated cells across multiple bacterial LPS's (t-test; $p < 0.05$). The flow cytometry data was also gated using cellular activation, derived by morphological changes in the cells (subgating on size and granularity of cellular subsets). This comparison also yielded statistically significant reduction in MFI and percent positive cells (t-test; $p < 0.05$). Flow cytometry data was then gated comparing activated and inactivated cell percentages and resulted in statistically significant reduction of activated cells and increase of inactivated cells in the treatment group (t-test; $p < 0.05$).

Conclusions: Baricitinib significantly reduces bacterial inflammation in an invitro model of sepsis at physiological concentrations in relevant primary human cells. With no currently approved treatment for the inflammatory dysregulation from sepsis, the utilization of JAK-STAT inhibition provides a novel treatment option.

Poster Number: 22

Disrupting SIV Reservoir Seeding by Targeting Stemness Pathways in Rhesus Macaques

Authors: Ruiz-Salinas, Inna; Hamid, Riri; Schoof, Nils; Lin, Alice; Goldy, Jordan; Silvestri, Guido; Chahroudi, Ann; and Mavigner, Maud.

Presenting Author: Inna Ruiz-Salinas, PhD

Background: Latently HIV-infected CD4+ T cells persist indefinitely through proliferation. We previously showed that inhibition of proliferation and induction of differentiation of the long-lived, self-renewing central (CM) and stem cell memory (SCM) CD4+ T cells can be achieved in ART-treated SIV-infected rhesus macaques (RMs) through modulation of the Wnt pathway.

Objective: We evaluated a combined approach targeting Wnt and Notch pathways during acute SIV infection of RMs to disrupt viral reservoir establishment.

Design/Methods: Five RMs were infected i.v. with SIVmac239 before receiving 8-week treatment with the Wnt inhibitor PRI-724 administered subcutaneously daily (18-20 mg/kg) in combination with the Notch inhibitor LY3039478 administered orally three times per week (2.5 mg/kg). ART was initiated 8 weeks post-infection (wpi) and PBMC were collected longitudinally to sort subpopulations of naïve, SCM, CM, transitional memory (TM) and effector memory CD4+ T cells. Levels of cell-associated total SIVgag DNA and unintegrated 2-LTR circles were measured by multiplex qPCR in sorted cells. A group of 7 SIVmac239-infected ART-treated RMs served as controls.

Results: The combined treatment PRI-724+LY3039478 demonstrated an acceptable safety profile and did not alter plasma viral load dynamics in SIV-infected RMs. After ART initiation, the decay in the SIV 2-LTR circles was greater in the CM at 12wpi and TM subsets at 12 and 20wpi from the PRI-724+LY3039478-treated RMs versus controls. The SIVgag/2-LTR ratio was higher in all subsets of memory CD4+ T cells from the treated RMs versus controls at 8 and 12wpi. Interestingly, a reduced CM contribution to the total SIV reservoir in CD4+ T cells was observed in the treated RMs at both 8 and 12wpi. This reduction was attributed to lower levels of SIVgag DNA in CM cells at 12wpi and decreased frequencies of CM cells within the CD4+ T cell pool at 8 and 12wpi in PRI-724+LY3039478-treated RMs versus controls.

Conclusion: This study suggests that the combined pharmacological modulation of Wnt and Notch pathways during acute SIV infection impacts viral reservoir seeding by transiently reducing the relative contribution of the CM cells to the peripheral CD4+ T cell compartment and to the pool of the infected CD4+ T cells.

Poster Number: 23

Characterizing spatio-temporal interactions of HIV-1 capsid with host factors

Authors: Sagadiev, Sara; Gifford, Levi; and Melikian, Gregory B.

Presenting Author: Sara Sagadiev, BS, PhD(c)

Despite the wealth of knowledge regarding HIV-1 infection, key early events of the virus' lifecycle, such as disassembly of its capsid (uncoating), virus trafficking, and nuclear import, remain poorly understood. Upon cell entry, HIV-1 interacts with a multitude of host dependency factors that provide protection against innate immune responses triggered by the host cell. The identity and basic functions of several host dependency factors have been determined; however, the order and timing of interactions between these factors and HIV-1 capsid remain unknown. We hypothesize that several of these factors, SEC24C, RBM14, and CPSF6, interact in a relay type mechanism with capsid for its optimal stability and transport from the cytoplasm to the nucleus. We endogenously tagged these factors with fluorescent proteins and visualized the spatial arrangement and temporal co-localization of these factors with fluorescently labeled HIV-1 capsid by single virus tracking in live cell. In addition to live cell imaging, capsid-host factor interactions are validated by other in situ methods such as proximity ligation assay (PLA). Another host dependency factor SUN1, which is localized to the nuclear membrane, has been shown to interact with HIV-1 capsid and selectively inhibit infection upon overexpression in target cells. However, the mechanism by which such restriction occurs remains unclear. We are currently testing the hypothesis that overexpression of SUN1 inhibits HIV-1 infection through capturing HIV-1 capsid at the nuclear pore using several advanced imaging techniques. This work was supported by the NIH R01 AI129862 grant to GBM.

Poster Number: 24

Clinical features, risk factors, and outcomes of COVID-19 in Immunocompromised adults hospitalized with acute respiratory infection

Authors: Taylor, Elizabeth Grace; Tippett, Ashley; Salazar, Luis W.; Hussaini, Laila; Choi, Chris; De Castro, Khalel; Reese, Olivia D.; Momin, Humerazehra; Lew, Ashley M.; Ciric, Caroline R.; Banerjee, Amrita; Keane, Amy; Puzniak, Laura A.; Hubler, Robin; Valluri, Srinivas; Wiemken, Timothy; Lopman, Benjamin; Kamidani, Satoshi; Anderson, Evan J.; and Rostad, Christina A.

Presenting Author: Elizabeth Grace Taylor, BS

Background: Individuals with immunocompromising conditions are at high risk of severe disease from COVID-19. The objectives of this study were to describe the clinical features, risk factors, and outcomes of COVID-19 in immunocompromised (IC) adults hospitalized with acute respiratory infection (ARI).

Methods: We enrolled patients ≥18 years of age hospitalized with ARI at two Emory University hospitals from May 2021 – Aug 2022. Patient interviews and medical abstractions were completed. Nasopharyngeal and oropharyngeal swabs were tested for SARS-CoV-2 using BioFire Respiratory Panel, and results of standard-of-care testing were recorded. IC was defined using comorbidities from the medical chart (cancer, HIV, organ/stem cell/bone marrow transplant, long-term steroid use, other immune decreasing conditions). IC patients were considered to have completed primary vaccination if they had 3 mRNA or 1 J&J + 1 other doses. Vaccine effectiveness (VE) was calculated using a test-negative case-control design. Multivariable logistic regression with stepwise selection yielded a final model controlling for employment, past COVID-19, and blood disorders. SAS v9.4 software was used.

Results: Of 1677 enrolled participants, 1653 had SARS-CoV-2 testing, of whom 850 (50.7%) were positive and 231 (27.2% of 850) were IC. Compared to non-IC patients with SARS-CoV-2, IC patients were significantly older (median 58, IQR [44-67)), male (57.1%), and had underlying comorbidities, including blood disorders (13.9%) and chronic kidney disease (36.8%). IC patients were more commonly infected with the Omicron variant, while non-IC patients were more commonly infected with Alpha or Delta. Compared to non-IC, IC patients had longer hospitalization duration (median 4.7, IQR [2.9-9.5]), required positive-pressure ventilation (CPAP/BiPAP) (13.9%, P=0.03), and died (6.5%). IC patients had less commonly received a full COVID-19 vaccine series (19.9% vs. 25.8%) and adjusted VE of primary COVID-19 vaccine series against hospitalization for ARI was lower in the IC (48.7 (17.9, 68.0)) vs. non-IC patients (76.0 (68.4, 81.7)).

Conclusions: Compared to non-IC hospitalized adults, COVID-19 VE against hospitalization for ARI was lower in IC patients, who were more likely to experience severe outcomes and death.