Center for Childhood Infections & Vaccines

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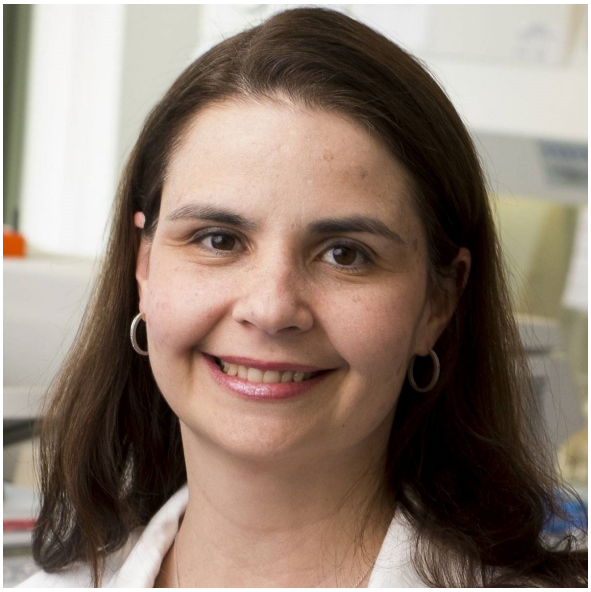
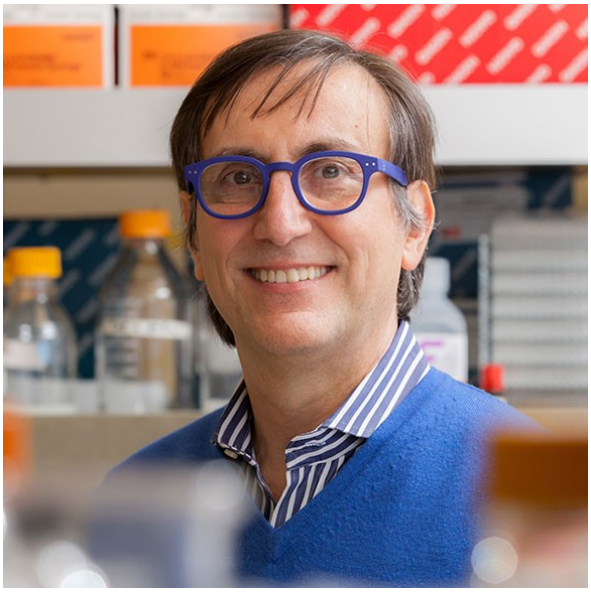




Symposium Recap

As in 2020, our symposium this year was virtual. While we missed the in-person interactions, the event was a great success. The virtual symposium drew over 130 registrants, 93 attendees, 2 keynote speakers, and 5 internal speakers. Thank you to all who participated in this year's symposium!

Our keynote speakers included Dr. Marina Caskey from The Rockefeller University (top left) and Dr. Alessandro Sette from La Jolla Institute for Immunology (top right).

Dr. Caskey's keynote was titled "Broadly Neutralizing Antibodies for HIV Prevention Therapy and Cure." Much of Dr. Caskey's research focuses on the development and clinical evaluation of novel immunotherapeutic strategies for HIV. Her talk in November covered a range of new HIV cure strategies that use bNabs to target, control, or eliminate viral reservoirs.

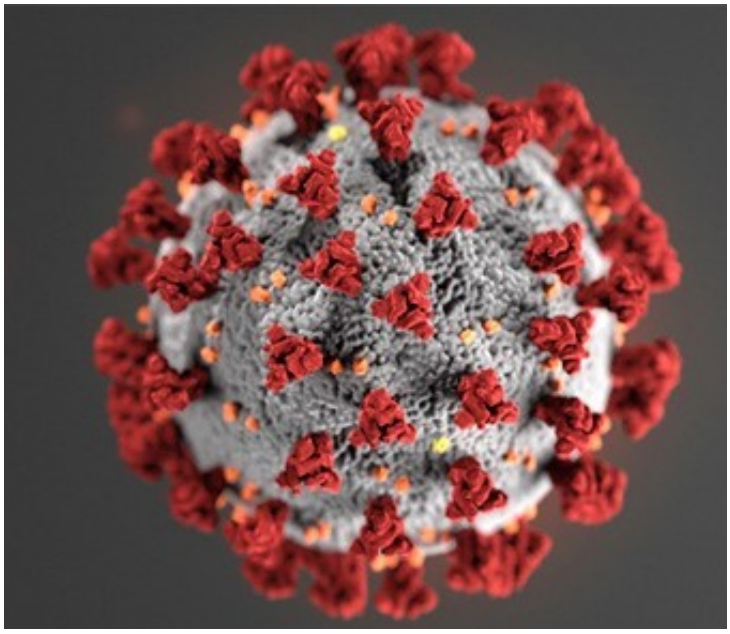
IN THIS ISSUE

Symposium Recap Cont,

Over the last 35 years, Dr. Sette worked to understand the immune response and develop disease intervention, with a recent focus on SARS-CoV-2. His talk, titled “Definition of Adaptive Responses to SARS-CoV-2 and Its Variants,” reviewed some of his lab’s major findings over the course of the pandemic, including the impact such findings had on the federal response. Dr. Sette also indicated some of his lab’s new work on SARS-CoV-2 variants and how their mutations affect spread, vaccine efficacy, and treatment strategies.

In between each keynote speaker, the symposium featured five internal speakers. Drs. Greg Melikian and Lisa Cranmer each gave short talks on their HIV-related work, while Dr. Satoshi Kamidani spoke about his recent research on influenza-associated hospitalizations. Finally, Drs. Anne Piantadosi and Jens Wrammert presented their recent findings on SARS-CoV-2, with the former focusing on variants and the latter on vaccines. §

COVID-19 & MIS-C



In the past year and a half, CCIV led the nation in SARS-CoV-2 research throughout the COVID -19 pandemic. A key component of that has been research on Multisystem Inflammatory Syndrome in Children (MIS-C).

MIS-C often results in PICU admission, with complications including myocarditis, cardiorespiratory failure, and death. Currently, MIS-C is thought to be a postinfectious response to SARS-CoV-2. Moreover, MIS-C often affects previously healthy children who have no underlying comorbidities, resulting in a growing number of COVID-19-related PICU admissions.

Being able to more quickly identify severe COVID-19 and MIS-C cases would help lead to improved patient care. Key advances in our understanding MIS-C, as it arises from COVID-19, come from CCIV researchers.

In Fall 2020, Dr. Christina Rostad started a Pediatric Research Alliance pilot grant investigating the relationship between COVID-19 and MIS-C. This pilot grant quickly led to additional funding on MIS-C with emphases on clinical phenotypes and biomarker identification.

One such award is the NIH funded PreVAIL study with PI Dr. Charles Chiu (UCSF). This study works to discover and validate predictive host biomarkers of pediatric COVID-19 and MIS-C severity using RNA sequencing and cell-free DNA methylation profiling. PreVAIL plans to apply machine learning-based classification strategies to generate diagnostic and predictive models of disease severity. Dr. Rostad is also part of a CDC MIS-C Phenotype Initiative Study and Extension. This study evaluates the longitudinal outcomes of children hospitalized

with MIS-C vs. COVID-19. The study will also assess the acceptance, uptake, safety, reactogenicity, and immune responses to COVID-19 vaccination in children with a history of MIS-C.

Dr. Rostad said, “the most rewarding aspect of our MIS-C research over the past year has been the opportunity to collaborate with investigators across the university and the country to improve our understanding of this novel condition and our approach to caring for children.”

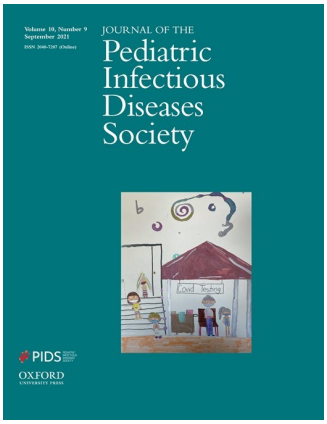
Such collaborations led several teams that included CCIV researchers to identify two MIS-C inflammatory biomarkers: secretory phospholipase 2 and plasma osteopontin. Previously, no evidence existed for a biomarker, a molecular indicator of disease severity enabling accurate treatment from onset, for COVID-19 positive children or MIS-C.

Partnering with Emory’s Pediatric Neurotrauma Lab and the Center for Clinical and Translational Research, investigators discovered that these inflammatory biomarkers typically identified in relation to Kawasaki disease or traumatic brain injuries respectively, were also elevated in SARS-CoV-2 positive and MIS-C patients. Findings from these studies were both published in *Experimental Biology and Medicine*.

The first study, published in July 2021, was funded by the Wilbur and Hilda Glenn Family Foundation, Michael and Natalie Beinenson, the Woodruff Health Sciences Center Synergy Award, and an Emory COVID-19 Cure award. The study led Children's and Emory researchers to conclude that secretory phospholipase 2 may be a potential biomarker of COVID-19 severity and MIS-C in children. The second study, published in September 2021 was funded by the Elaine and John C. Carlos Chair Fund and a grant from the National Institutes of Health (NIH). This study identified that plasma osteopontin may also be a biomarker.

CCIV investigators also collaborated with other pediatric divisions, especially Cardiology, to uncover a greater understanding of MIS-C. Dr. Preeti Jaggi (right) has been a key player in much of this collaborative effort.

Through collaborations with Dr. Matt Oster in the Division of Cardiology, Dr. Jaggi helped to study symptomatic acute myocarditis and giant coronary aneurysms associated with MIS-C and COVID-19 patients.



Key findings from these studies focused on potential symptoms of MIS-C that could contribute to diagnostic efforts. For instance, a study in *Journal of the Pediatric Infectious Diseases Society* found that 28% of MIS-C patients experienced neck pain and other symptoms affecting the ear, nose, and throat. As a result, the team proposed that neck pain could be a distinct clinical observation associated with a MIS-C diagnoses.

The ongoing COVID-19 pandemic means that treatment for MIS-C is also evolving as more is learned about the condition. While larger follow-up studies are still needed, these discoveries open the door to the more timely diagnoses for pediatric patients, as well as the development of new and more effective treatments.§

PROFILE: COVID-19 Vaccine Research Team

Over the last year, the Emory Children's Center — Vaccine Research Clinic (ECC-VRC), which includes the Emory Vaccine Treatment and Evaluation Unit (VTEU), led by Dr. Evan Anderson, played a critical role in the pediatric COVID-19 vaccine trials. The ECC-VRC's dedication over the past year led to their recognition by the Department of Pediatrics with the 2021 "Rising to the Occasion" award.

The VTEU conducted the Pfizer pediatric and Moderna Kid-COVE Phase II—III studies. These ongoing studies continue to enroll children from 6 months through 11 years. The ECC-VRC has been integral to both the blinded and unblinded portions, as well as key components related to dosage selection and vaccine efficacy.

This fall, Pfizer obtained FDA emergency use authorization for the 5-11 age range, and Moderna recently released data on their vaccine for 6-11 year old children.

As the pandemic continues, the VTEU faces the challenge of managing many different trials, including the Moderna and Janssen Phase 3 adult studies, the Moderna Phase 1 study, and the Mix 'n Match booster study, in addition to the aforementioned pediatric studies. One of the biggest challenges, for the ECC-VRC is the rapid turnaround needed during the pandemic. Through long hours, days, nights, and weekends, the ECC-VRC team dedicated most of the past 2 years to fighting COVID.

Their hard work is evident in the continued success of these clinical trials. Dr. Anderson said that "seeing children (including my own) that are 5-11 years of age able to receive this vaccine is really rewarding." Echoing Dr. Anderson's sentiments, Clinical Trials Director Laila Hussaini, MPH, said, "one of the most rewarding parts of the trial is to see the excitement and willingness of the kids . . . The shear enthusiasm of the participants was enough to show us that adults and kids can make a difference during the pandemic."

One day, the team hopes to return to their pre-pandemic work that includes RSV and influenza vaccines in children. For now, the VTEU team will continue their COVID work to ensure a greater understanding of pediatric response to vaccination in the months and years ahead. §

Research Highlights

CCIV members continued to advance knowledge about and treatment of major pediatric infectious diseases, including influenza, RSV, and HIV.

HIV

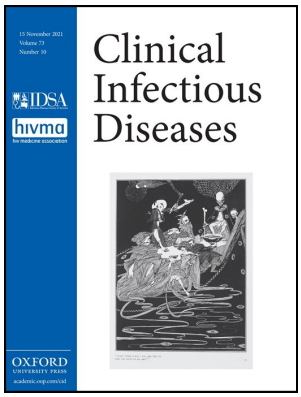
The Pediatric Adolescent Virus Elimination (PAVE) Martin Delaney Collaboratory (MDC) became the only pediatric MDC funded by the NIH this year. PAVE is led by Dr. Ann Chahroudi and her co-director, Dr. Debbie Persaud from Johns Hopkins University. Over the next five years, PAVE will use cutting-edge science to establish a deep and broad understanding of the immunopathogenesis of pediatric HIV-1 reservoirs across the age spectrum, and to demonstrate the safety and efficacy of novel therapeutics to purge and control viral reservoirs.

SARS-CoV2

In addition to work on MIS-C and vaccine clinical trials, CCIV researchers including Drs. Mehul Suthar and Jens Wrammert contributed to a number of other publications on SARS-CoV2 immunity. Dr. Suthar contributed to a number of publications investigating antibodies related to both vaccines and variants. Several of these studies were published in major journals like *Nature* and *Science*. Dr. Wrammert also contributed to the evolving understanding of SARS-CoV-2 antibodies through his work published in the *Journal of Clinical Microbiology* and the *Journal of Immunology*.

RSV

Dr. Larry Anderson contributed to a number of publications on RSV, many with a particular emphases on immune response, such as an article published in the *Journal of Virology* and another in *The Journal of Allergy and Clinical Immunology*.



Influenza

Drs. Christina Rostad and Evan Anderson, along with a team of scientists including previous CCIV faculty, Drs. Inci Yildirim and Carol Kao, published findings on influenza vaccine effectiveness in relation to hospitalizations in *Clinical Infectious Diseases* this November. They found that influenza vaccination decreased the risk of influenza-related pediatric hospitalizations by >50% across 5 influenza seasons.

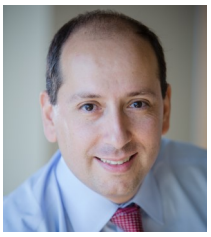
Arenavirus

Dr. Greg Melikian's lab published their findings on arenavirus in *PLOS Pathogens* in September. This study shows that productive arenavirus entry into cells is specifically enhanced by a late endosome-resident lipid, which promotes late steps of virus-cell fusion. The work was funded by two of Dr. Melikian's R01s (AI053668 and AI129862). Both R01s study virus-cell fusion.

Awards & Accomplishments

Both Drs. **Ann Chahroudi** and **Greg Melikian** were recipients of NIH Merit Awards, which affords them the freedom and stability to pursue their long-term research goals.

Dr. **Ann Chahroudi** was also named the Co-Director for Basic Science of the Emory Center for AIDS Research (CFAR).



Dr. **Andres Camacho Gonzales** was elected to the society for Pediatric Research and named the Associate Director of CFAR Clinical Research Core.

Dr. **Andi Shane** was appointed as Deputy Editor and then acting Editor-in-Chief for the *Journal of the Pediatric Infectious Diseases Society* (*JPIDS*).

Dr. **Evan Anderson** was also selected as a Fellow of both the Pediatric Infectious Diseases Society and the Infectious Disease Society of America.

Dr. **Christina Rostad** was selected for the Infectious Diseases Clinical Research Consortium Mentorship Program.

Dr. **Matt Linam** was appointed Children's Medical Director of Outcomes and Analytics. Dr. Linam also joined the Emory Professional Leadership Enrichment and Development Program.

Drs. **Mehul Suthar** and **Jens Wrammert** were awarded the 2021 Innovation of the Year from the Emory Office of Technology Transfer for their technology "Serological test for SARS-CoV-2." They also earned the DOP 2021 Faculty and Staff Award for Best Scientific Publication—Clinical/Translational.

Dr. **Brian Zanoni** was selected to serve on the NIH-CDC-HIVMA/IDSA panel which writes the guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Dr. Zanoni also joined the Global Health Institute Scholars Award Program, as well as the Emory Professional Leadership Enrichment and Development Program.

Dr. **Larry Anderson** and Dr. **Murali Kaja** were named as members of the MilliPub Club.

Dr. **Maud Mavigner** was awarded an NIH R56 award (R56 AI165149) to study long-lived cells that serve as an HIV reservoir. The objective of this proposal is to evaluate novel pharmacologic agents targeting the Wnt/β-catenin signaling pathway that controls the self-renewal of long-lived memory CD4+ T cells.

Upcoming Events

CCIV Weekly Seminars

CCIV Monday Seminars are held every Monday from 1-2 PM. Check out the most current seminar schedule and find the Zoom link to participate on the CCIV website.

COVID Force Seminars

January 28, 2022—REGISTER HERE!

> "Successful Research Takes a Village: Insight gained from the Longitudinal Surveillance of SARS-CoV-2 Antibodies in Pediatric Healthcare Workers Study" from Claudia Morris, MD, FAAP, Miriam Vos, MD, MSPH, and Jens Wrammert, PhD

CCIV Research Grand Rounds

Our Research Grand rounds, featuring Donna L. Farber, Ph.D. from Columbia University College of Physicians and Surgeons, will be on 4/20/2022. More information to come!

Resources

CCIV and Children's Publication Citation

Remember to cite CCIV and Children's Healthcare of Atlanta in your publications. This is vital to ensure recognition of our work by both Emory and Children's. This request/requirement applies to all center members, whether lab-based on non-lab based. Children's has been a significant supporter of the research operations that make all of our work possible and should be acknowledged.

The proper affiliation citation is: Center for Childhood Infections and Vaccines (CCIV) of Children's Healthcare of Atlanta and Emory University Department of Pediatrics, Atlanta, GA USA.

CCIV's Website got a remodel!

Do you have a profile on our website you want to update? Fill out this form to do so.

Social Media: @EmoryCHOA_CCIV

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