

# 11TH ANNUAL PEDIATRIC RESEARCH SYMPOSIUM

FRIDAY APRIL 29, 2022  
8:00AM - 5:00PM

Poster Sessions at:  
12:10PM-1:40PM  
3:40PM-5:00PM

## LOCATION:

RADY CHILDREN'S HOSPITAL  
EDUCATION & OFFICE BUILDING  
(EOB) ROOM 1900  
7960 BIRMINGHAM DRIVE  
SAN DIEGO, CA 92123

## KEYNOTE SPEAKERS

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- **Elizabeth Winzeler, PhD**  
University of California, San Diego
- **Carrie Byington, MD**  
University of California, Office of  
the President

## PRESENTERS

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### Session 1: Pediatric COVID

- Alessandro Sette, Dr.Biol.Sci
- Xin Sun, PhD
- Natasha Martin, DPhil/PhD

### Session 2: Pediatric Cancer

- Judith Varner, PhD
- Catriona Jamieson, MD, PhD
- Jing Yang, PhD

### Session 3: Congenital Heart Disease

- Stephanie Lindsey, PhD
- Andrew McCulloch, PhD

**UC San Diego**  
SCHOOL OF MEDICINE  
Department of Pediatrics

**Rady  
Children's**  
Hospital  
San Diego

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## Program Schedule

Friday, April 29, 2022

8:00 - 8:10	<b>Welcome</b> <b>Gabriel Haddad, MD</b> Distinguished Professor of Pediatrics and Neurosciences Chair, Department of Pediatrics University of California, San Diego Physician-In-Chief & Chief Scientific Officer Rady Children's Hospital - San Diego	(10)
8:10 - 8:20	<b>Patrick Frias, MD</b> President and Chief Executive Officer Rady Children's Hospital - San Diego	(10)
8:20 - 8:55	<b>Keynote Address: "The Malaria Drug Accelerator – a Model for Finding New Therapies for Underserved Diseases"</b> (Introduction by Gabriel Haddad, MD) <b>Elizabeth Winzeler, PhD</b> Professor of Pediatrics Divisions of Host-Microbe Systems and Therapeutics Department of Pediatrics University of California, San Diego	(35)
<b>COVID</b> <b>Moderator Welcome: Victor Nizet</b> (8:55-9:00 - Clinical Relevance)		
9:00 - 9:20	<b>"Adaptive Responses to SARS Cov2 Infection and Vaccination"</b> <b>Alessandro Sette, Dr.Biol.Sci.</b> Professor Center for Autoimmunity and Inflammation, Center for Infectious Disease and Vaccine Research La Jolla Institute for Immunology	(20)
9:20 - 9:40	<b>"Lung in COVID-19 and other Respiratory Viral Diseases"</b> <b>Xin Sun, PhD</b> Professor of Pediatrics & Biological Sciences Division of Respiratory Medicine Department of Pediatrics Department of Biological Sciences University of California, San Diego	(20)

9:40 - 10:00	<p><i><b>"UC San Diego's Return to Learn COVID Response: Insights from Modeling"</b></i></p> <p><b>Natasha Martin, DPhil/PhD</b>  Associate Adjunct Professor of Medicine  Division of Infectious Diseases and Global Public Health  University of California, San Diego</p>	(20)
10:00 - 10:25	<i><b>PANEL DISCUSSION + Adri Tremoulet, Mark Sawyer</b></i>	(25)
10:25 - 10:40	<i><b>Break</b></i>	(15)
<p style="text-align: center;"><b>CANCER</b>  <b>Moderator Welcome: Ezra Cohen</b>  <i>(10:40-10:45 - Clinical Relevance)</i></p>		
10:45 - 11:05	<p><i><b>"Targeting Macrophages to Improve Cancer Therapy"</b></i></p> <p><b>Judith Varner, PhD</b>  Professor of Pathology and Medicine  Divisions of Hematology, Oncology &amp; Blood and Marrow Transplantation  University of California, San Diego</p>	(20)
11:05 - 11:25	<p><i><b>"Detection and Eradication of Pediatric Acute Myeloid Leukemia Stem Cells"</b></i></p> <p><b>Catriona Jamieson, MD, PhD</b>  Deputy Director, UC San Diego Moores Cancer Center  Professor of Medicine and Chief, Division of Regenerative Medicine  Koman Family Presidential Endowed Chair in Cancer Research  University of California, San Diego</p>	(20)
11:25 - 11:45	<p><i><b>"Epithelial-Mesenchymal Plasticity in Tumor Metastasis"</b></i></p> <p><b>Jing Yang, PhD</b>  Professor of Pharmacology and Pediatrics  Division of Hematology-Oncology  University of California, San Diego</p>	(20)
11:45 - 12:10	<i><b>PANEL DISCUSSION + Bill Roberts, Peter Zage</b></i>	(25)

12:10 - 1:40    ***Lunch and Poster Session***    (90)  
***Poster Session - Room 1900***  
***Please see booklet for abstracts***

**CARDIAC**  
**Moderator Welcome: Bob Ross**  
(1:40-1:45 - Clinical Relevance)

1:45 - 2:05    ***"Mechanics of a Broken Heart"***    (20)  
**Stephanie Lindsey, PhD**  
Assistant Professor, Mechanical and Aerospace Engineering  
University of California, San Diego

2:05 - 2:25    ***"Intersections of Pediatrics and Engineering Science at UC San Diego"***    (20)  
**Andrew McCulloch, PhD**  
Shu Chien Chancellor's Endowed Chair in Engineering and Medicine  
Director, UC San Diego Institute for Engineering in Medicine  
University of California San Diego

2:25 - 2:50    ***PANEL DISCUSSION + Chris Davis, Beth Printz, Paul Grossfeld***    (25)

2:50 - 3:25    ***Closing Keynote: "The Future of Research: Collaboration is Key"***    (35)  
(Introduction by Gabriel Haddad, MD)  
**Carrie Byington, MD**  
Executive Vice President  
University of California Health  
University of California Office of the President

3:25 - 3:40    ***Closing Remarks and Award Winners Announced***    (15)

3:40 - 5:00    ***Poster Session***  
***Room 1900***  
***Please see booklet for abstracts***

# KEYNOTE SPEAKER BIO

## **Elizabeth Ann Winzeler, Ph.D.**

Professor of Pediatrics

Divisions of Host-Microbe Systems and Therapeutics

Department of Pediatrics

University of California, San Diego



Elizabeth Ann Winzeler is a Professor at the University of California, San Diego, School of Medicine. She leads a group that uses systematic, data intensive methods to solve problems at the interface of host pathogen biology typically involving large collections of chemical screening data and whole genome sequencing at UC San Diego.

She is a fellow of the American Academy in Microbiology. She has published more than 175 publications. She has received awards from the Keck Foundation, the Ellison Medical Foundation, and the Bill and Melinda Gates Foundation. She has received the 2014 Bailey-Ashford Medal, 2017 Medicines of Malaria Venture Project of the year, 2018 Alice and C.C. Wang Award, 2018 William Trager Award, 2020 Rady Children's Hospital Awards of Excellence in Basic Research, the 2020 UCSD Health Sciences Women Leadership Award and was recently elected to the National Academy of Medicine.

# KEYNOTE SPEAKER BIO

## **Carrie L. Byington, M.D.**

Executive Vice President

University of California Health

University of California Office of the President

Professor of Pediatrics

University of California, San Francisco



Dr. Carrie L. Byington is the Executive Vice President (EVP) for the University of California's health enterprise and a Professor of Pediatrics at the University of California, San Francisco. In her role as EVP, Dr. Byington leads the country's largest public academic health care system. UC's health delivery and education enterprise is comprised of six academic health centers which include 12 hospitals and 20 health science schools, many of which are ranked among the country's best. In her role, she has led the COVID-19 response for the UC System including preparing hospitals for surge, protecting ~ 100,000 health care workers, developing testing, supporting the health and safety of ~ 600,000 students and employees on 10 campuses, coordinating the COVID vaccine roll-out, and partnering with the state of California to provide expertise and capacity for pandemic response.

Trained as a pediatrician specializing in the treatment of infectious diseases, Dr. Byington is a member of the National Academy of Medicine. She is a patent holder and member of the National Academy of Inventors. She previously served as Chair of the American Academy of Pediatrics' (AAP) Committee on Infectious Diseases (2014-2018) and is an expert on bacterial and viral respiratory pathogens, pathogens with pandemic potential, and vaccine-preventable infections. In her role with the AAP, she has been an external advisor and technical expert to the CDC on evaluation of children with suspected or confirmed Ebola, EVD68, influenza, and Zika viruses and other infectious diseases. Her research team contributed to the development of the FDA-cleared BioFire diagnostic platform which includes an EUA for the Respiratory Panel 2.1 which tests for SARS-CoV2 and 21 other pathogens. She chairs the Association of Academic Health Centers President's Council on Health Security.

Dr. Byington has had a distinguished career in academic medicine. Prior to assuming leadership and faculty positions with the University of California, Dr. Byington served simultaneously as Vice Chancellor for Health Services to the Texas A&M System and Senior Vice President for Health Sciences and Dean of the College of Medicine at Texas A&M University. Prior to those roles, Dr. Byington was a Professor of Pediatrics at the University of Utah and served as Associate Vice President of Faculty and Academic Affairs for the University of Utah Health Sciences Center and Vice Dean for Academic Affairs and Faculty Development to the University of Utah School of Medicine.

As a Mexican-American woman in academic medicine, she has worked throughout her career to end health disparities and increase health equity. She has also worked for a more inclusive academy. In her administrative roles, she has developed and supported faculty mentoring programs and policies and processes for faculty diversity, salary equity, and parental leave. Dr. Byington has created pipeline programs for under-represented students interested in health professions, has held training grants that support research and career development experiences for American Indian undergraduates, and has mentored more than 100 students, trainees, and faculty members, the majority of whom are under-represented in academics or medicine. She is a member of the scientific advisory board of the Robert Wood Johnson Harold Amos Program and the Board of Directors of the Commonwealth Fund, both dedicated to ending disparities.

Dr. Byington is a graduate of Texas A&M University (BS Biology) and the Baylor College of Medicine, both with honors. She completed a residency in pediatrics at Baylor College of Medicine, where she was a neonatal chief resident, and a fellowship in infectious diseases at UCSF.

# PRESENTER ABSTRACT

## *ADAPTIVE RESPONSES TO SARS COV2 INFECTION AND VACCINATION*



Alessandro Sette, Dr.Biol.Sci  
Professor of Pediatrics  
Director, Recurrent Fever Disorders Clinic  
Division of Allergy, Immunology & Rheumatology  
University of California, San Diego  
Rady Children's Hospital – San Diego

I will present data from several studies performed in the last two years. The results show that SARS CoV2 infection induces a multi-specific and multifunctional adaptive responses which is durable over the 6-8 months period. Neutralizing antibodies are likely key to protect from infection, but substantial contributions of T cells are likely at the level of protection from disease. Side-by-side longitudinal comparison of different vaccine platforms reveals durable B and T cell responses, and allow correlation with vaccine efficacy. T cell reactivity is largely preserved at the level of SARS CoV2 variants, including Omicron and Delta.

# PRESENTER ABSTRACT

## *"LUNG IN COVID-19 AND OTHER RESPIRATORY VIRAL DISEASES"*



### **Xin Sun, PhD**

Professor of Pediatrics & Biological Sciences  
Division of Respiratory Medicine  
Department of Pediatrics  
University of California, San Diego

The lung is at the center of severe acute respiratory syndrome corona virus 2 (Sars-CoV-2) infection. The types of lung cells susceptible to SARS-CoV-2 infection, their acute response to infection, and the long-term consequence of infection (long-haul COVID) are only some of the questions at the center of investigation by the lung community. Through studies down to single cell resolution, our findings provided insights to these questions. Continued investigation of lung and Sars-CoV-2 interplay will minimize COVID-19 impact and promote the return to lung and human health.

# PRESENTER ABSTRACT

## *UC SAN DIEGO'S RETURN TO LEARN COVID RESPONSE: INSIGHTS FROM MODELING*



**Natasha Martin, DPhil/PhD**

Associate Adjunct Professor of Medicine

Division of Infectious Diseases and Global Public Health

University of California, San Diego

The UC San Diego Return to Learn program is a data-driven, adaptive COVID mitigation program, which has provided support to the campus and wider community throughout the pandemic. This talk will describe the core components of the strategy, technological innovations developed through the program, and partnerships with the county health department. In particular, this talk will focus on the innovative epidemic modeling and wastewater initiatives, which have informed the COVID response.

# PRESENTER ABSTRACT

## *TARGETING MACROPHAGES TO IMPROVE CANCER THERAPY*



### **Judith Varner, PhD**

Professor of Pathology and Medicine  
Divisions of Hematology, Oncology & Blood and Marrow  
Transplantation  
University of California, San Diego

Solid tumors develop as a result of inherited or acquired mutations and are characterized by impaired anti-tumor immune responses. The new immune based therapies such as T cell checkpoint inhibitors and chimeric antigen receptor T cells have been able to reactivate anti-tumor immunity in some patients, and the technology is offering great promise to cancer patients. However, most patients do not respond to these immune-based therapies. A major source of resistance to T cell-based therapeutics is the presence of myeloid cells in the tumor microenvironment. Studies from our laboratory and many others have shown that monocytes, macrophages and neutrophils accumulate in tumors via recruitment from the circulation or by proliferation from resident myeloid cells. Tumor associated myeloid cells create an immune suppressive and tumor-promoting, wound-healing type microenvironment that inhibits T cell survival and stimulates tumor cell aggression. Our lab identified a key myeloid cell signaling protein, PI3Kgamma, that regulates the trafficking of myeloid cells into the tumor microenvironment and promotes the immune suppressive, wound-healing transcriptional program that leads to resistance to chemotherapeutics and immune therapeutics. A novel investigational PI3Kgamma inhibitor, eganelisib, developed in collaboration with our group, re-activates anti-tumor immune responses and synergizes with chemotherapy and immune checkpoint blockade. Eganelisib has shown promise in cancer clinical trials. Currently in Phase 3 clinical trials for the treatment of triple negative breast cancer, the PI3Kgamma inhibitor eganelisib represents a new avenue to therapy for many cancer patients.

# PRESENTER ABSTRACT

## *DETECTION AND ERADICATION OF PEDIATRIC ACUTE MYELOID LEUKEMIA STEM CELLS*



### **Catriona Jamieson, MD, PhD**

Deputy Director, UC San Diego Moores Cancer Center

Professor of Medicine and Chief, Division of Regenerative Medicine

Koman Family Presidential Endowed Chair in Cancer Research

University of California, San Diego

While chromosomal aberrations and somatic DNA mutations can drive therapy resistant adult leukemia stem cell (LSC) generation in adult acute myeloid leukemia (AML), alternative splicing deregulation has emerged as a key arbiter of antecedent pre-malignant hematologic disorder transformation, in part through acquisition of splicing factor gene mutations. In contrast to adult AML, splicing factor mutations have rarely been detected by next generation sequencing (NGS) analysis of bulk populations of cells in pediatric AML, which is plagued by high levels of therapeutic resistance and relapse. To elucidate molecular drivers of the LSC generation in pediatric AML, we coupled single cell multi-omics analysis with whole transcriptome hematopoietic stem cell (HSC) and hematopoietic progenitor cell (HPC) RNA sequencing (RNA-seq). Notably, both analyses revealed marked splicing deregulation and a relation to embryonic gene expression profiles. Most interestingly, we found significant reduction in embryonic alternative splicing repressor, RBFOX2, expression and an embryonic stem cell-like pattern of exon skipping in pediatric AML derived HSCs and HPCs compared with non-leukemic samples. In addition, we found that splicing deregulation, as a consequence of decreased RBFOX2 expression, could render pediatric AML derived HSCs and HPCs inherently vulnerable to Rebecsinib thereby providing the impetus for therapeutics.

# PRESENTER ABSTRACT

## *EPITHELIAL-MESENCHYMAL PLASTICITY IN TUMOR METASTASIS*



### **Jing Yang, PhD**

Professor of Pharmacology and Pediatrics  
Division of Hematology-Oncology  
University of California, San Diego

During metastasis, epithelial tumor cells dissociate from each other, disseminate into the systemic circulation, and then establish secondary tumors in distant sites. A developmental program termed Epithelial-Mesenchymal Transition (EMT) is implicated in promoting the dissemination of single carcinoma cells during metastasis. Our previous work shows that activation of the EMT transcription factor Twist1 is sufficient to promote carcinoma cells to undergo EMT and disseminate into blood circulation. Importantly, in distant sites, turning off Twist1 to allow reversion of EMT is essential for disseminated tumor cells to proliferate and form macrometastases. These data indicate that EMT is dynamically regulated during tumor metastasis. Our recent studies aim to understand how EMT is dynamically regulated in response to signals from the tumor microenvironment to impact EMT and tumor metastasis.

Breast tumors are often detected through manual palpation due to their apparent “hardness” compared to normal tissue. Increase in tissue stiffness is correlated with distant metastasis and poor outcome in breast cancer patients. Several studies, including ours, show that increasing matrix stiffness can induce Epithelial-Mesenchymal Transition (EMT) and cancer cell invasion in human and mouse 3D mammary epithelial organoids, suggesting that mechanical properties of extracellular matrix (ECM) directly regulate tumor metastasis. Using 3D reconstituted extracellular matrixes that recapitulate the range of physiological stiffness from normal mammary glands to breast tumors, we identified TWIST1 as a key player driving EMT and invasion in response to increasing ECM stiffness. I will present our recent progress in understanding the Twist1 mechanotransduction pathway that senses and transmits mechanical cues from extracellular matrix in the tumor microenvironment to promote EMT and invasion during tumor progression. I will also discuss the involvement of this pathway in Ewing’s Sarcoma metastasis.

# PRESENTER ABSTRACT

## *MECHANICS OF A BROKEN HEART*



### **Stephanie Lindsey, PhD**

Assistant Professor, Mechanical and Aerospace Engineering  
University of California, San Diego

Congenital heart defects (CHDs) are among the most severe congenital abnormalities, accounting for over 29 percent of deaths from developmental abnormalities. Of these, approximately 25 percent require palliative surgery in the first year of life. While the precise origins of CHDs remain unknown, they arise from disturbances in cardiac morphogenesis, a complex interconnected process involving changing hemodynamic forces concomitant with cellular and molecular signaling. Despite advances in surgical and medical management, their potential to restore cardiac function remains compromised, largely due to continued complications from implanted devices. To that end, I explore innovative ways to advance treatment options for patients suffering from CHD, through the identification of new mechanistic insights into the origin of such defects and the optimization of current treatment options. To understand causation, I rely on the chick embryo as a mechanical model of development. Towards optimization, I explore patient specific and subject specific simulations of tissue engineered vascular grafts in single ventricle physiology patients.

# PRESENTER ABSTRACT

## *INTERSECTIONS OF PEDIATRICS AND ENGINEERING SCIENCE AT UC SAN DIEGO*



### **Andrew McCulloch, PhD**

Shu Chien Chancellor's Endowed Chair in Engineering and Medicine  
Director, UC San Diego Institute for Engineering in Medicine  
University of California San Diego

UC San Diego has a long and enviable tradition of interdisciplinary collaboration between engineering and both basic health sciences and translational medicine. The Institute of Engineering in Medicine has 320 members from engineering and health sciences and 14 centers. About half are disease focused like the Cardiac Biomedical Science and Engineering Center (CBSEC) and the Center for Engineering in Diabetes. The others are technology focused including the Center for Mobile Health Systems and the Center for Multiscale Imaging. Collaborations of engineering with Pediatrics and Rady Children's Hospital have grown significantly in recent years, and include projects in medical imaging, congenital heart disease, musculoskeletal diseases and sports medicine, mobile health monitoring, infectious disease research, medical device development and genomics. I will summarize some of this work, preview new initiatives in type 1 diabetes and sports medicine, and give a more in-depth example of how AI and computational biology are creating new opportunities to improve the management of patients with congenital heart diseases.

## ABSTRACTS: POSTER PRESENTATIONS

### ACADEMIC GENERAL PEDIATRICS, DEVELOPMENTAL/BEHAVIORAL PEDIATRICS & NEWBORN NURSERY

#### Poster #1:

#### **“Think Globally, Act Locally” (TGAL): A cross-border global health residency elective**

Vanessa P. Scott<sup>1</sup> , Michelle Rivera-Vega<sup>1</sup> , Shannon O'Donnell, Rebeca Rivera-Gomez, Angelica Martinez, Paula Aristizabal<sup>2</sup> , Chris Cannavino<sup>2</sup>

**Background:** Global health (GH) experiences during residency have been shown to improve confidence in physical exam and communication skills, cultural sensitivity, and better understanding of needs in underserved populations. While participation in GH electives has increased, most experiences are 1-2 months, require long-distance travel, and are costly. There are very few, if any, short-term, accessible, and low-cost pediatric residency GH electives.

**Objective:** To assess outcomes of a unique, local 2-week global health elective, “Think Globally, Act Locally” (TGAL), which exposes residents to the diverse cross-border, immigrant and refugee populations in San Diego, California and Tijuana, Mexico (Table 1).

**Methods:** After finishing the elective, residents completed a retrospective pre-post evaluation assessing confidence in providing care in various settings (using a 5-point Likert scale) and five open-ended questions focused on satisfaction and feedback. Frequency statistics were used to describe the characteristics of the participants and survey responses. Mean pre- and post-rotation confidence scores were compared to assess change in resident confidence. A paired sample t-test was run for each pair of mean confidence pre- and post- scores, and a significant difference was noted with  $p < 0.05$ . Resident and program cost was assessed. SAS 9.4 used for analysis.

**Results:** Of the 9 residents who experienced the TGAL elective, 8 completed the survey (89%). Most were in their second year of residency (78%), non-Hispanic White (89%), female (66%) and ages ranged from 28-34 years old. Self-reported resident confidence significantly increased for almost every domain assessed (Figure 1). The domains which showed the most significant increase included providing ongoing outpatient care to refugee, immigrant and cross-border populations, providing routine refugee health assessments, and sending patients to hospitals in Tijuana to receive adequate patient care. Overall elective assessments were positive. Key themes included learning about the challenges of serving diverse cross border populations, difficulties immigrants/refugees face, and differences between healthcare systems in the United States vs Mexico. Resident highlights included “working with Mexican physicians at the Tijuana hospitals, seeing the pathology, and refugee health assessments.” (Table 2) Participant cost was \$0-\$200 per resident.

**Conclusion:** This unique GH elective improved resident confidence for providing care in resource-limited settings to a diverse cross-border and immigrant/refugee population. Resident satisfaction was overall excellent and the program cost was minimal

## ADOLESCENT MEDICINE

### Poster #2:

#### Exploring Perceived Facilitators and Barriers to using Telemedicine for Gender-Affirming Care: A Qualitative Study

David J. Inwards-Breland MD MPH, Debra Yeh MD, Tay Richardson BSW, Bixby Marino-Kibbee LCSW, Maja Marinkovic MD, Kay Rhee MD

**Background:** Telemedicine use for gender-affirming medical interventions has increased. There is a paucity of research in the use of telemedicine for gender care and TNB perspectives on its use. Our objective was to explore perspectives of TNB youth in the use of telemedicine for gender-affirming care.

**Methods:** Participants aged 13-21 years, who identified as TNB, were recruited from the Center for Gender Affirming Care to participate in a semi-structured interview and demographics survey. Interviews were audio-recorded and transcribed verbatim. Survey results were analyzed using descriptive statistics. Two independent coders reviewed the transcripts, developed a coding scheme, and reached consensus on discrepancies. ATLAS.ti® was used for thematic analysis.

**Results:** 30 participants completed an interview/survey. Mean age was 17-years, with 30% identifying as female/trans female, 47% male/trans male, and 23% identifying as nonbinary or gender fluid. Several key themes emerged 1) participants favored in person visit over telemedicine because of connection with known provider; 2) low perceived knowledge about telemedicine despite having good working knowledge; 3) advantages included convenience, and disadvantage included a lack of provider's ability to fully assess their treatment progress; 4) telemedicine is good for risk/benefits of hormone therapy (initial visit not requiring a physical exam), lab results, dose change discussions and top surgery evaluations with social worker; 5) mixed feelings of clinic staff's role in telemedicine; and 6) little concerns around confidentiality and having a secure line.

**Conclusions:** Despite participant's preference for in person visits with providers, telemedicine is a viable option for TNB youth in receiving gender-affirming medical care because of convenience, confidentiality and ideal for initial and follow up visits. Efforts in increasing telemedicine use could center on education in its use as well as role of clinic staff and could be an ideal venue to use patient reported outcomes measures (PROM) to track clinical progress.

### Poster #3:

#### Healthcare and community needs assessment for transgender and non-binary youth and their caregivers at the Center for Gender Affirming Care at Rady Children's Hospital San Diego

Byron Maltez MS4; Maya Kumar, MD; David Inwards-Breland, MD; Maja Marinkovic, MD

**Background:** Transgender and nonbinary (TNB) youth experience disproportionately high rates of psychiatric and medical comorbidities. The health of TNB youth is in part influenced by their caregivers, who carry significant impact on support and access to care. However, the lived experiences and precise needs of TNB youth in our community and their caregivers remain to be fully elucidated.

**Methods:** Upon obtaining appropriate consent, an anonymous survey was administered to assess the needs of TNB youth (age ≥13y) and their caregivers at the Center for Gender Affirming Care (CGAC).

**Results:** A total of 41 subjects (19 TNB youth, 22 caregivers) participated. Most youth reported living in their affirmed gender all the time at home [15/19 (79%)] and at school [11/18 (61%)]. While 11/19 (58%) youth reported feeling affirmed at home all the time, only 6/18 (33%) felt similarly at school. Most desired greater access to name-change resources [9/14 (64%)] and in person support groups [7/14 (50%)], and expressed interest in discussing mental health, access to trans-competent providers, and healthy eating with their clinicians. Importantly, only a minority strongly agreed that they felt comfortable presenting to the Emergency Department [5/19 (26%)] or discussing their gender identity with their primary care physician [8/18 (44%)]. Only 36% (8/22) of caregivers reported having adequate support at home all the time. Most desired greater access to support groups [14/19 (74%)] and educational opportunities [10/19 (53%)]. Over half strongly agreed that they felt confident affirming their child's gender identity at home [13/22 (59%)], at school [12/21 (57%)], and in public [12/22 (55%)]. 95% of youth (18/19) and caregivers (21/22) felt supported by CGAC overall.

**Conclusions:** Per our study at CGAC, TNB youth and their caregivers felt well-supported overall, however, most desired additional resources and support—at home, at school, and within healthcare settings

### *ALLERGY/IMMUNOLOGY/RHEUMATOLOGY*

#### **Poster #4:**

#### **Asthma Symptom Action Plan: A Standardized Form for San Diego County Schools**

Devon Ball, MD and Susan Laubach, MD

**Background:** Asthma is one of the most common chronic medical conditions affecting school-aged children. One in two children with asthma report school absences due to asthma per year. SAMPRO (School-based Asthma, Allergy & Anaphylaxis Management Program) endorses standardized asthma action plans (AAP) in schools. A coalition of physicians, school nurses, and parents developed a standardized Asthma Symptom Action Plan across San Diego county school districts based on one of SAMPRO's plans. Little is known about the variety of forms currently in use in San Diego (SD) County.

**Methods:** Data was collected from the main websites for all 42 SD county school districts. Information regarding health forms was documented including types of forms and ease of access to these forms. All forms were compared for similarities and to assess any standardized form used across schools.

**Results:** Only thirteen of forty-two (31%) SD county school district sites had an easily accessible link to an AAP. Of these thirteen forms, six (46%) met all nine "essential features" of a school-related AAP (from SAMPRO). For the sites that did not have an easily accessible AAP, six (14%) had medication authorization or "self-carrying" medication forms available- which allow students to "self-medicate" (applicable for older students), but do not give guidance regarding treatment instructions. Twenty-one (50%) sites were without easily accessible forms- two (5%) sites provided links to the school-based asthma treatment form from the American Lung Association.

**Conclusions:** Currently, there is not a standardized form for asthma symptom treatment across SD county schools. Our results highlight the need for a standardized asthma symptom action plan across SD County schools to improve management of asthma exacerbations in students. We have initiated a quality improvement project to encourage adoption of the standardized form developed by our Coalition, including easy online access to the form on district websites.

## ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

### Poster #5:

#### Kawasaki disease in the time of COVID-19

Jennifer A. Burney, PhD<sup>1</sup>, Samantha C. Roberts, MS<sup>3</sup>, Laurel L. DeHaan, MS<sup>2</sup>, Chisato Shimizu, MD<sup>3</sup>, Emelia V. Bainto, BS<sup>3</sup>, Jane W. Newburger, MD<sup>4</sup>, Samuel Dominguez, MD<sup>5</sup>, Pei-Ni Jone, MD<sup>5</sup>, Preeti Jaggi, MD<sup>6</sup>, Jacqueline R. Szmuszkovicz, MD<sup>7</sup>, Anne H. Rowley, MD<sup>8</sup>, Nichole Samuy, MD<sup>9</sup>, Paul Scalici, MD<sup>9</sup>, Adriana H. Tremoulet, MD, MAS<sup>3</sup>, Daniel R. Cayan, PhD<sup>2</sup>, Jane C. Burns, MD<sup>3</sup> and the KIDCARE Study Investigators

<sup>1</sup> School of Global Policy & Strategy, University of California San Diego, La Jolla, CA, USA

<sup>2</sup> Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA, USA

<sup>3</sup> Department of Pediatrics, University of California San Diego and Rady Children's Hospital San Diego, La Jolla, CA, USA

<sup>4</sup> Department of Cardiology, Boston Children's Hospital, and Department of Pediatrics, Harvard medical School, Boston, MA, USA

<sup>5</sup> Department of Pediatrics, Pediatric Cardiology, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

<sup>6</sup> Emory University, Department of Pediatrics and Children's Healthcare of Atlanta

<sup>7</sup> Division of Pediatric Cardiology, Children's Hospital Los Angeles, Keck School of Medicine of the University of Southern California, Los Angeles, CA

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**Background:** Public health measures implemented during the COVID-19 pandemic had widespread effects on population behaviors, transmission of infectious diseases, and exposures to environmental pollutants. This provided an opportunity to study how these factors potentially influenced the incidence of Kawasaki disease (KD), a self-limited pediatric vasculitis of unknown etiology.

**Methods:** For the multicenter (28 US centers) study, we collected date of fever onset for each KD patient (diagnosed between January 1, 2018 to December 31, 2020). For Rady Children's Hospital San Diego (RCHSD), we collected detailed demographic and clinical data of KD patients (diagnosed from January 1, 2002-November 15, 2021) and publicly available, anonymized mobile phone data and median household income by Census Block Group.

**Results:** Total KD cases for the multicenter study were as follows: 2018: 894; 2019: 905; 2020: 646. The 28% decline in KD cases during 2020 was uneven across the U.S. For RCHSD, there was a disproportionate decline in KD cases for children 1-5 years, males, and children of Hispanic or Asian descent. Mobility data did not suggest that shelter-in-place measures influenced the number of KD cases. School closures, masking mandates, decreased ambient pollution, and decreased circulation of respiratory viruses all overlapped to different extents with the period of decreased KD cases. KD in San Diego rebounded in the spring of 2021 coincident with lifting of mask mandates.

**Conclusions:** Nationwide, KD cases fell by 28% during the pandemic, and remained low during the period of masking and school closure. Mobility data indicated that differential intensity of sheltering in place was not associated with KD incidence. These findings demonstrate that social behavior has a strong influence upon the exposure to the agent(s) that trigger KD and support a respiratory portal of entry for the agent(s).

## ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

### Poster #6:

#### Implementation of a Severe Asthma Program Clinic Improves Patient Symptoms, Education, and Asthma Control

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**Background:** Inadequate clinic time for patients with severe asthma can lead to insufficient care, poor disease control, reduced quality of life, increased ED visits/hospital admissions, and higher treatment costs. Establishing a specialized multidisciplinary program for patients with severe asthma can increase patient knowledge, improve symptoms and asthma health outcomes.

**Methods:** The Severe Asthma Program (SAP) consisting of Allergy/Immunology, Pulmonology, clinical pharmacy, respiratory therapy, case management, and quality analyst was started for comprehensive coordinated evaluation, therapy, and education of patients with severe/uncontrolled asthma. We analyzed pre/post-education quiz scores, ED visits/hospitalization days, Asthma Therapy Assessment Questionnaire (ATAQ) scores, and PROMIS Asthma Impact scores using paired t-tests.

**Results:** The study population currently includes 66 patients with severe uncontrolled asthma seen in the multidisciplinary SAP Clinic. The mean number of ED visits and hospitalization days from the year before to the year after joining SAP decreased from 1.71 to 0.98 ( $p < 0.001$ ;  $n = 66$ ) and 2.24 to 1.05 ( $p < 0.001$ ;  $n = 66$ ), respectively. The ATAQ scores from the most recent clinic visit before joining SAP to the most current score decreased from 4.53 to 2.15 ( $p < 0.001$ ;  $n = 55$ ). Pre- and post-educational module quiz scores improved after the 1st visit from 2.70 to 2.94 ( $p < 0.001$ ;  $n = 50$ ), after the 2nd visit from 3.16 to 3.92 ( $p < 0.001$ ;  $n = 25$ ), and after the 3rd visit from 3.0 to 3.79 ( $p < 0.001$ ;  $n = 14$ ). PROMIS Asthma Impact scores improved from 20.42 at visit 1 to 17.8 at visit 2 to 16.0 at visit 3. These results allowed us to quantify the clinic's effectiveness.

**Conclusions:** Implementation of SAP led to better asthma education, symptom control, and health outcomes as demonstrated by significant improvements in pre/post- educational module quiz scores, ED visits/hospitalization days, ATAQ scores, and PROMIS Asthma Impact scores.

### Poster #7:

#### Immune phenotype and SARS-CoV-2-specific T cell responses in multisystem inflammatory syndrome in children (MIS-C)

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We studied SARS-CoV-2-specific T cell responses in 33 subacute MIS-C children enrolled from May 2020 to March 2022 using peptide pools derived from SARS-CoV-2 spike or non-spike proteins. Coordinated CD4<sup>+</sup> and CD8<sup>+</sup> SARS-CoV-2-specific T cells were detected in ten subjects (30.3%). CD4<sup>+</sup> T helper responses only were detected in 16 subjects (48.5%); and CD8<sup>+</sup> cytotoxic T cell responses alone were documented in 2 subjects (6.1%). Six subjects did not respond to any of the peptide pools. The chemokine receptor CCR6, which determines homing to the endothelium, was highly expressed on SARS-CoV-2-specific CD4<sup>+</sup> but not CD8<sup>+</sup> T cells. CD4<sup>-</sup> CD8<sup>-</sup> double negative T cells were abundant in circulation and responded to SARS-CoV-2 peptide pools, especially in children who had very low T cell numbers in circulation. To address possible T cell exhaustion in these lymphopenic, inflamed children that may have caused downregulation of the CD4 and CD8 coreceptor, we studied the expression of Programmed Cell Death 1 (PD1) on SARS-CoV-2-specific CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells, which was expressed in over 30% of CD4<sup>-</sup> CD8<sup>-</sup> T cells. However, PD1 expression on CD4<sup>-</sup> CD8<sup>-</sup> SARS-CoV-2-specific could not be caused by exhaustion, but it may define a functional T cell subset as reported for CD8<sup>+</sup> T cells in COVID-19 convalescent adult subjects.

We also studied Vb 23.1 T cell receptors (TCRs) that other groups reported to be pathogenic in MIS-C and found this TCR expressed in up to 2.7% of the T cells in circulation, including CD4<sup>+</sup>, CD8<sup>+</sup> T cells. Only a small % Vb 23.1 T cells expanded in response of SARS-CoV-2 peptides suggesting that their fine specificity is not only within the anti-viral T cell response. Finally, we studied the immune phenotype of antigen presenting cells (APC) and enumerated monocytes, macrophages and dendritic cells (DC) lineages to assess the state of the innate immunity. We found very low cell precursors, especially tolerogenic CD14<sup>+</sup> cDC2 and CD4<sup>+</sup> ILT-4<sup>+</sup> tmDC suggesting an underlying defect in the innate immune regulation and validating the hypothesis of ongoing antigen presentation to T cells several weeks after SARS-CoV-2 infection

## ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

### Poster #8:

#### Predictive Histologic Biomarkers For Recurrent Eosinophilic Esophagitis

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Seema Aceves, M.D., Ph.D., Professor, Pediatrics and Medicine, Division of Rheumatology, Allergy, Immunology, University of California, San Diego, Rady Children's Hospital, San Diego

**Background:** Eosinophilic esophagitis (EoE) is an eosinophilic inflammation of the esophagus with  $\geq 15$  intraepithelial eosinophils per high power field (eos/HPF) in an esophageal biopsy. It is a chronic allergic /immune disease that immune hypersensitivity responses to allergens can cause. There are no surrogate markers for disease activity or severity, and no prognostic indicators for disease progression. The mechanisms behind disease relapse and loss of response to therapy are unclear. We hypothesize that alteration of the histological elements of the esophageal biopsy can be predictive markers of EoE patients' response to therapy and their disease trajectory. This study aimed to understand EoE patients' histologic patterns associated with their response to therapy and their disease trajectory.

**Method:** The study sample was 73 pediatric patients with EoE diagnosed histologically and clinically at the Eosinophilic Gastrointestinal Disorders Clinic at Rady Children's Hospital San Diego. We used a linear mixed effect model to investigate the basal cell hyperplasia effect on EOS mean at different time points defined as EGD.

**Results:** There were significant differences between groups among average Eosinophil counts. There was a significant association between average EoE count and BZH with time.

**Conclusion:** Basal cell hyperplasia could be a predictive marker for EoE therapy response

### Poster #9:

#### Reducing Emergency Department Observation Time for Patients with Low-Risk Anaphylaxis

Susan Laubach, MD; Stephanie Schroter, MD; Lindsay Heitzman, MSN, RN, CNS, CPEN; Deven O'Crump, MISM; Amy Bryl, MD

**Background:** Historically, patients with anaphylaxis are observed for 4 to 6 hours after intramuscular epinephrine (epi) administration to monitor for biphasic reactions. In April 2020, new guidelines identified specific risk factors for biphasic reactions and recommended a 1-hour observation time for patients without risk factors.

**Objective:** We conducted a quality improvement project with the aim to decrease our pediatric emergency department observation (ED obs) time for patients with low-risk anaphylaxis from a mean of 4 to 2 hours by May 31, 2021.

**Methods:** We reviewed charts for patients diagnosed with anaphylaxis to identify risk factors. A multidisciplinary team of allergy and ED physicians and nurses identified barriers to early discharge. Plan-Do-Study-Act cycle interventions included: education of ED physicians and nurses regarding the guideline; a poster in the ED and an electronic medical record banner listing the low-risk criteria and recommending discharge after being asymptomatic for 1 hour; standardized discharge instructions; and provider specific feedback. Balancing measures included return visits within 72 hours of ED discharge. We used statistical process control to analyze changes in measures over time.

**Results:** Between June 2020 and May 2021 the mean ED obs time for patients with low-risk anaphylaxis decreased from 229 to 142 minutes. There was no change in the ED obs time for patients with risk factors. The median ED length of stay for all discharged patients increased by 22 minutes during the same period. During the intervention period, there were 5 biphasic reactions: 2 were in patients with low-risk anaphylaxis but neither required IM epi and neither would have been identified within a 4-hour ED visit.

**Conclusion:** Using QI methodology, we successfully reduced the mean ED obs time for patients with low-risk anaphylaxis by 87 minutes (38%). Our next step is to seek parental feedback regarding their experience with the decreased observation time.

### ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

#### Poster #10:

#### Disease Improvement In Atopic Dermatitis Through A Multidisciplinary Approach With Allergy, Dermatology, And Clinical Pharmacy

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**Background:** Severe and difficult to control Atopic Dermatitis (AD) patients often persist without disease improvement due to disjointed dialogue between specialties. The substantial population of these patients establishes a need for coordination of care across specialties.

**Methods:** The Multidisciplinary Atopic Dermatitis Program (MADP) was established to treat severe and difficult to control AD with equal involvement of Dermatology and Allergy/Immunology and coordination with Clinical Pharmacy. Program design includes monthly clinic visits and integrates educational modules and assessment of patient and provider reported outcomes, including EASI, BSA, vIGA (validated Investigator Global Assessment), Pruritus, CDLQI and POEM scores.

**Results:** Out of 26 subjects, 85% achieved an EASI 50 within a year and 77% within 6-months. 58% of patients achieved an EASI 75 within a year and 53.85% within 6-months. EASI scores increasingly declined over visits, starting with a mean decrease of 13.09 at visit 2 ( $p<0.001$ ) to the largest mean decrease of 20.16 at visit 4 ( $p<0.001$ ). BSA trended negatively with mean decreases of 31.96% by visit 2 ( $p=0.003$ ), 47.69% by visit 3 ( $p<0.001$ ), and 57.80% by visit 4 ( $p=0.002$ ). vIGA dropped by 1.08 by visit 2 ( $p<0.001$ ) and 1.81 by visit 4 ( $p=0.002$ ). POEM and CDLQI scores decreased significantly up to visit 3. Pruritus was the only parameter to not achieve clinical significance, mean difference of 2.94 by visit 3 ( $p<0.001$ ).

**Conclusion:** Coordination between specialties simultaneously in a multidisciplinary setting with emphasis on compliance and patient education resulted in significant disease improvement based on patient and provider reported outcomes.

### *ALLERGY/IMMUNOLOGY/RHEUMATOLOGY*

**Poster #12:**

**Neutrophils Perpetuate the Inflammatory Phenotype in Cryopyrin Associated Periodic Syndromes**

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**BACKGROUND:** CAPS (Cryopyrin-Associated Periodic Syndromes) is a monogenic autoinflammatory disease caused by autosomal dominant mutations in NLRP3 resulting in interleukin (IL)-1 driven systemic inflammation affecting multiple tissues. We previously generated Nlrp3 gain of function mutant mice that mimic the phenotypic spectrum of human CAPS, including inflammatory cell infiltration of tissues, and elevation of serum inflammatory markers. While we have determined that the pathogenesis of CAPS is driven primarily by innate immune cells, the specific cells contributing to disease have not been identified. We hypothesize that neutrophils play a vital pathogenic role in CAPS. **METHODS:** We used our knockin model to generate conditional CAPS mice with isolated expression of the mutation in neutrophils and evaluated survival and weight gain as measures of systemic inflammation. To investigate the CAPS phenotype in mice with significant neutropenia, we generated CAPS mutant mice that are deficient for IL-6, granulocyte colony stimulating factor (GCSF), or both.. To translate our findings to human disease, we performed CyTOF analysis of white blood cells isolated from CAPS patients. **RESULTS:** In our murine models, CAPS mice with neutrophil-specific expression of mutant NLRP3 developed a severe inflammatory phenotype similar to that of CAPS mice with universal or innate immune cell expression. Significant reduction in neutrophils due to deficiency of GCSF or GCSF/IL-6 resulted in partial rescue of the phenotype. CyTOF analysis of CAPS white blood cells revealed an expansion of neutrophil progenitors, that was independent of disease activity. **CONCLUSIONS:** Neutrophils play a significant role in the pathogenesis of murine CAPS. Neutrophil development is altered in CAPS patients with increased presence of progenitor cells which may contribute to persistent inflammation.

## ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

### Poster #13:

#### **RNA-seq reveals beneficial effects of atorvastatin on endothelial cells in acute Kawasaki disease**

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**Background:** Damage to the coronary arteries during the acute phase of Kawasaki disease (KD) is linked to inflammatory cell infiltration, myointimal proliferation, and endothelial cell (EC) dysfunction. To understand the response of ECs to KD treatment, we studied the genome-wide transcriptional changes in cultured ECs incubated with KD sera before and after treatment with or without atorvastatin.

**Methods:** RNA sequencing was performed on human umbilical vein endothelial cells (HUVECs) incubated with pooled sera from acute KD patients pre-treatment or after treatment with IVIG and infliximab with or without atorvastatin. Selected differentially expressed genes were validated using RT-PCR in independent experiments using individual KD sera.

**Results:** RNA sequencing of HUVECs incubated with pooled sera from acute KD patients pre-treatment or after treatment with IVIG and infliximab revealed differentially expressed genes in IL1, TNFa, and inflammatory cell recruitment pathways. Subacute sera pooled from patients treated with IVIG, infliximab, and atorvastatin uniquely induced expression of NOS3, KLF2 and KLF4 (promotes EC homeostasis and angiogenesis) and ZFP36 and SOCS3 (suppresses inflammation), and suppressed expression of TGFB2 and DKK1 (induces endothelial-mesenchymal transition (EndMT)) and SPHK1 and CXCL8 (induces inflammation).

**Conclusions:** ECs incubated with pre-treatment sera from KD patients upregulated IL1 and TNFa pathway genes that were dramatically suppressed after treatment with IVIG and infliximab. ECs incubated with post-treatment sera from patients who also received atorvastatin upregulated expression of genes involved in EC homeostasis and suppression of inflammation and downregulated genes involved in promoting inflammation and EndMT. These results suggest that atorvastatin treatment of acute KD patients improves EC health and may block KD-induced myofibroblast proliferation.

### Poster #14:

#### **Esophageal Fibroblasts Are Players in the Interferon Response in Eosinophilic Esophagitis**

Amanda Wu BS, Quan Nhu MD, PhD, Austin Chiang PhD, Mario Manresa PhD, Richard Kurten PhD, Nathan E. Lewis PhD, Seema S. Aceves MD, PhD

**Background:** Eosinophilic Esophagitis (EoE) is a Th2 predominant disease of increasing prevalence in children and adults. Recent studies have demonstrated conserved interferon (IFN) signals in pediatric and adult biopsies, but the cells responsible for these signals remain unclear. Here, we investigated the ability of esophageal fibroblasts to respond to interferons and whether type I and II IFN signals are conserved in EoE esophageal fibroblasts.

**Methods:** Publicly available datasets of human active EoE biopsies were analyzed to identify differential expression of genes in the IFN pathways. Fibroblasts were isolated from esophageal biopsies of healthy donors or pediatric patients with active EoE. Flow cytometry was used to determine the presence of IFN and IFN receptors. RNA-sequencing and qRT-PCR were used to investigate the relative expression of genes in IFN signaling pathways.

**Results:** Flow cytometry demonstrated that both normal and active EoE fibroblasts expressed type I and II IFN receptors. RNA-sequencing data demonstrated an upregulation of several IFN genes that were conserved between EoE biopsies and fibroblasts, particularly IFNAR, IFI27, RSAD2, OAS2, and IRF1 (FDR  $p < .05$ ). qRT-PCR confirmed significantly increased expression of these transcripts in active EoE, as compared to normal, esophageal fibroblasts under basal conditions ( $p < .05$  for each). Treatment of esophageal fibroblasts with IFN $\alpha$  or IFN $\gamma$  induced transcription of these type I and type II IFN signaling pathway genes.

**Conclusion:** Esophageal biopsies and fibroblasts from active EoE patients have an overlapping and enhanced IFN gene expression signature. This highlights the role of fibroblasts as potential pro-inflammatory cells responsible for IFN responses in EoE inflammation.

## ALLERGY/IMMUNOLOGY/RHEUMATOLOGY

### Poster #15:

#### **Immune response to intravenous immunoglobulin in patients with Kawasaki disease and MIS-C**

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**Background:** Multisystem inflammatory syndrome in children (MIS-C) is a rare but potentially severe illness that follows exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Kawasaki disease (KD) shares several clinical features with MIS-C, which prompted the use of intravenous immunoglobulin (IVIG), a mainstay therapy for KD. Both diseases share a robust activation of the innate immune system, including the IL-1 signaling pathway, and IL-1 blockade has been used for the treatment of both MIS-C and KD. The mechanism of action of IVIG in these 2 diseases and the cellular source of IL-1 $\beta$  have not been defined.

**Methods:** The effects of IVIG on peripheral blood leukocyte populations from patients with MIS-C and KD were examined using flow cytometry and mass cytometry (CyTOF) and live-cell imaging.

**Results:** Circulating neutrophils were highly activated in patients with KD and MIS-C and were a major source of IL-1 $\beta$ . Following IVIG treatment, activated IL-1 $\beta$ <sup>+</sup> neutrophils were reduced in the circulation. In vitro, IVIG was a potent activator of neutrophil cell death via PI3K and NADPH oxidase, but independently of caspase activation.

**Conclusion:** Activated neutrophils expressing IL-1 $\beta$  can be targeted by IVIG, supporting its use in both KD and MIS-C to ameliorate inflammation.

## CARDIAC SURGERY

### Poster #16:

#### Contemporary Outcomes for Early Repair of Symptomatic Tetralogy of Fallot

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**Background:** Recent studies suggest that staged repair (SR) for symptomatic neonates with tetralogy of Fallot (TOF) is preferable to early repair (ERep). Evolution of catheter based strategies (CBS) including ductal and right ventricular outflow tract (RVOT) stenting has also increased interest in SR. However, the use of SR exposes patients to brittle interstage physiology (with combined operative aorto-pulmonary shunt and interstage mortality of at least 7%), cumulative risks of additional procedures and exposure to both aggressive antiplatelet therapy and risks of vascular access for neonates treated with CBS. Most reports for ERep are from prior eras and demonstrate excellent survival but significant morbidity. The goal of this study is to determine our center's contemporary early and intermediate outcomes for ERep.

**Methods:** Retrospective chart review of all who underwent ERep for TOF or similar morphology  $\leq 4.1$  kg at our institution (3/1/2017 - 1/1/2021) yielded 16 patients. Diminutive pulmonary arteries, pulmonary artery arborization abnormalities, or multiple arterial pulmonary collaterals were exclusion criteria. Abstracted data included demographics, history, imaging, operative reports, inpatient and outpatient notes. Data were analyzed with descriptive statistics. Outcomes included length of stay, complications, survival and reinterventions. Follow up was complete at a median of 23.2 (IQR 10- 37) months.

**Results:** Among the 16 consecutive patients, there were no SRs performed during the study period. Median weight and age were 3.3kg (IQR 2.9 – 3.9) and 26 days (IQR 9.8 – 44.8), respectively. Demographics and procedural data are in Table 1. All patients were symptomatic or Prostaglandin E dependent. ERep was performed emergently on 3, with 2 on preoperative extracorporeal membrane oxygenation (ECMO). RVOT reconstructions are in figure 1. All but 1 had trans-ventricular repair, 4 had branch pulmonary arterioplasty and 1 patient had concomitant arch repair. Despite the tenuous preoperative status, all patients returned from ERep without ECMO. Delayed sternal closure was utilized for 3. There was 1 post ERep diaphragm plication and 1 surgical site infection. All patients were weaned from mechanical ventilation and discharged home. Postoperative echocardiograms showed no significant residual RVOT obstructions, tricuspid valve regurgitation or residual ventricular septal defects and excellent biventricular function. There were no deaths, cardiac arrests, or cardiac reoperations. Patients have thrived and had stable echocardiographic findings at follow-up.

**Conclusions:** Contemporary ERep has excellent survival, limited morbidity, and low re-intervention rates making it a highly effective and versatile treatment for symptomatic TOF. ERep may be preferred over SR because it avoids risks of inter-stage physiology and additional procedures and exposures.

### CARDIAC SURGERY

#### Poster #17:

#### Stage 2 Palliation after Ductal Stenting for Single Ventricles with Duct Dependent Pulmonary Blood Flow

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**Background:** Patent ductus arteriosus stenting (PDAS) for ductal dependent pulmonary blood-flow (DDPBF) provides a new paradigm for managing neonates with single ventricles (SV). Currently, sparse data exists regarding outcomes for subsequent palliation. We describe our experience with inter-stage care and stage 2 (S2P) conversion with PDAS in comparison to a prior era of patients who received surgical aortopulmonary shunts (APS).

**Methods:** Retrospective review of 18 consecutive DDPBF SV patients treated with PDAS between 2016 and 2021 was done and compared with 9 who underwent APS from 2010 to 2016. Patient care outcomes and pulmonary artery (PA) growth was analyzed.

**Results:** S2P was completed in all 18 with PDAS with no cardiac arrests and one post-S2P mortality. In the 9 APS patients, there was one cardiac arrest requiring ECMO and one mortality interstage. Off cardiopulmonary bypass strategy was utilized in 10/18 in the PDAS and 1/9 in the APS group ( $p=0.005$ ) at S2P. Shorter ventilation time, earlier PO feeding and shorter hospital stay was noted in the PDAS group ( $p=0.01$ ,  $p=0.006$ ,  $p=0.03$ ). Median Nakata index increase inter-stage was not significant between the two groups 94.1 versus 71.7 mm<sup>2</sup>/m<sup>2</sup> ( $p=0.94$ ), however median change in PAS was -0.02 and -0.24 which was statistically significant ( $p=0.008$ ). Neurodevelopmental outcomes were better in the PDAS group compared to the APS group ( $p=0.02$ ).

**Conclusions:** PDAS provides excellent PA growth, inter-stage survival, progression along multistage single ventricle palliation and favorable post Glenn physiology. Most patients can be transitioned through 2 stages of palliation without CPB.

## CARDIAC SURGERY

### Poster #18:

#### Hypoplastic Left Heart Syndrome Surveillance and Early Intervention Program May Improve Survival

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**Background:** Studies have shown that the HLHS cohort are the highest risk single ventricle patients with continuous attrition of survival 2-3 years post Norwood procedure. There has been improvement in mortality over the past few decades but this remains a complex and resource intensive patient population. The aim of our study is to capture all HLHS patients that are at risk using an objective marker of risk and intervening early to improve outcomes.

**Methods:** Our institution started a HLHS Surveillance Committee and created a risk scoring system based on graded echocardiographic criteria (TR 0-3, Aortic Arch gradient 0-3 and Single ventricle function 0-2). A maximum score of 8 represents the highest risk category. Inclusion criteria were all HLHS patients at all stages and ages dating back 2 years until present who had at least 1 risk scored echo. A snapshot of their score was obtained every 6 months and this was used to track their progress as well as capture at risk patients. Patients with a score  $\geq 3$  were referred for advanced imaging and early intervention.

**Results:** 78 patients were identified for inclusion in our surveillance program of which 2 are in Stage 1, 17 are in Stage 2 and 54 are in stage 3. Current median age and weight for the entire cohort is 9.4 (4.4 – 15.6) years and 26.7 (15.5 – 47) kg. Survival was 95% (71/75) over the 2 year period with 3 mortalities and 1 transplant (figure 1). Mean (IQR1-IQR3) risk score over the 2 year period for the entire cohort was 2.30 (2.18 – 2.45). Over the entire study period a mean of 43% of patients had a risk score  $\geq 3$ . During our final 6 month snap shot 22 patients decreased their risk score and 6 patients increased their risk score. Figure 2 illustrates risk score proportions during 6 month intervals. All patients with a score  $\geq 4$  had interventions and 22% had referrals to the heart failure team for optimization and possible transplant consideration during that time frame.

**Conclusion:** Patient surveillance utilizing an echo based risk score system to identify and intervene in HLHS patients throughout their palliation pathway can improve decision making in this high risk cohort. This objective approach can provide a bird's eye view of the different risk profiles of patients in a HLHS program and can hopefully lead to proactive intervention by heart teams.

## CARDIOLOGY

### Poster #19:

#### Deep Learning Left Ventricular Mechanical Analysis and Unsupervised Phenotypic Clustering in Patients with Tetralogy of Fallot

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**Background:** Patients with repaired tetralogy of Fallot (rTOF) are at increased risk for left (LV) and right ventricular (RV) dysfunction, which have been linked to adverse outcomes. Consequently, we sought to investigate regional patterns of LV mechanics in rTOF patients using deep learning synthetic strain (DLSS), a new algorithm for the regional assessment of myocardial strain developed by our lab.

**Methods:** We retrospectively collected a multi-institutional cohort of 191 patients with rTOF from five international institutions. Using DLSS, we calculated measures of LV contraction strength and timing across 16 AHA segments. Next, we performed a hierarchical clustering analysis of LV mechanical patterns to identify core phenotypic clusters of patients. To further characterize these groups, we related these clusters with traditional global metrics of volume, function, and valvular regurgitation.

**Results:** Hierarchical clustering of patients identified three unique patterns of LV mechanics. Clusters 1 (n=29) and cluster 3 (n=139) were characterized by decreased strain in the septal regions, though cluster 1 also showed increased measures of mechanical dispersion. In contrast, cluster 2 (n=18) was characterized by globally depressed LV strain, particularly in the lateral segments of the LV. In concordance with the DLSS metrics, clusters further showed significant differences in indexed RV end-diastolic volume (RVEDVi) ( $162 \pm 29.7$  vs.  $131 \pm 19.4$  vs.  $125 \pm 34.4$  mL/m<sup>2</sup>,  $p < 0.001$ ), pulmonary regurgitation fraction (PRF) ( $43.4 \pm 7.6$  vs.  $27.1 \pm 20.1$  vs.  $30.6 \pm 18.8\%$ ,  $p < 0.001$ ), and LV ejection fraction (LVEF) ( $55.6 \pm 8.3$  vs.  $52.8 \pm 6.9$  vs.  $59.1 \pm 7.0\%$ ,  $p < 0.01$ ).

**Conclusions:** Patients with rTOF exhibit several distinct patterns of regional LV mechanics, which generally correlate with known phenotypic patterns amongst patients with abnormal PRF and RVEDVi following repair. However, clustering also revealed an additional cohort of patients with depressed LV strain but normal LVEF, which may represent a subclinical detection of LV systolic dysfunction. Consequently, these phenotypes may benefit the stratification of patients under consideration for pulmonary valve repair.

### Poster #20:

#### Prenatal Diagnosis Rate of Critical Congenital Heart Disease Remains Inadequate with Important Racial Disparities and Technical Barriers

Arpine Davtyan, Heidi Ostler, Heather Sun

**Background:** Prenatal diagnosis (PreDx) of critical congenital heart disease (CCHD) has been shown to decrease morbidity and mortality. In 2013, revision of obstetrical fetal cardiac imaging guidelines aimed to increase rates of preDx. We sought to determine the contemporary rate of preDx in infants with CCHD and identify maternal-fetal factors and variations in prenatal care that may be potential barriers.

**Methods:** This retrospective study evaluated maternal demographics and characteristics of infants with CCHD (defined as requiring cardiac catheterization or surgical intervention before 6 months-old) from October 2016 to December 2019. Prospective telephone surveys ascertained prenatal care information from mothers of infants who underwent or died prior to intervention within the first month of life. Infants with isolated VSD, vascular ring, or branch pulmonary artery anomalies were excluded.

**Results:** Overall, 58% (197/339) of infants with CCHD had preDx. Infants with preDx were more likely to have mothers who were 35 or older ( $p=0.028$ ), had family history of CHD ( $p=0.017$ ), had health insurance ( $p=0.002$ ), or saw a perinatologist for anatomic scan ( $p<0.001$ ). Hispanic infants were less likely to have preDx (45.6%) compared to African American (73%), Asian (63.6%), or Caucasian (63.6%) infants ( $p=0.005$ ). PreDx rates were higher in infants with preDx of extracardiac/genetic anomalies ( $p<0.001$ ) and significantly different between subtypes of CCHD ( $p=0.024$ ). In infants without preDx, 21% had CCHD detectable by fetal four chamber view and 54% had CCHD detectable by adequate outflow tract imaging; 30% of their mothers had indication for, but did not receive, fetal echocardiogram during the pregnancy.

**Conclusions:** PreDx rates of CCHD remains inadequate across subtypes detectable by the standard fetal cardiac screening views. Outreach to primary obstetrical providers and education regarding fetal cardiac imaging and indications for fetal echocardiogram, particularly in uninsured and Hispanic communities, should be prioritized to increase rates of preDx of CCHD.

## CARDIOLOGY

### Poster #21:

#### **Pulmonary Atresia with Intact Ventricular Septum: From Radiofrequency Perforation to Transcatheter Pulmonary Valve**

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**Objectives:** We intend to describe an entirely transcatheter management pathway for patients with pulmonary atresia with intact ventricular septum (PA/IVS).

**Background:** PA/IVS is a rare cyanotic congenital heart lesion traditionally palliated with multiple procedures and surgeries. Entirely non-surgical transcatheter management from infancy to adulthood may be possible; however, the pathway from neonatal radiofrequency (RF) pulmonary valve perforation to later transcatheter pulmonary valve replacement (TPV) is not well described.

**Methods:** This retrospective study was performed at a pediatric cardiac center between 2007-2018. All patients with PA/IVS who were managed exclusively with catheterization-based interventions as neonates (RF perforation, pulmonary valvuloplasty, or ductal stenting) were analyzed. Demographic, procedural and clinical data were collected.

**Results:** Fifteen patients had exclusively catheterization-based RV decompression as neonates, seven (7/15) of whom did not require subsequent surgery. Six (6/15) patients required a right ventricular outflow tract (RVOT) augmentation later in life; all were born before 2013. All six later had a TPV placed. Two (2/15) patients underwent a surgical Glenn shunt alone. Of the seven patients that never had surgery, three have since undergone a TPV, and four are awaiting candidacy for TPV placement. No patients with PA/IVS have had an RVOT augmentation at our institution since 2012.

**Conclusions:** Patients with PA/IVS that underwent catheterization-based neonatal interventions can make it to TPV without requiring surgery. At our institution, there has been a shift in management over the last eight years favoring entirely non-surgical transcatheter management from infancy to adulthood.

### Poster #22:

#### **Neonatal myocardial infarction: A proposed algorithm for coronary arterial thrombus management**

Hannah El-Sabroun BSa, Srujan Ganta MDa, Peter Guyon MDa, Kanishka Ratnayaka MDa, Gabrielle Vaughn MDa, James Perry MDa, Amy Kimball MDc, Justin Ryan PhDd, Courtney D. Thornburg MD MSe, Suzanne Tucker MDf, Jun Mo MDf, Sanjeet Hegde MD, PhDa, John Nigro MDa, Howaida El-Said MDa

**Background:** Neonatal myocardial infarction (NMI) is rare and is associated with a high mortality of (40-50%). We report our experience with NMI, including presentation, management, outcomes, and our current patient management algorithm.

**Methods:** We reviewed all infants admitted with a diagnosis of coronary artery thrombosis, coronary ischemia or myocardial infarction between January 2015-May 2021.

**Results:** We identified 21 patients; median age and weight 1day (IQR 0.25-9.00) and 3.2kg (IQR 2.9-3.7). Presentation included respiratory distress (16), shock (3), and murmur (2). Regional wall motion abnormalities by echocardiogram were a key criterion for diagnosis and were present in all 21 with varying degrees of depressed left ventricular (LV) function [severe (8), moderate (6), mild (2), and low normal (5)]. Ejection Fraction (EF) ranged from 20-54% (median 43%, IQR 34-51%). Mitral regurgitation was present in 19 (90%). Left atrial dilation in 15 (71%) and pulmonary hypertension in 18 (86%). ECG was abnormal in 19 (90%). Median Troponin-I was 0.18 ng/ml (IQR 0.12-0.56). Median BNP 2100 pg/ml (IQR 924-2325).

Seventeen had documented coronary thrombosis by cardiac catheterization. 17 (81%) were treated with intracoronary tissue plasminogen activator (tPA) followed by systemic heparin, antithrombin (AT) and intravenous (IV) nitroglycerin, and 4 (19%) were treated with systemic heparin, AT, and IV nitroglycerin alone. 19/21 recovered. One died (also had infra-diaphragmatic-total anomalous pulmonary venous return). One patient required a ventricular assist device and later underwent heart transplant; this patient was diagnosed late at 5-weeks-of-age and did not respond to tPA. 19/21 (90%) regained normal LV function (EF 60-74%) (mean 65%, IQR 61-67%) at latest follow up [median 6.8 months (IQR 3.58-14.72)]. 2/21 (10%) had residual trivial mitral regurgitation. After analysis of these results, we present our current algorithm, which developed and matured over time, to manage neonatal MI.

**Conclusions:** We experienced a lower mortality rate for infants with neonatal infarction than that reported in the literature. We propose a post hoc algorithm that may lead to improvement in patient outcomes following coronary artery thrombus.

## CARDIOLOGY

### Poster #23:

#### Leveraging Video Game Development Experience in a Healthcare Facility

Parham Gholami, Chris Abe, Justin Ryan

**Background:** The introduction of 3D printing into healthcare has led to innovations in advanced imaging, education, and surgical/interventional preprocedural planning. 3D printing in healthcare facilities (HCFs) has primarily been built on the infrastructure intended from other domains such as automotive, aerospace, defense, and consumer products. For example, there exist few software suites designed specifically for manufacturing with an HCF. Software packages often lack user-first design principles, especially when the end-user is often a clinician or surgeon who may not have 3D experience. We sought to develop software that avoids shortcomings common to the field by leveraging pedagogical practices from software and videogame development.

**Methods:** We adopted user-first design principles in the Webster Foundation 3D Innovations Lab, focusing on addressing the needs of the broadest range of users and creating an approachable user experience. We reinforced this approach by organizing regular user testing to refine the experience and ensure we maximize the software's usability. During the development process, we considered and reviewed project specifications via iterative design. Rather than build out the entire application based on a strictly defined design document, we emphasized building a minimal viable product that could be quickly iterated and refined. This process focuses on implementing features with the highest user impact.

**Results:** We found user-focused designs to significantly contribute to a project's success, including leveraging pilot groups and user testing – both techniques employed in video game and software development. This approach facilitated the development of tools that can provide the greatest value and impact for the end-users.

**Conclusions:** Our experience in building on pedagogical methods and platforms generated initially for video games, leveraging user-first design principles, and shaping our development pipeline to support iterative development can benefit the PoC manufacturing community.

### Poster #24:

#### Selective Use of Pulmonary Vasodilators in Patients with Fontan Physiology

Thomas Glenn, Nicole Duster, Jerry Dwek, Jose Silva-Sepulveda, Howaida G. El-Said

**Background:** Fontan associated liver disease is a well-known sequela following the Fontan procedure for patients living with Single Ventricle heart disease. Pulmonary vasodilators, such as phosphodiesterase type 5 inhibitors, have emerged as a potential therapeutic option for lowering central venous pressures by reducing pulmonary vascular resistance.

**Method:** We performed a single-center retrospective review of Fontan patients who were placed on pulmonary vasodilator therapy with pre- and post-hemodynamic, MR elastography, and histologic assessments.

**Results:** A total of 125 patients with Fontan circulation underwent surveillance with cardiac catheterization during the review period. Fifty-three (42%) patients, who did not have increased end diastolic pressures at the time of cardiac catheterization, were started on phosphodiesterase type 5 inhibitor therapy. Nine patients (17%) underwent post-therapy follow up catheterization.

The mean Fontan pressure decreased from  $15.4 \pm 3.3$  mmHg to  $13.3 \pm 2.5$  mmHg ( $p = 0.026$ ), after initiation of pulmonary vasodilatory therapy. There was no change in end diastolic pressure, transpulmonary gradient, wedge pressure, pulmonary vascular resistance, cardiac index, or saturation. Eleven patients (21%) underwent pre-therapy MR elastography testing with post-therapy follow up MR elastography. We found no improvement in liver stiffness score following the application of pulmonary vasodilators. Three patients underwent pre- and post-therapy liver biopsy, with variable histological changes observed within the hepatic parenchyma.

**Conclusions:** This data suggests promising results for selective use of pulmonary vasodilators but highlights the need for large prospective randomized control trials of pulmonary vasodilator therapies to fully assess the benefit of such therapies in Fontan associated liver disease.

## CARDIOLOGY

### Poster #25:

#### Institutional Trend in Device Selection for Transcatheter PDA Closure in Premature Infants

Peter Guyon MD1, Nicole Duster MD2, Anup Katheria MD3, Caitlyn Heyden DO1, Danica Griffin MS1, Ronald Steinbergs RT1, Andres Moreno Rojas MD1, Kanishka Ratnayaka MD1, Howaida G. El-Said MD PhD1

**Objectives:** We report our experience with transcatheter patent ductus arteriosus (PDA) closure in premature infants and compare patients grouped by the device used for closure: the Microvascular Plug, "MVP" (Medtronic, Minneapolis, MN); Micro Plug Set, "Micro Plug" (KA Medical, Minneapolis, MN); and Amplatzer Piccolo Occluder, "Piccolo" (Abbot, Santa Clara, CA). We also report trends in device selection over time.

**Background:** Studies examining outcomes according to device selection for PDA closure in premature infants are lacking.

**Methods:** We performed a retrospective review of all percutaneous PDA closures in premature infants at a single center (June 2018 - May 2021). Patients were grouped by initial device selected for PDA closure (intention to treat). Institutional Review Board approval was obtained.

**Results:** 58 premature infants [MVP (n=25), Micro Plug (n=25), and Piccolo (n=8)] underwent successful transcatheter PDA closure (mean gestational age 27 weeks 2 days; mean weight at procedure 1.4kg; mean age at procedure 28 days). Pre-procedural demographics, procedural data, and follow up data were similar between groups. There were no significant procedural adverse events. Three devices (2 MVP, 0 Micro Plug, 1 Piccolo p=0.27) embolized after the procedure. One other device was removed for concern for aortic obstruction. Device selection evolved, with a clear trend towards the Micro Plug device over time.

**Conclusions:** Demographic, procedural, and follow up data were similar between the MVP, Micro Plug, and Piccolo groups. The Micro Plug did not require exchange for sub-optimal fitting or embolize and became our preferred device in most cases.

### Poster #26:

#### Simultaneous stenting with Edwards SAPIEN percutaneous pulmonary valve implantation

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**Background:** Pre-stenting of the landing zone for percutaneous pulmonary valve implantation (PPVI) with a balloon-expandable valve can dilate a stenotic right ventricular outflow tract (RVOT), prevent paravalvular leak (PVL), and protect against conduit tear. Simultaneous stenting (SS) with the Melody valve has been described, but to our knowledge, SS with a SAPIEN valve has not been reported. We report share our experience with this novel technique.

**Methods:** Retrospective chart review of patients who underwent PPVI at Rady Children's hospital and UCSD Medical Center. Subjects were included if they had a SAPIEN PPVI with SS. The technique is described in Figure 1. Rationale for stent choice is: bare metal stent to increase landing zone length, and covered stents to prevent PVL or to protect against conduit tear.

**Results:** A total of 15 cases were identified. The majority of RVOTs were transannular patches (n= 9, 64%) with minimum diameter of 20 mm  $\pm$  5 mm, and the most common valve placed was an Edwards SAPIEN 26mm (n=8, 50%). The procedure was successful in all patients, with no conduit tears and no PVL. Minor complications occurred in 3 (20%).

**Conclusions:** Simultaneous stent deployment with a SAPIEN PPVI is an alternative one-step technique for patients that require pre-stenting. Simultaneous stenting simplifies the procedure, has low complication rates, and offers the benefits of increased radial strength and decreased PVL.

## CARDIOLOGY

### Poster #27:

#### SARS-CoV-2 variants and differences in MIS-C clinical course

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**Background:** Infection with SARS-CoV-2 in children has been associated with a severe inflammatory syndrome now recognized as Multisystemic Inflammatory Syndrome in Children (MIS-C). SARS-CoV-2 has gone through different mutations that have changed infectivity, transmission, and severity of the clinical presentation. Very little information has been reported regarding if those mutations have also changed the presentation and severity of MIS-C.

**Methods:** This is a single-center, retrospective study including all patients admitted with MIS-C at RCHSD between May 2020 and March 2022. Statistical analysis was performed with R statistical software.

**Results:** 109 patients were included. Four MIS-C waves were identified, and patients were divided into four groups. The third and fourth waves coincided with Delta and Omicron variants, respectively. (Figure 1)

There were no significant differences in age, sex, or race among groups. All patients presented with similar initial laboratory results. Wave 2 was more likely to require ICU admission ( $p=0.001$ ), inotropic support ( $p=0.002$ ), and decreased cardiac function (LVEF  $<55\%$ ,  $p=0.04$ ) when compared to waves 1 and 3. Wave 4 had more patients admitted to the PICU (56% vs. 45% and 20%) and with cardiac dysfunction (47% vs. 35% and 28%) than waves 1 and 3, but no statistical significance was achieved.

For all the waves, patients admitted to the PICU had higher BNP levels ( $p=0.0002$ ) and lower LVEF on presentation ( $p=0.00001$ ). Troponin, ferritin, and platelet count were not different in patients admitted to the ICU vs. patients admitted to the floor.

**Conclusions:** This study suggests that different variants of SARS-CoV-2 triggered MIS-C with differing severities. The second wave had a more severe clinical course than the first and third waves. Larger numbers of patients from centers across the U.S. will be needed to expand on these preliminary observations.

## CARDIOLOGY

### Poster #28:

#### **Modeling Single Ventricle Morphology of Congenital Heart Diseases with a HLHS-Specific Biventricular Template to Enhance Statistical Shape and Biomechanics Analysis**

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**Background:** Hypoplastic left heart syndrome (HLHS) is a condition with underdeveloped left heart structures. Creating three-dimensional (3D) patient-specific models for single ventricular morphologies of HLHS has been challenging. The morphology has been modeled using a left ventricular template for the dominant right ventricle or using a generic biventricular template. Both methods compromise the numerical accuracy of statistical shape and biomechanical analyses. Thus, we aimed to develop a HLHS-specific biventricular template that captures HLHS morphology in patient-specific models with less distortion and higher accuracy to empower analysis and disease management.

**Methods:** A previously characterized generic biventricular template was interactively registered onto HLHS CT data to obtain a biventricular finite element template<sup>1</sup>. Angle and length of each element in the HLHS-specific mesh template were computed for quality characterization. A subdivision surface scheme was subsequently utilized<sup>2</sup>. Accuracy was assessed by the average root mean square errors (RMSE) between cardiac magnetic resonance (CMR) images and the subdivision surface. Mesh quality and accuracy were compared between templates.

**Results:** A HLHS-specific biventricular finite element template including four valves was successfully constructed and subdivided. Less deformed elements were observed using the HLHS-specific template to analyze HLHS data than the generic template. Distortion of HLHS-specific template on HLHS data, measured by edge angle (SD=20.55) and aspect ratio (SD=0.61), showed no significant deviation ( $p>0.05$ ) from the generic template on healthy data (SD=18.45, SD=0.97). The RMSE (1.69cm) of the generic subdivision surface on healthy data will be used for accuracy comparison of HLHS data analyzed by the generic and the HLHS-specific subdivision surface.

**Conclusions:** A HLHS-specific biventricular finite element template was successfully developed, characterized, and subdivided for creating 3D patient-specific models. Statistical shape and biomechanical analyses based on patient-specific models will provide insights on how surgical techniques affects ventricular shape and function at different stages of the palliative HLHS treatment.

## CARDIOLOGY

### Poster #29:

#### **Exercise stress echocardiography in Kawasaki Disease patients with coronary aneurysms**

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**Background:** The most significant sequelae of Kawasaki Disease (KD) are coronary artery aneurysms, which can lead to risk of future myocardial ischemia. Exercise stress echocardiography allows for non-invasive assessment of myocardial dysfunction. We reviewed our single center experience with exercise stress echocardiography in patients with previous history of KD with coronary aneurysms.

**Methods:** We reviewed the records of 53 KD patients with coronary aneurysms who underwent exercise stress echocardiography from 2000-2020. Abnormal stress echocardiograms were defined as those showing a lack of increase in biventricular systolic function post-exercise, or regional wall motion abnormalities. Cardiac computed tomography (CT) and cardiac magnetic resonance imaging (CMRI) were reviewed for patients with abnormal stress echocardiograms. Clinical data including advanced imaging were reviewed in the same patients and correlated with stress echocardiogram results.

**Results:** Three of 53 (5.7%) patients had abnormal exercise stress echocardiograms. All three of the patients were classified as AHA Risk Level 4 or 5 by coronary Z-score (internal dimension normalized for body surface area) and were confirmed to have coronary aneurysms, stenosis, or myocardial tissue perfusion defects on cardiac CT or CMRI that could account for the results seen on stress echocardiogram.

**Conclusions:** Exercise stress echocardiography detected signs of myocardial ischemia in a subset of high-risk patients with Kawasaki disease and coronary aneurysms.

### Poster #30:

#### **Endothelial loss of ETS1 causes coronary vascular development and ventricular non-compaction**

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**Background:** Jacobsen syndrome (JBS) is a rare chromosomal disorder caused by deletions in the long arm of human chromosome 11, resulting in multiple developmental defects including congenital heart defects (CHDs). Combined studies in humans and genetically engineered mice implicate that loss of ETS1 is the cause of CHDs in JBS, but the underlying molecular and cellular mechanisms are unknown.

**Methods:** ETS1 global and endothelial-specific knockout mice were used. Phenotypic assessments, RNA sequencing and chromatin immunoprecipitation analysis were performed together with expression analysis, immunofluorescence and RNAscope in situ hybridization to uncover phenotypic and transcriptomic changes in response to loss of ETS1.

**Results:** Loss of ETS1 in endothelial cells causes ventricular non-compaction, reproducing the phenotype arising from global deletion of ETS1. Endothelial-specific deletion of ETS1 caused a coronary vasculature developmental defect in association with decreased compact zone cardiomyocyte proliferation. Loss of ETS1 in endocardium increased extracellular matrix (ECM) expression in the trabecular layer, in association with increased trabecular cardiomyocyte proliferation.

**Conclusions:** These results demonstrate the importance of endothelial and endocardial ETS1 in cardiac development. Delineation of the gene regulatory network involving ETS1 in heart development will enhance our understanding of the molecular mechanisms underlying ventricular and coronary vascular developmental defects, and will lead to improved approaches for the treatment of patients with congenital heart disease.

## CHILD ABUSE PEDIATRICS

### Poster #31:

#### The acceleration of illicit ingestions in young children

Natalie Laub MD MSHP 1,2 and Jeannie S. Huang MD, MPH 1,2

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2. Rady Children's Hospital

**Background:** Due to the COVID-19 pandemic, mandated social isolation measures were initiated in the spring of 2020. While these measures reduced the spread of COVID-19, data suggest that this had a negative effect on child maltreatment, including exposure of young children to illicit drugs. Isolated pediatric centers reported increases in their rates of children hospitalized for illicit drug ingestions. However, the national impact of Covid-19 on illicit ingestions in young children remains unknown.

**Methods:** Using the Pediatric Health Information System database, we compared hospital encounters for drug ingestions in children ages 0-5 years. We identified these encounters through International Classification of Diseases 10th Revision diagnosis codes for cocaine, heroin, opioids, hallucinogens, methamphetamine, cannabis, and benzodiazepine ingestion. We excluded birth-related hospitalizations and those patients requiring NICU stay or complex care. We included encounters discharged from January through May during the years 2017 through 2021. We also collected patient demographic data (sex, age, race, ethnicity, and insurance). Absolute numbers of and annual proportions of specific illicit substance encounters were determined and calculated. Chi-squared were used to compare the categorical data. P-values <0.05 were considered statistically significant.

**Results:** 2,375 encounters were included in the analysis. The median age was 1 year. There was no statistical difference in age, race, or gender between the years. Total ingestions demonstrated a 2% decrease in the pre-COVID years (2017-2019) with a subsequent 69% increase in the post COVID years (2020-2021) THC products make up the greatest proportion of the change accounting for 14% of ingestions prior to COVID-19 and 46% of ingestions after.

**Conclusions:** Illicit ingestions in young children have increased over the study time frame with a substantial increase noted in the COVID-19 years (2020-2021) vs pre COVID years. This overall increase was attributable primarily to an increase in cannabis ingestions comparing to pre-COVID to COVID years.

## CHILD & COMMUNITY HEALTH

### Poster #32:

#### **Creating a System to Achieve Equitable Health Outcomes through an Asthma Pilot**

Monica Angeles, Dani Staub, MPH, Carolina DiGregorio, RT, Jacob Parker, Mary Perez, Rhonda Sparr-Perkins, BSN, MBA, Keri Carstairs, MD, MBA, FACEP, FAAP

**Background:** Rady Children's Hospital – San Diego was awarded a grant to develop an Asthma Health Equity Index to redefine capture and display of equity related data to create a standardized approach to monitor health equity related improvements. RCHSD piloted this index on the severe asthma population recently seen in the Emergency Department (ED) as it is a disproportionately underserved population. Many of the children live in neighborhoods commonly associated with inequities related to poverty, air quality and other socioeconomic and cultural factors.

**Methods:** Children with poorly controlled asthma recently seen in the ED were contacted by a Patient Care Coordinator to identify disparities through Social Determinants of Health (SDOH) screenings for food insecurity, housing, transportation, and tobacco use. SDOH and demographic data were compiled to build a health equity index to identify, track, and prioritize care gaps and develop appropriate interventions for all children seen in the ED. The index offers valuable insights detailing location (geo-mapping), race and ethnicity, gender, language, age, payor type, household income, Prior ED visits, SDOH, and school information to easily identify gaps, communities in need, and develop targeted interventions.

**Results:** Among those who completed the SDOH screening, 4.9% identified transportation issues, 10.4% reported food insecurity, 18.2% experienced housing instability, and 20.9% disclosed passive smoke exposure. Race/Ethnicity was strongly associated with food insecurity ( $p < .001$ ), unstable housing ( $p < .001$ ), and tobacco use ( $p < .001$ ). When compared to Non-Hispanic Whites, patients who were Hispanic, Non-Hispanic Black and Non-Hispanic Other were 3-5 times more likely to experience unstable housing ( $p < .001$ ); Hispanic patients were 3 times more likely to experience food insecurity ( $p < .001$ ) and transportation issues ( $p < .001$ ); Non-Hispanic Blacks were 2 times more likely to experience smoke exposure ( $p < .001$ ).

**Conclusions:** The index allows teams to apply a necessary health equity lens to interventions, metrics, and outcomes and is scalable to other conditions and populations.

### DYSMORPHOLOGY

#### Poster #33:

#### **Associations of prenatal exposure to non-steroidal anti-inflammatory drugs with preterm birth and small-for-gestational age among women with autoimmune disorders**

Erin Delker, Ann Kelly, Christina Chambers, Diana Johnson, Gretchen Bandoli

**Background:** Prenatal non-steroidal anti-inflammatory drug (NSAID) use is common, especially in early gestation prior to pregnancy recognition and among people with autoimmune conditions. We estimated associations between prenatal NSAID exposure and preterm birth and small-for-gestational age (SGA).

**Methods:** Participants were enrolled in the MotherToBaby prospective cohort study. We included participants with an autoimmune disorder (52% rheumatoid arthritis, 19% psoriasis, 34% irritable bowel syndrome, 2.7% lupus) and a singleton live birth after 20 weeks gestation (n=2009). We characterized self-reported NSAID exposure over gestation for timing, duration, and average daily dose, and examined two outcomes: preterm birth (i.e. <37 weeks gestation) and SGA (<10th percentile birthweight). We used multivariable Poisson regression to estimate associations between each NSAID exposure variable and study outcomes adjusting for maternal age, race/ethnicity, education, and prenatal cigarette, alcohol, disease-modifying antirheumatic drug, acetaminophen, oral corticosteroid use (Model 1), and self-reported disease severity at baseline (Model 2).

**Results:** Overall, 15% of women reported NSAID use in pregnancy, with 14% reporting use in the first trimester, 5% in the second trimester, and 2% in the third trimester. NSAID use was not associated with risk of preterm birth. Any NSAID use (RR = 1.7, 95% CI 1.2, 2.5), first trimester use (RR=1.8, 95% CI 1.2, 2.6), and second trimesters use (RR = 1.8, 95%CI 1.0, 3.1) were associated with greater risk of SGA. Greater duration of use, average daily dose, and greater cumulative dose of use were also associated with greater risk of SGA. Though, all effect estimates were attenuated towards the null after adjusting for disease severity at baseline.

**Conclusions:** NSAID use in pregnancy is associated with SGA but not preterm birth. Future research should explore causal mechanisms that may explain these findings. Future research must also consider alternative explanations for these associations such as confounding by autoimmune disease severity.

# ABSTRACTS: POSTER PRESENTATIONS

## EMERGENCY MEDICINE

### Poster #34:

#### **Pediatric Cardiac Standstill by Point-of-Care Ultrasound, A Simulation Based Skill Assessment**

Nicole Barbera, DO; Atim Ekpenyong, MD; Sheetal Khiyani, MD; Mylinh Nguyen, MD; Kathryn Pade, MD

**Background:** In pediatric cardiac arrest, pulse check by palpation is unreliable and causes significant pauses during resuscitative care. A potential alternative to improve accuracy and timeliness of pulse checks is by cardiac Point-of-Care Ultrasound (POCUS).

The aim of this study is to determine the ability of Pediatric Emergency Medicine (PEM) physicians to obtain and interpret cardiac POCUS images for cardiac standstill in simulated pediatric resuscitation scenarios following a brief video training session.

**Methods:** This is a prospective, simulation-based research study on the use of cardiac POCUS for pulse check by PEM attending and fellow physicians at a single center. All subjects will complete pre-training and post-training questionnaires as well as perform cardiac POCUS on model patients before and after a brief training video. Subjects will also provide interpretation of pre-recorded cardiac POCUS images. Data will be analyzed to determine the mean time to obtain images before and after the training video, percentage of correctly interpreted images, mean time of image interpretation, and changes in pre and post-training confidence scores.

**Results:** Data collection is planned to be obtained during the month of April 2022, with data collection on the model patients scheduled for April 19, 2022. Following the brief training video, we anticipate to see a decrease in the time it takes PEM physicians to obtain cardiac POCUS images to assess for cardiac standstill and a high percentage of correctly interpreted images. Additionally, we anticipate an increase in confidence scoring in performing cardiac POCUS for assessment of cardiac activity after the training session.

**Conclusions:** We aim to demonstrate that a brief video training session is sufficient to teach Pediatric Emergency Medicine (PEM) physicians to accurately and efficiently use cardiac Point-of-Care Ultrasound (POCUS) to evaluate for cardiac standstill.

### Poster #35:

#### **Comparison of Patient Health Questionnaire Screening Results Prior to and Following the Covid-19 Pandemic Lockdown, Rady Children's Hospital - San Diego**

Bialostozky M, Holt J, Garcia I, Sanderson K, Mueller S, Costa E, Billman G, Davis C, Kuelbs CL, Hollenbach K

**Background:** To assess the effect of the COVID-19 pandemic lockdown on adolescent mental health, we examined PHQ screening results before and after the pandemic lockdown.

**Methods:** We compared Patient Health Questionnaire (PHQ) screening results completed across RCHSD Integrated Delivery Network during two time periods related to the COVID-19 lockdown: September 2018-March 2019 (pre) and April 2019-October 2021 (post). Patient data included minimum and maximum PHQ-2 and PHQ-9 scores, number of screenings and presence of a behavioral health diagnosis (BHD) in their problem list during each of the time periods. Data were analyzed using MATLAB (Natick, MA) and STATA16 (College Station, TX). Comparisons were made between pre post periods by overall screens and by patients. Matched statistical comparisons were made between patients with at least one screening in each the pre and post COVID-19 lockdown periods.

**Results:** A total of 63,418 patients completed at least one PHQ-2 and/or PHQ-9 screening prior to the lockdown compared to 91,741 patients post lockdown and 29,897 had at least one screen in each of the study time periods. Among patients with scores in both the pre and post period, the median (25th, 75th percentile) number of screenings completed was 1 (1,2) in pre and 2 (1,3) in post periods. 13.5% (n = 8533) of patients screened in the pre lockdown period had a behavioral health diagnosis on their problem list compared to 15.1% (n = 13,838) during the post lockdown period. Patients were 7% more likely to be positive for self-harm post-lockdown relative to pre (95% CI = 1.01, 1.14).

**Discussion:** Data demonstrate the effect the COVID-19 pandemic lockdown had on adolescent mental health as measured by PHQ screenings as well as the importance of examining data by patient as opposed to population based screening results.

## EMERGENCY MEDICINE

### Poster #36:

#### **Antibiotic Use Patterns in Patients Presenting to Pediatric Emergency Department and Pediatric Urgent Cares for Dental Related Complaints in a Specialized Children's Hospital Division**

Heather Conrad MD; Fadra Whyte DMD, MPH; Elizabeth Haddad BS; Andrew Richardson MS; Noelle Johnson BS; Kathryn Hollenbach PhD, MPH

**Background:** 20-27% of children in the US suffer from dental caries. Despite the Affordable Care Act, barriers in access to dental care for children remain. In patients presenting with non-traumatic dental diagnoses (NTDD), antibiotic use is limited to infection not confined to pulp tissue or close surrounding areas. Unnecessary and over prescribing of antibiotics for NTDDs is a concern in an ED/UC setting. There remains room for improvement in care of NTDD.

**Objective:** Evaluate medical treatment of NTDD patients presenting to PED/UC to determine whether antibiotics were prescribed according to American Academy of Pediatric Dentists (AAPD) Guidelines to identify areas for improvement.

**Design/Methods:** Retrospective electronic medical records review of patients aged 0-18 presenting to the PED/UC for non-traumatic dental reasons from January 1, 2019 to December 31, 2020. Dental diagnosis, exam, antibiotic treatment (type and dose), demographics, and visit history were abstracted. Non-dental diagnoses and trauma were excluded. Antibiotic need was classified as indicated (acute facial swelling, and/or abscess with fever) or not indicated (caries, pulpitis with no systemic signs of infection). Statistical comparisons were made using t-test, chi square or Fisher's exact tests (STATA 16).

**Results:** 768 patients met study eligibility criteria with antibiotics indicated in 40.8%. Indicated and non-indicated patients had similar race, ethnicity, insurance, gender, and age. 95.2% of antibiotic indicated patients were appropriately treated and 42.2% of not indicated patients were unnecessarily prescribed antibiotics ( $p < 0.001$ ). Of those treated, 21.6% of indicated and 34.4% of not indicated patients were incorrectly dosed.

**Conclusions:** Patients with NTDD are often prescribed antibiotics when not indicated. When antibiotics are indicated most medical providers are appropriately prescribing antibiotics. Incorrect antibiotic dosing is found in both indicated and not indicated patient groups. Improving the coordination of care between dental and medical providers creates an opportunity to improve antibiotic stewardship.

### Poster #37:

#### **Geographical Distribution of Extended Spectrum Beta-lactamase (ESBL) Urinary Tract Infections (UTIs) within San Diego County**

Vanessa Tamas MD, Mario Bialostozsky MD, Margaret Nguyen MD

**Background:** Pediatric urinary tract infections (UTIs) account for approximately 5-14% of all pediatric emergency department (ED) diagnoses. Extended spectrum beta-lactamase (ESBL) producing uropathogens have been increasing in prevalence. These organisms are no longer constrained to pediatric patients with urinary tract abnormalities, recent and recurrent hospitalizations, or those requiring antimicrobial prophylaxis. This observation suggests an ecologic cause. In this study we identify geographic patterns of pediatric ESBL urinary tract infections in San Diego County and characterize the sociodemographic and environmental profiles where ESBL uropathogens are found.

**Methods:** We queried the medical record for children <18 years treated for a UTI at a tertiary urban children's hospital emergency department or associated urgent care centers from 2013-2018. A positive urine culture was defined as  $\geq 50,000$  CFUs/ mL of a single urinary pathogen obtained by catheterization or  $\geq 100,000$  CFUs/ mL single pathogen obtained by clean catch. Urine cultures with growth of normal flora, mixed organisms, or less than 50,000 CFU/mL of a pathogen were considered negative. We obtained census data from the Center for Disease Control Social Vulnerability Index (SVI) 2018 and environmental data from CalEnviroScreen (CES) 3.0. We mapped patient home addresses and aggregated locations by census tracts to protect privacy. The primary outcome was the proportion of positive ESBL urine cultures of all the ESBL-capable producing urine cultures for the census tract. We used Wilcoxon rank sum test to compare SVI and CES variables between census tracts with positive ESBL UTIs and census tracts with no ESBL UTIs. The Anselin Local Moran's I statistic was performed in ARC GIS to assess the geographic distribution of statistically significant spatial clusters and outliers.

**Results:** Our study sample included 7,281 culture-confirmed UTIs, with 6,529 UTIs with a valid geocoded San Diego county address (Figure 1). Of these, 6,000 UTIs were ESBL-capable uropathogens. Median age of the geocoded sample was 3 years (0-8 IQR) with 5,153 (78.9%) female. Census tracts with ESBL-producing UTIs were statistically disadvantaged in SVI themes of socioeconomics, household composition, minority status and language, and housing and transportation (all  $p < .001$ ). ESBL-producing census tracts also demonstrated higher particulate matter of <2.5 microns (PM<sub>2.5</sub>) than non-ESBL producing census tracts ( $p < .001$ ). Spatial statistical analysis revealed four census tracts identified as high clusters and ten high outliers (Figure 2).

**Conclusion:** Specific census tracts within San Diego are characterized by having a high rate of ESBL producing positive urine cultures and are disadvantaged in the four domains of the social vulnerability index and are also disproportionately burdened by pollution.

## EMERGENCY MEDICINE

### Poster #38:

#### Sexual History Documentation and Screening in Adolescent Females with Suicidal Ideation in the Emergency Department

Tatyana Vayngortin, MD<sup>1,2</sup>, Katie Clark, BS candidate,<sup>1</sup> Kathryn Hollenbach, PhD<sup>1,2</sup>

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<sup>2</sup>Department of Pediatrics, University of California, San Diego School of Medicine, La Jolla, California

**Background:** Adolescents with mental illness often seek care in the emergency department (ED) and are more likely to engage in risky behaviors such as substance abuse and unprotected sex, increasing the risk of sexually transmitted infections (STI), unintended pregnancy, and non-consensual sex.

**Methods:** We retrospectively identified 312 females aged 13-18 years presenting to the pediatric ED with chief complaint of suicidal ideation from February-May 2018. From electronic medical records, we abstracted demographics, psychiatric history, sexual history, and testing for pregnancy and STI. The primary outcome was documentation of presence or absence of prior sexual activity. Secondary outcomes included aspects of sexual history documented, and pregnancy and STI testing performed in ED. We compared groups using chi-square, Fisher's exact or t-tests, as data indicated.

**Results:** Of the 320 eligible females seen in the ED during the study period, 8 were excluded for altered mental status and 144 (46.2%) had documented sexual history. Of those with documented sexual history, 50 (34.7%) were sexually active. Sexual history documentation was not associated with patient age, race, ethnicity, insurance, or gender of ED provider. A history of anxiety and recent suicide attempt were associated with lack of sexual history documentation ( $p = 0.03$ ). Of the sexually active patients, 28 (56%) had documentation of contraception use. Pregnancy testing was done in 67.3% of all patients and 80% of sexually active patients. Only 10 patients had STI testing in the ED with most testing in those with sexual history documentation ( $p = 0.007$ ).

**Conclusions:** More than half of females with suicidal ideation in our ED had no documentation of sexual history, and when documentation was completed, it was often missing important elements including screening for pregnancy, STI, non-consensual sex, and contraception use. Since the ED visit provides an opportunity to address the reproductive health needs of this high-risk population, further work is needed to determine ways to improve provider documentation and sexual health screening.

### Poster #39:

#### Optimizing Education During Pediatric Resident Mock Code Sessions

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**Introduction:** Most pediatric residents have limited opportunities to manage cardiac arrest. We used simulation to fill that educational void. Given work hours and other obligations, resident education sessions must be high-yield. We examined the effectiveness of adding formal standardized education to mock code sessions on resident knowledge and confidence in managing pediatric arrest.

**Methods:** Convenient groups of 3-8 pediatric residents completed a simulation session with the identical scenario: a 3-month-old infant with pulseless ventricular tachycardia and then pulseless electrical activity. All residents completed pre and post-tests which consisted of open-ended knowledge questions from the American Heart Association's (AHA) Pediatric Advanced Life Support (PALS) guidelines and confidence Likert scale assessments. Resident groups were assigned to one of three educational models: Experiential-only: participation in the mock, Traditional: mock code participation with standardized education after mock code, or Reinforced: standardized education before and after mock code participation.

**Results:** Ninety-five residents participated. Collectively, residents demonstrated a median 2 (interquartile range (IQR) = 1,4) point increase in knowledge (test maximum score 10) after they attended a mock simulation session ( $p < 0.0001$ ); however, there were no statistically significant differences noted between educational modalities. All residents also demonstrated a 4-point median increase in confidence (test maximum score 25) after completing their simulation session (IQR = 3,6) ( $p < 0.001$ ), but no differences were seen by type or amount of accompanying education.

**Conclusion:** Residents had gains in confidence and knowledge of pediatric arrest management after participation in the mock code. Formal educational sessions and reinforced formal education sessions accompanying the mock code did not significantly increase knowledge or confidence.

## ENDOCRINOLOGY

### Poster #40:

#### **Disparities in Telemedicine Use Among Pediatric Patients with Type 1 and Type 2 Diabetes**

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Despite increasing telehealth services during the COVID-19 pandemic, disparities in telemedicine (TM) use remains. Our Diabetes Clinic serves 1400 patients with Type 1 Diabetes (T1D) (46% publicly insured) and 375 patients with Type 2 Diabetes (T2D) (88% publicly insured). We have shown a significantly lower number of completed TM encounters between January and July 2020 among publicly versus privately insured patients ( $p$  value = 0.03523) and a threefold increase in no-shows and same-day TM visit cancellations by the publicly insured group.

Of the 707 patients who received care in our clinic between January and March 2021, 22.8% had never attended a TM visit. To better understand barriers to TM use, we surveyed 39 families from this group. Among these patients, 84.6% had T1D and 15.4% had T2D, 48.7% had public insurance, 23.1% had no EMR access, and 15.4% did not speak English as their primary language. There were 46.2% who self-identified as Non-Hispanic White, 35.9% as Hispanic, 5.1% as Asian, 2.6% as Non-Hispanic Black, and 10.3% as Other.

Reported reasons not to attend a TM visit included: preference for in-person care (43.6%), not being offered a TM visit (17.9%), technology issues (12.8%), scheduling conflicts or forgetting the appointment (17.9%) and 20.5% did not provide a reason. In conclusion, more than half of our surveyed patients with diabetes who never attended a TM visit were from racial and ethnic minority groups. The COVID-19 pandemic has highlighted disparities related to access to and use of technology to improve diabetes care. Our results show the importance of ensuring all families are aware of TM options and receive support with TM technology. Further research into TM perception and adoption barriers should be conducted to prevent disparities in care and to close health equity gaps.

### Poster #41:

#### **Health Disparities and Food Insecurity in Pediatric Type 1 and Type 2 Diabetes: The Role for Empathy and Compassion**

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Diet plays a critical role in type 1 (T1D) and type 2 diabetes (T2D) management. Food insecurity is on the rise in the US putting patients with diabetes especially at a risk. Providers, medical staff, and patients have reported discomfort discussing food insecurity due to the associated stigma. Here we aimed to use compassion as a tool to improve the experience and perspective of patients and medical staff regarding food insecurity screening (FIS).

A retrospective review was conducted on patients with T1D or T2D screened for food insecurity at RCHSD from July 2020 to June 2021. Information on sociodemographic variables and diabetes outcomes were extracted from the EMR. Caregivers were surveyed about their comfort level regarding FIS pre and post a 30 min Empathy and Compassion Training Session (ECTS) provided to the medical assistants (MAs) who administer the screening. MAs were surveyed about their own comfort level when administering the screening before and after ECTS.

Of the 806 patients screened, 13% (80 with T1D and 23 with T2D) were positive for food insecurity. Among those, 83% were from minority racial/ethnic groups. Patients with a positive food insecure screening were more likely to have T2D, have public insurance, speak a language other than English, have a higher BMI and a higher HbA1c. Surveyed caregivers ( $n=50$ ) reported feeling judged (9.6%), uncomfortable or very uncomfortable (7.9%) when screened for food insecurity during the pre-intervention period. After the intervention 57 caregivers were surveyed and 3.5% reported feeling judged while 7.1% felt uncomfortable or very uncomfortable during FIS.

In conclusion, this study highlights social disparities in achieving adequate glycemic management and the importance of addressing food insecurity to improve health equity in children and adolescents with diabetes. Empathy and compassion interventions have the potential to improve caregivers food insecurity screening experience.

## ENDOCRINOLOGY

### Poster #42:

#### **Integrated glycoproteomic and metabolomic network analysis reveals subnetworks associated with insulin resistance.**

Tyler Kim, Yixuan Xie, Quiongyu Li, Carlito B Lebrilla, John W Newman, Nancy L Keim, Nathan E Lewis, Sridevi Krishnan

**Background:** Precision health aims to customize the prevention and treatment of diseases. Multi-omic knowledge of the systems involved in the disease process is necessary to achieve this goal.

**Methods:** Forty-four women, 21 with insulin resistance (IR) and 23 without (non-IR), were given a high-fat meal challenge test. Fasting and postprandial (60min, 180min, and 360min) blood draws were collected. Fasting samples were used to measure the serum glycoproteome of 28 circulating glycoproteins (associated with inflammation and metabolic syndrome) by LC-MS/MS analysis. Both fasting and postprandial samples were used to measure circulating metabolomic markers – acylcarnitines, amino acids, and fatty acids. Data were used in network analyses generating graphical (sparse LASSO) models, comparing women with IR vs non-IR. These generated graphical models were evaluated using isomorphism tests, to evaluate differences in global network structure.

**Results:** The network for IR and non-IR were both sparse, with a density score of 0.052 and 0.059 respectively. The network for IR had 148 nodes and 568 edges and non-IR had 148 nodes and 642 edges out of a possible 10,878 total. Both IR and non-IR networks were isomorphic, however, subgraph analysis revealed differences between IR and non-IR in their connectivity between glycoproteins, lipids, and amino acids. Arachidonic acid (dietary meat, eggs) was positively associated with monosialylated apoCIII (the form of apo CIII that is linked to hypertriglyceridemia) in IR but not in non-IR. Serine, asialylated apoM, disialylated heparin cofactor-2, and vaccenic acid (found in dairy foods) formed a negatively associated sub-network in IR, but not in non-IR suggesting a link between dietary dairy and insulin resistance.

**Conclusions:** These unique subgraphs likely reveal interactions that are representative of the link between lifestyle and metabolic status. Investigating metabolic networks using multi-omic integrated approaches can identify interactions that have previously been unreported, inching closer to the goal of precision health.

### Poster #43:

#### **Impact of Gender-Affirming Care Learning Module on Medical Students' Knowledge and Self-Efficacy**

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**Background:** While evidence supports the need for increased provider education on gender-affirming care, few medical curricula address the healthcare needs of transgender and non-binary (TGNB) patients. To bridge this knowledge gap, we developed an online learning module to educate medical students (MS) in the care of this underserved population. The module included topics such as TGNB health disparities, gender dysphoria, and gender-affirming therapy. We hypothesized that learners would possess greater knowledge and self-efficacy following completion of the module.

**Methods:** A cohort of 272 first- (MS1) and second-year medical students (MS2) from a single institution received protected time during their academic training to complete the mandatory online module (total duration: 60 minutes). Of those, 90 learners consented to participate in our IRB approved study and completed pre- and post-module surveys. Surveys assessed the impact of the educational module on self-reported knowledge and self-efficacy pertaining to learning objectives.

**Results:** Most participants self-identified as cisgender (97%), while 40% of those who chose to answer reported being part of LGBTQIA+ community. Baseline knowledge scores ranged from 7 (not knowledgeable) to 35 (knowledgeable). Following completion of the module, the median knowledge score significantly increased by 9 points (23 to 32;  $p < 0.0001$ ). At baseline, self-efficacy scores ranged from 9 (not confident) to 45 (confident) and similarly increased by 9 points (31 to 40;  $p < 0.0001$ ). Feedback from participants indicated that the module was well-received.

**Conclusion:** Our data showed that an online educational module on gender-affirming care was successful in increasing knowledge and self-efficacy in surveyed MS1 and MS2 at our institution. Education of healthcare providers is a key step towards mitigating health disparities among TGNB patients. Therefore, more institutions should adopt formal curricula for MS on gender-affirming care. Similar modules could be offered to practicing clinicians and support staff to ensure a more gender-inclusive healthcare environment.

## ENDOCRINOLOGY

### Poster #44:

#### **A human pluripotent stem cell model of HNF4a/MODY1 provides mechanistic insights into disease phenotypes**

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**Background:** Heterozygous mutations in the transcription factor HNF4a cause maturity onset diabetes of the young (MODY). Clinically, HNF4a/MODY1 mutations are associated with postnatal hyperinsulinemic hypoglycemia (HI), evolving into diabetes later in life.

**Methods and Results:** To gain insight into disease mechanisms of HNF4a/MODY1, we introduced the heterozygous HNF4aR141X point mutation into human pluripotent stem cells (hPSC) and differentiated HNF4aR141X/+ and control cells into pancreatic islet cells (SC-islet). We observed no impact of the HNF4aR141X mutation on islet cell differentiation. However, HNF4aR141X/+ SC-islets exhibited insulin hypersecretion in basal and high glucose, which was reversed by diazoxide treatment and resolved during SC-islet maturation. These findings are consistent with the HI phenotype and treatment in the MODY1 patients. To understand HNF4a-dependent gene regulatory programs in beta cells, we compared transcriptomes and chromatin accessibility in HNF4aR141X/+ and control SC-islets at single cell level. Beta cell-specific analyses revealed reduced expression of NEUROD1 and ion channels, consistent with reported insulin hypersecretion in loss-of-function models for these genes. In addition, HNF4aR141X/+ SC-beta cells exhibited reduced expression of pro-survival genes (BCL2L1, SERPINA1, HSPA5, ANKS4B), which are known to compensate for ER stress. Through gene regulatory network analyses, we identified BCL2L1 and SERPINA1 as direct target genes of HNF4a in beta cells. In agreement with these molecular findings, HNF4aR141X/+ SC-beta cells were more prone to undergo apoptosis in response to thapsigargin-induced ER stress, a phenotype that was rescued by supplementing SERPINA1 protein. These results suggest that beta cells in HNF4a/MODY1 patients are more susceptible to stress-induced cell death, providing a possible mechanism for progression to diabetes.

**Conclusions:** Our hPSC-based HNF4a/MODY1 model recapitulates key aspects of the HNF4a/MODY1 phenotypes. By providing mechanistic insight into HNF4a-regulated cellular processes in beta cells, our work identifies opportunities for therapeutic intervention for MODY1 patients.

### Poster #45:

#### **Change in Incidence of Central Precocious Puberty Treated with GnRHa During COVID-19 Pandemic: Single-center Retrospective Review**

Marcela Vargas, MD, Tiranun Rungvivatjarus, MD, Karen O. Klein, MD

**Background:** We studied the incidence of new central precocious puberty (CPP) patients treated with GnRH agonist (GnRHa) during Covid. (1-3).

**Methods:** We performed a retrospective comparison of the incidence of newly diagnosed CPP with GnRHa treatment during the COVID-19 pandemic (5/2020–4/2021) versus pre-COVID (5/2018–4/2019). CPP was defined by random LH >0.3 IU/L, GnRH stimulated LH >5 IU/L, or GnRH stimulated estradiol >40 pg/mL. Girls had onset of breast development at < 8 years-old and boys had testicular size >4 ml at <9 years-old. We evaluated time from diagnosis to GnRHa order, and time from GnRHa order to onset of treatment. We compared bone age (BA) chronological age (CA), BA/CA and BA-CA between groups.

**Results:** During pre-COVID period, 28 children (1 boy, 27 girls) were treated with GnRHa for CPP out of 2340 new Endocrinology visits (1.2%). During COVID years, 64 children (7 boys, 57 girls) were treated out of 2261 new visits (2.8%). The incidence of new CPP cases on GnRHa during COVID more than doubled that of pre-COVID ( $p < 0.01$ , Chi Square). There were no significant differences between groups in age, time between diagnosis and treatment order, time between order and treatment, degree of BA advancement, or BMI (Tables 1-2). CPP incidence was consistent between 26–37 cases/year over the past 4 years pre-COVID. Cases per month did not correlate with peaks of COVID cases (Figure).

**Conclusions:** CPP cases requiring GnRHa treatment significantly increased during the first year of COVID-19 compared to pre-COVID. There was no delay in presentation or treatment initiation during COVID based on BA. Preliminary data didn't show a significant difference in rate of BA progression, time from diagnosis to treatment, or changes in BMI during the COVID pandemic.

## ENDOCRINOLOGY

### Poster #46:

#### **Integration of single-cell multiomic measurements across disease states with genetics identifies mechanisms of beta cell dysfunction in type 2 diabetes**

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**Background:** Islet endocrine cell types, in particular the insulin-producing beta cells, are known to regulate glucose homeostasis. Functional failure and beta cell loss are hallmark features of type 2 diabetes (T2D), which results from the interplay of both genetic and environmental factors. Despite substantial efforts to define the molecular events underlying T2D pathogenesis, we still lack a thorough understanding of the gene regulatory programs driving T2D progression in beta cells.

**Methods:** We conducted single-cell analysis of chromatin accessibility and gene expression in pancreatic islets from 34 non-diabetic, pre-T2D and T2D donors. We then performed integrative analyses with genetic association data, and data from combined single-cell gene expression and functional measurements to define gene regulatory programs involved in T2D pathogenesis in beta cells. We used machine learning and gene regulatory network (GRN) analysis to identify gene regulatory changes causal to beta cell dysfunction in T2D.

**Results:** We identify two transcriptionally and functionally distinct beta cell subtypes that undergo an abundance shift in T2D. Through GRN analysis, we show that feedback loops between transcription factors (TFs) establish subtype identity. Genetic analysis revealed enrichment of subtype-defining active chromatin for T2D risk variants, suggesting a causal contribution of subtype identity to T2D. Both subtypes exhibit activation of a stress-response transcriptional program and functional impairment in T2D. The stress-response transcriptional program is driven by nutrient-responsive TFs, indicating secondary changes due to the T2D-associated metabolic environment.

**Conclusions:** Our findings suggest that a beta cell subtype shift from a subtype secreting less insulin to a subtype that is more highly secretory has a causal role in T2D. This result lends support to the debated hypothesis in T2D research that insulin hypersecretion has a causal role in T2D. Our study demonstrates the power of multimodal single-cell measurements combined with machine learning for identifying mechanisms of complex diseases.

## GASTROENTEROLOGY

### Poster #47:

#### Analysis of Gastric Emptying Scans in Eosinophilic Esophagitis

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**Purpose:** Gastric emptying studies can be indicated in eosinophilic esophagitis (EoE) when there are persistent symptoms of esophageal dysfunction such as reflux, nausea/vomiting, weight loss, early satiety, anorexia, abdominal discomfort, and bloating. Given the potential for esophageal dysmotility, which could extend beyond the esophagus, in EoE patients, a concomitant diagnosis of delayed gastric emptying should be considered. We sought to understand the results of nuclear medicine scans in EoE patients with persistent symptoms and whether or not there is a correlation between having eosinophilic inflammation, symptoms of esophageal dysfunction in EoE and delayed gastric emptying.

**Methods:** We identified and reviewed the records of 84 patients who had been diagnosed with EoE and were enrolled into our IRB approved EoE database who had a clinically indicated nuclear medicine gastric emptying scan. At our institution, the clinical definition of a normal study is based on a half emptying time of less than 60 minutes. A result greater than 90 minutes is considered delayed, and between 60-90 minutes is borderline delayed. Based on the nuclear medicine scan's result, these 84 patients were divided into these three groups; normal, borderline delayed, and delayed. Among these 84 patients, 23 patients were placed on erythromycin, a therapy that is known to improve delayed gastric symptoms.

**Results:** There were 28 patients in the "normal" group, 24 patients in the "delayed" group, and 31 patients in the "borderline delayed" group. In terms of gender, 86% male in the normal group, 64% male in the delayed group, and 55% male in the "borderline" delayed group.

The average half emptying time was 39 min in the normal group, 126 minutes in the delayed group and 74 minutes in the borderline delayed group. There was a significant difference between their half emptying time ( $P < 0.0001$ ). There was no significant difference in BMI ( $P = 0.71$ ), weight ( $P = 0.32$ ), or height ( $P = 0.059$  between the 3 groups).

There was no statistically significant difference between the number of eosinophils in different regions of the esophagus between the three groups, although distal eosinophils trended towards being significantly higher in normal group. [distal ( $p = .07$ ), proximal ( $p = 0.75$ ), mid ( $p = 0.583$ )]

Erosions were found at similar rates in the normal 10/28 (36%), delayed 7/25 (28%), and borderline 9/31 (29%) groups.

**Symptoms:** There was a variable distribution of symptoms throughout the 3 groups. The only statistically significant symptom of note was the frequency of constipation in the delayed vs normal group. ( $P = 0.018$ )

**Erythromycin:** 23 patients started erythromycin, 16 delayed, 5 borderline and 2 normal. Nine of these patients (8 delayed, 1 borderline) had post-treatment EGD's. Four of patients had improved distal eosinophilia following treatment (mean of 43 eos/hpf to a mean 1 eos/hpf;  $p = 0.028$ ).

**Conclusions:** Only constipation was associated with persistent EoE symptoms and delayed gastric emptying studies. Interestingly there were fewer GEJ erosions seen in the delayed group than in the borderline and normal groups, suggesting a non-motility based reason for reflux in the normal group. Further studies are needed to help determine which EoE patients are most likely to benefit from a gastric emptying study. Persistent EoE symptoms and delayed gastric emptying in the context of a child with concurrent constipation may suggest the presence of a more global esophagogastrintestinal dysmotility.

## GASTROENTEROLOGY

### Poster #48:

#### Unraveling the Risks of Total Body Fat versus Location of Fat versus Muscle Mass Volume for Hepatic Steatosis in Children

Ghattas J. Malki, Nidhi Goyal, Patricia Ugalde-Nicalo, Lauren F. Chun, Jasen Zhang, Ziyi Ding, Yingjia Wei, Cynthia Knott, Danielle Batakis, Claude B. Sirlin, Michael S. Middleton, and Jeffery B. Schwimmer

**Background:** Ectopic lipid accumulation in hepatocytes is the basis of Nonalcoholic Fatty Liver Disease (NAFLD). NAFLD has a prevalence of 5-10% in children and is associated with adverse hepatic, endocrine, and cardiovascular outcomes. Controversy remains about the effect of body composition on ectopic liver fat. Possible factors include total amount of body fat, preferential localization of fat as visceral adipose, or insufficient muscle mass. The influence of adipose and lean mass on pediatric NAFLD have not previously been assessed together, making it difficult to compare their relative importance.

**Methods:** In 227 children ages 8-17, we tested the association of total body fat (by DXA), visceral and subcutaneous adipose (by MRI), and lean body mass (by DXA) with hepatic steatosis (by MRI proton density fat fraction). Multivariate analysis and multivariable regression models were used to determine the relative significance of these associations.

**Results:** Liver fat was positively associated with total-body adipose mass, centralized adipose regionalization, and muscle mass ( $p < 0.001$ ). Liver fat was negatively associated with lean mass percentage ( $p < 0.001$ ). After adjusting for weight, hepatic steatosis only remained positively associated with markers of centralized adipose distribution, such as the trunk-to-limb fat mass ratio ( $R^2 = 0.43$ ,  $p < 0.001$ ) and the percent of abdominal adipose stored viscerally ( $R^2 = 0.35$ ,  $p < 0.001$ ). Comparing these three indices against each other, visceral adipose had the strongest association with hepatic steatosis compared with total-body adipose or muscle mass ( $p < 0.001$ ).

**Conclusions:** Hepatic steatosis is more strongly associated with adipose regionalization than total adipose amount, and the association of lean mass is not independent of fat mass or body weight. Thus, interventions that preferentially decrease visceral adipose may be more effective for addressing fatty liver than those targeting weight loss or muscle gains. Clinical trials should test this hypothesis.

### Poster #49:

#### Tumor necrosis factor receptor 2 (TNFR2) regulates colonic epithelial dynamics in homeostasis and repair

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**Background:** In inflammatory bowel disease, cytokines play key roles in epithelial damage and intestinal barrier dysfunction. However, cytokines can also benefit the epithelium by promoting cell proliferation and regeneration. Tumor necrosis factor (TNF) exemplifies this duality. In mouse models of colitis, TNF receptor-2 (TNFR2) expression is increased in intestinal epithelium, and deletion of TNFR2 exacerbates the injury. To understand the molecular mechanisms of TNF function, we studied TNFR2's impact on colonic epithelial morphology and wound healing.

**Methods:** Tnfr2 was ablated in colonic epithelium of Tnfr2<sup>flox/flox</sup>;Vil1::Cre mice. Colon tissues were scored for colitis and compared with controls (Tnfr2<sup>flox/flox</sup>). To induce acute colonic injury, mice were exposed to dextran sulfate sodium [3.5% DSS (6d)]. Colonic levels of Tnfr2 and Ly6a were analyzed through in situ hybridization, RT-qPCR, and flow cytometry. Cultures were established from the distal colons of wildtype and Tnfr2<sup>ko</sup> mice (8w/o). The size and the number of organoids were analyzed daily.

**Results:** Epithelial ablation of TNFR2 showed colitis and crypt loss ( $*P < 0.05$ ;  $n = 5$ ), an increase in proliferation (pH-H3), and a decrease in goblet cells ( $***p < 0.001$ ) compared to controls. Tnfr2<sup>ko</sup> colonoids had a higher organoid forming efficiency, grew 1.5-fold faster with larger structures ( $****p < 0.0001$ ) compared to wildtype controls. In DSS colitis, colonic Tnfr2 transcript was specifically upregulated in crypts adjacent to inflamed mucosal erosions (days 10-14;  $***p = 0.0001$ ), and it was reduced at day 20 when the tissue is largely recovered. Flow cytometric analysis showed that TNFR2<sup>hi</sup> epithelial cells (days 9-14) are markedly enriched for LY6A, a fetal-like marker.

**Conclusions:** A combination of organoid and TNFR2-ablated studies suggests that loss of epithelial TNFR2 results in hyperproliferation. During an acute injury, TNFR2 expression is induced in the colonic epithelium and may represent a regulatory adaptive change in response to an injury. This study reveals added functions for TNF beyond the inflammatory responses.

## GASTROENTEROLOGY

### Poster #50:

#### Development of a Clinical Prediction Rule For Moderate to Severe Fibrosis in Children with Nonalcoholic Fatty Liver Disease

Andrew Wang, Amanda Blackford, Cynthia Behling, Kimberly P. Newton, Laura Wilson, Jeffrey B. Schwimmer

**Background:** Liver fibrosis is an important determinant of clinical outcomes for patients with chronic liver disease. Fibrosis is a common feature in children with nonalcoholic fatty liver disease (NAFLD) and assessment depends on liver histology. Current non-invasive models to assess fibrosis in NAFLD have not been validated for use in children. Study aims were to validate existing fibrosis models and if they did not perform well, to develop a more accurate clinical prediction tool.

**Methods:** This is a multi-center study of children with biopsy-proven NAFLD including consensus review of liver histology. Liver fibrosis was staged as 0 = none; 1 = mild; 2 = moderate; 3 = bridging; 4 = cirrhosis. We tested the existing models PNFS, PNFI, and FIB-4. We developed a model to discriminate moderate-to-severe (stage 2-4) fibrosis from none or mild (stages 0-1) using spline modeling, logistic regression, 100-fold cross-validation, and least absolute shrinkage and selection operator.

**Results:** We evaluated 1055 children with NAFLD with mean age of 13 (SD 2.7) years. The distribution of fibrosis was none: 34.7%, stage 1: 39.4%, stage 2: 12.9%, stage 3: 11.9%, stage 4: 1.1%. Existing NAFLD fibrosis models all performed poorly in classifying fibrosis in children with area under the receiver operator curves ranging from 0.57 to 0.64. Our prediction model was based upon age, sex, weight, height, ALT, AST, GGT, bilirubin, albumin, HDL, non-HDL, HbA1c, total WBC, and hematocrit. The model had an AUC of 0.81 (95% CI: 0.78 to 0.84) and provided 77% sensitivity and 72% specificity for moderate-to-severe fibrosis.

**Conclusions:** Existing NAFLD fibrosis prediction models do not perform well in children. Our newly developed fibrosis model has performance characteristics that offer clinical utility to identify moderate to severe fibrosis and may help to guide patient selection in future clinical trials

### Poster #51:

#### Effect of Pediatric IBD-Associated Commensal Bacteria on Epithelial Barrier Function

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**Background:** With growing rates of inflammatory bowel disease (IBD), a better understanding of the pathogenesis of IBD is needed. Studies exploring the role of the microbiome have shown alterations to the mucosal barrier and mucosal bacterial communities, and an association of gut dysbiosis with IBD; however, it remains unclear whether these changes are a cause or consequence of disease. We aimed to provide insight into the role of commensal bacteria in the pathogenesis of IBD and hypothesized commensal bacteria from pediatric IBD specimens would decrease barrier function in wild-type murine enteroids.

**Methods:** Colonic biopsies were collected from pediatric patients undergoing colonoscopy for gastrointestinal symptoms and IBD. Mucosal bacteria adherent to biopsy specimens were identified via 16s rRNA sequencing. The bacterial community from actively inflamed tissue of a treatment-naïve patient with ileocolonic Crohn's disease was isolated, consisting of *Fusobacterium ulcerans*, *Escherichia coli*, *Bacteroides fragilis*, *Veillonella parvula*, *Bacteroides xylanisolvens*, and *Bacteroides thetaiotaomicron*. Wild-type murine enteroid-derived monolayers (EDM) were infected with the Crohn's bacterial community at a multiplicity of infection of 10. Effects on barrier function were assessed by analyzing transepithelial electrical resistance (TEER), paracellular permeability utilizing the FITC-dextran flux assay, and RNA expression of tight junction proteins using qRT-PCR.

**Results:** Compared to untreated controls, EDMs treated with the Crohn's bacterial community, exhibited significantly decreased TEER at 24 and 48 hours post-treatment ( $p < 0.0001$ ) as well as significantly increased permeability ( $p = 0.002$ ). RNA expression of tight junction protein genes (ZO1, occludin, and claudin-7) was evaluated with occludin found to be significantly decreased ( $p = 0.032$ ).

**Conclusions:** Our findings suggest that commensal bacteria in the setting of pediatric IBD may contribute to pathogenesis by disrupting barrier function. Further studies are needed to better elucidate the mechanism(s) by which bacteria contribute to the pathophysiology of IBD, thereby allowing for improved management and treatment of this increasingly prevalent disease.

## GENETICS

### Poster #52:

#### **Hematopoietic stem cell gene therapy for Mucopolysaccharidosis type IIIC**

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Mucopolysaccharidosis type IIIC (MPSIIIC) is a lysosomal storage disease (LSD) characterised by the accumulation heparan sulphate. MPSIIIC is a progressive childhood neurodegenerative disease due to the loss of the lysosomal transmembrane protein Heparan-a-glucosamine N acetyltransferase (HGSNAT) with no current therapy. This disease presents with missing developmental milestones, hyperactivity, loss of neurons and motor function, culminating with early death from neurodegeneration in adolescence. Our group has previously shown transplantation of hematopoietic stem and progenitor cell (HSPC) rescues cystinosis, another LSD due to a lysosomal transmembrane protein. The main mechanism of rescue involved lysosomal cross-correction from HSPC-derived macrophages to the disease cells via tunnelling nanotubes (TNTs). We believe that the same principles could be used to treat MPSIIIC. We generated a new MPSIIIC mouse model which displayed disease phenotypes such as accumulation of glycosaminoglycans, enlarged liver, distended bladder, increase in urine volume, and the presence of disease specific non-reducing end carbohydrates biomarkers. The mice also present with kidney defects such as glomerular hyaline bodies, glomerular sclerosis and fibrosis, and dilated tubules. We transplanted MPSIIIC mice with HSPC from wild-type GFP mice. Preliminary results show engraftment of HSPC-derived cells in tissues and a trend decrease in liver and bladder size as well as a trend decrease in bladder urine content. In parallel, we have generated self inactivated (SIN)-lentivirus vector containing human HGSNAT cDNA which will be used for autologous gene corrected HPSC transplants. Previous studies of MPSIIIA, a similar LSD, reported limited improvement mice following wild-type HSPC transplant, while strong therapeutic benefits were obtained with the gene therapy approach. We believe the gene therapy approach will deliver strong therapeutic effect due to higher expression of the HGSNAT protein in cells derived from the lentivirus treated HSPC. Overall, our results show we have successfully generated an MPSIIIC mouse model with characteristic MPSIIIC phenotypes that can be used to test the efficacy of HPSC gene therapy.

## GENETICS

### Poster #53:

#### Identification of a novel exonic deletion in the GALNS gene causing Morquio syndrome.

Kathryn DeLong<sup>1</sup>, Annette Feigenbaum<sup>1,4</sup>, Laura Pollard<sup>2</sup>, Andrew Lay<sup>2</sup>, Tim Wood<sup>3</sup>

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<sup>4</sup>University of California San Diego

**Background:** Mucopolysaccharidosis (MPS) IVA or Morquio syndrome is a rare lysosomal storage disorder caused by N-acetylgalactosamine-6-sulfatase deficiency. The condition is characterized by intracellular accumulation of glycosaminoglycans keratan sulfate and chondroitin-6-sulfate, which leads to progressive development of clinical features. A diagnosis can be provided by the identification of reduced N-acetylgalactosamine-6-sulfatase activity and detection of compound heterozygous or homozygous pathogenic variants in GALNS.

**Case Presentation:** We present a case of two sisters with a severe classical phenotype of Morquio syndrome who were born to healthy nonconsanguineous parents of Indian background. Both were diagnosed following identification of low or absent N-acetylgalactosamine-6-sulfatase activity. Prior genetic testing for MPS IVA, which utilized next generation sequencing (NGS), did not identify sequence variants associated in GALNS, however it was noted that a large region of GALNS corresponding to exon 9 was not covered in the sequencing data. After establishing care with our center, subsequent polymerase chain reaction (PCR) amplification of the coding exons for GALNS produced an appropriate product for all exons with the exception of exon 9 and we hypothesized that a deletion encompassing exon 9 was present in our patients. An allele specific PCR assay was designed to confirm the exon 9 deletion and determine the precise deletion breakpoints (c.899-397\_1003-18632del) for our patients.

**Conclusions:** To our knowledge, the pathogenic deletion identified in our patients has not been reported in the literature. Various deletions encompassing at least one exon have been reported in GALNS, however none encompassing only exon 9. The gold-standard for diagnosis of MPS IVA is detection of reduced N-acetylgalactosamine-6-sulfatase activity, however molecular analysis is useful to confirm a biochemical diagnosis and assist with genetic counseling and familial testing. Recognizing limitations of molecular testing is important to ensure proper diagnosis and subsequent treatment for individuals with Morquio syndrome is completed in a timely manner.

### Poster #54:

#### Glucose consumption in human brain organoids, a first step in using brain organoids as models to study neonatal hypoglycemia

Laura Forero, Ariel Lee, Cedric Snethlage, Lynne M. Bird, Bruce A. Barshop, Alysson R. Muotri

**Background:** Cortical organoids are 3D tissue cultures of the human cerebral cortex. Pluripotent stem cells from human subjects are differentiated into self-organizing neuronal tissue. These structures offer a unique opportunity to study neuronal tissue. However, their fidelity as models for human brain pathology is unclear. Their metabolism, specifically glucose utilization, has not yet been characterized.

**Methods:** Our objective was to find the average glucose consumption of an in-vitro organoid and compare this with the glucose consumption of an in-vivo human brain. We used 230 15–17-week brain organoids divided into six wells, each with 3mL standard neurobasal media. 100 organoids were weighed to establish an average weight. Glucose was measured using a YSI analyzer at 2 points in time approximately 48 hours apart, and glucose consumption was calculated per gram of tissue per day. Results were compared to previously reported human brain glucose consumption values.

**Results:** The average organoid weight was 2.2 mg with a range of 0.69 – 4.88 mg, with an apparently normal distribution. At time A, the total glucose media in sampled wells was 28.35 mg, and at time B (2627 minutes after) was 21 mg, with a difference of 7.35 mg. There was an average of 116 organoids in the wells, yielding 15.79 mg of glucose consumed per gram of tissue per day. Prior studies have estimated that a newborn human brain consumes between 14.2 mg (preterm) and 18.9 mg (term) of glucose per gram of tissue per day.

**Conclusions:** Glucose consumption rate of brain organoids is comparable to preterm and term neonatal brain glucose consumption. In this respect, brain organoids may be useful models to study the metabolic effects of hypoglycemia on the neonatal brain. Our findings may profoundly impact translational research for metabolic diseases associated with brain injury mediated by hypoglycemia.

## GENETICS

### Poster #55:

#### IDENTIFYING BARRIERS TO GENETIC TESTING

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**Background:** Racial and ethnic disparities are evident among health care services, and concerns have been raised that advanced and expensive genetic testing are likely to escalate these disparities.(1,2) Inconsistent insurance coverage doesn't appear to be the only barrier. Previous studies revealed that African Americans and Hispanics are less likely to know about the availability of genetic testing and more likely to view genetic testing as interfering with their cultural and religious beliefs than Caucasians.(3,4) Distrust in the medical system, and lack of adequate information have also been suggested as significant barriers.(2,5)

**Methods:** The electronic medical record at Rady Children's Hospital San Diego was searched for common genetic tests ordered between 1/1/2021 and 1/31/2021. We recorded 1) whether the test was authorized or not authorized, 2) whether test was performed or not performed, 3) demographic characteristics including race, ethnicity, preferred language, zip code 4) insurance type to determine whether there are any disparities in access to genetic testing.

**Results:** Four hundred and twenty nine unique genetic testing orders were found for three hundred and twenty unique patients. Duplicate orders and parental samples that were part of a child trio whole exome sequencing were removed from the cohort. Analysis showed no differences between rate of testing performance with respect to ethnicity (Hispanic vs. non-Hispanic), zip code of residence or preferred language.

**Conclusions:** Preliminary results suggest that genetic testing access at Rady Children's Hospital San Diego does not differ based on ethnicity, preferred language or zip code of residence. We intend to analyze a larger sample to see if some apparent trends become statistically significant. We will interrogate whether insurance type influences the likelihood of obtaining authorization, and examine specifically those in the cohort for whom authorization was obtained, but testing was never accomplished to see if barriers can be identified and overcome.

### Poster #56:

#### Renal Fanconi Syndrome and Cystinosis: an unresolved puzzle

Veenita Khare, Jay Sharma, Jean-claude Farre, Sergio Caatz, Stephanie Cherqui

Renal Fanconi Syndrome is a pathological condition of the proximal renal tubules of the kidneys. It is characterized by a defect in proximal tubular reabsorption of amino acids, glucose, phosphate, uric acid and bicarbonate ( $\text{HCO}_3^-$ ). This is the earliest manifestation in cystinosis before structural anomalies or cystine storage occurs. Cysteamine, the current treatment for cystinosis, that decrease cystine build up, does not treat the renal Fanconi syndrome. This strongly suggests another specific function of cystinosin in the proximal tubular cells beyond lysosomal cystine transport. Our objective is to decipher the underlying molecular mechanism behind the development of the renal Fanconi syndrome in cystinosis. A high-throughput screen in *Saccharomyces cerevisiae* identified an interaction between the only ortholog of cystinosin (Ers1) and the sodium/hydrogen (Na/H) exchanger (Nhx1). This interaction in yeast was confirmed by Dr. Jean-Claude Farre, at UCSD, an expert in autophagy and organelle homeostasis in yeast. By using Ers1-GFP and a pulse-chase of FM4-64, we determined that Ers1S is localized in the endocytic vesicles and at the vacuole (equivalent to lysosome in yeast). Interaction and colocalization of cystinosin and NHE3 was also confirmed in mammalian cells. In proximal tubular cells derived from cystinosis patients, we observed that NHE3 was mislocalized. Here, we report a novel interaction of cystinosin with a transport exchanger protein (NHE3) in the PTCs. Also, Cystinosin has a role in the subcellular localization and/or function of NHE3 in the PTCs, and in its absence, NHE3 homeostasis is dysregulated, potentially participating to the proximal tubulopathy. This knowledge may advance the understanding of the renal Fanconi syndrome pathogenesis in cystinosis leading to new therapeutic approaches for cystinosis.

## GENETICS

### Poster #57:

#### **Transplantation of wild-type hematopoietic stem and progenitor cells rescue Alzheimer's disease in a mouse model and highlights the central role of microglia in disease pathogenesis**

Priyanka Mishra<sup>1</sup>, Alexander Silva<sup>1</sup>, Jay Sharma<sup>1</sup>, Jacqueline Nguyen<sup>1</sup>, Donald P Pizzo<sup>2</sup>, Debashis Sahoo<sup>1,3,4</sup> and Stephanie Cherqui<sup>1\*</sup>

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Alzheimer's disease (AD) is the most prevalent cause of dementia but still no effective treatment exists. Microglia have been implicated in AD, but their role is still matter of debate. Our study represents direct evidence that microglia play a key role in disease progression, and that replacing diseased APP/PS1 microglia via single wild-type (WT) hematopoietic stem and progenitor cell (HSPC) transplantation rescue AD in the 5xFAD mice. Cell therapy led to complete rescue of the neurocognitive impairment, and significant decrease of Ab plaque burden in the hippocampus and cortex of the 5xFAD mice. Proliferation and activation of microglia were apparent in the 5xFAD mice untreated or transplanted with APP/PS1 HSPCs, whereas distinct reduction in number and activation of microglia was observed in WT HSPC-transplanted mice. Further, transcriptomic analysis revealed significant decrease of "disease-associated microglia" in the cortex and "neurodegeneration associated endothelial cells" in the hippocampus of the WT HSPC-transplanted 5xFAD mice compared to diseased controls. Therefore, this work strongly suggests that HSPC gene therapy to correct known familial mutations in AD could be a promising therapeutic approach for treating AD.

### Poster #58:

#### **Patient-derived iPSC-neurons and cerebral organoid for modeling Friedreich's Ataxia disease**

Alexander Silva, Priyanka Mishra, Anusha Sivakumar , Avalon Johnson, Emily A. Hansen, Jacqueline Nguyen, Nicole Coufal and Stephanie Cherqui

Department of Pediatrics University of California, San Diego, La Jolla, California

Friedreich ataxia (FA) is an autosomal recessive neurodegenerative disease. Most patients carry homozygous GAA expansions in the first intron of the frataxin gene causing reduction in frataxin (FXN) expression. FXN is a mitochondrial protein, and its deficiency leads to mitochondrial iron overload, defective energy supply and generation of reactive oxygen species. In this study, our aim is to establish a new human model system to advance the understanding of FA pathogenesis. We differentiated multiple FA patient-derived induced pluripotent stem cell (iPSC) lines to neurons, and cortical organoids as well as control lines. All iPSC lines have been characterized using well-established immunostaining assays and were found to be karyotypically normal. Interestingly, when we differentiated iPSCs into neurons, we observed a striking phenotype in FXN-deficient neurons. We identified no homogenous microtubule staining along the neurites or in neuronal cell bodies of FA neurons, and instead noted periodic breaks of neuronal immunostaining called blebbing while only few blebbing could be observed in the control cell lines. Similar results were obtained in the FA cortical organoids as compared to the control organoids. Dendritic blebbing is a feature of apoptotic neurons. In addition, Cleaved-caspase-3, a marker for apoptosis, was increased in both FA neurons and organoids compared to controls. Mitochondrial function was also found abnormal in these two FA models. Overall, this study provides a platform to advance the understanding of FA pathogenesis.

## GENETICS

### Poster #59:

#### **CRISPR/Cas9 edited hematopoietic stem and progenitor cells for Friedreich's ataxia**

Anusha Sivakumar<sup>1</sup>, Joseph N. Rainaldi<sup>1</sup>, Rita Wan<sup>1</sup>, Celine J. Rocca<sup>1</sup>, Stephanie Cherqui<sup>1</sup>

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Friedreich's ataxia (FRDA) is an autosomal recessive neurodegenerative disorder caused by homozygous GAA repeat expansion in first intron of the frataxin gene (FXN). This mutation reduces expression of frataxin, a mitochondrial protein, required for respiratory complex assembly and iron homeostasis. Symptoms like ataxia and muscle weakness begin between 5-15 years of age and patients are wheelchair bound by 10-15 years from onset. The predominant cause of death in FRDA patients is cardiomyopathy and currently, there is no treatment. We have previously shown that transplantation of wild-type HSPCs could prevent the neurological, muscular and cardiac complications, in mouse model of FRDA and that tissue rescue was mediated by transfer of frataxin from HSPC-derived microglia/macrophages to the diseased cells. With the objective of developing an autologous HSPC transplantation approach, we ex vivo gene edited CD34<sup>+</sup> HSPCs from FRDA patients and showed increased frataxin expression and better mitochondrial function. The current study investigates the in vivo therapeutic potential of our CRISPR/Cas9 editing in YG8s(GAA)<sup>>800</sup> mice expressing human FXN transgene carrying >800 GAA repeats. The analogous bone marrow Sca1<sup>+</sup> cells isolated from diseased mice were ex vivo gene edited, transplanted into irradiated, diseased mice and assessed at 2- and 6-months, post-transplant. Sca1<sup>+</sup> HSPCs show an average 25% hFXN gene editing efficiency. Primary organs affected during FRDA such as heart, spinal cord and brain also show modest gene editing, confirming engraftment and migration of edited cells to the affected organs. Increased frataxin protein levels were seen in bone marrow cells, heart, brain and spinal cord of animals receiving edited cells. This preliminary data demonstrates efficient and specific gene editing of hFXN in murine HSPCs, repopulation and proliferation of edited cells within the bone marrow niche for successful engraftment in the diseased organs and confirms that our CRISPR-Cas9 gene editing strategy could achieve clinically relevant frataxin levels in HSPCs for future ex vivo gene therapy clinical trial for FRDA.

### Poster #60:

#### **BUILDING THE FOUNDATION OF A PRECISION GENOMIC MEDICINE CLINIC FOR ULTRA-RARE AND UNDIAGNOSED NEUROLOGICAL DISORDERS AT RADY CHILDREN'S HOSPITAL**

Kristen Wigby<sup>1,2</sup>, Jerica Lenberg<sup>2</sup>, Matthew Bainbridge<sup>2</sup>, Charlotte Hobbs<sup>2</sup>, Marilyn Jones<sup>1</sup>, Stephen Kingsmore<sup>2</sup>, Soofia Khan<sup>2</sup>, Elizabeth Kiernan<sup>2</sup>, Viridiana Murillo<sup>2</sup>, Hung Nguyen<sup>2</sup>, Jong Rho<sup>3</sup>, Mari Tokita<sup>2</sup>, Jennifer Friedman<sup>2,3</sup>

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**Background:** Genomic sequencing provides unparalleled opportunities for increased diagnostic efficacy and therapeutic interventions for rare genetic disorders. Herein we describe the Precision Medicine Clinic (PMC) at Rady Children's Hospital-San Diego: a multi-disciplinary model integrating genomic sequencing, translational studies, and clinical care in the ambulatory setting. The PMC is a partnership of physicians and scientists interested in helping families navigate the diagnostic and therapeutic odyssey for rare genetic disorders. Our team is composed of physicians representing genetics and neurology, a genetic counselor, a nurse coordinator and genomics investigators.

**Methods:** The clinic leverages deep phenotyping, genomic sequencing, independent review of genomic data, and research collaborations to diagnose rare and ultra-rare disorders. All families are offered the opportunity to participate in research. Multi-disciplinary case discussions with other specialists are conducted.

**Results:** The PMC was founded in June 2020 and has evaluated 103 medically complex children with rare neurologic phenotypes. Over 70% were seen for ongoing diagnostic evaluation (n=74); other referrals included genotype-phenotype correlation (n=8) and rare disorder consultation and/or therapeutics consultation (n=21). As of March 2022, of 74 children undergoing diagnostic evaluation, a new genetic diagnosis was identified for 26 patients (35%) including ultra-rare and/or newly described genes in seven children. Diagnoses included coding variants and a deletion identified through WGS and not detected by other clinical testing (n=4) and variants identified by independent genomic data analysis by PMC investigators (n=2). Summaries of patient phenotypes and outcomes of evaluation will be presented for undiagnosed cases. Research collaborations with external institutions have been initiated for several patients.

**Conclusions:** These preliminary data highlight the benefit of a multi-disciplinary approach for rare neurological disorders. As PMC grows, we aim to expand research collaborations for candidate genes and undiagnosed cases and to connect rare disease families to emerging individualized therapies.

## *GENOME INFORMATION SCIENCES*

### **Poster #61:**

#### **AI Driven Real-time Cytometry**

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Artificial intelligence (AI) has achieved unreal performance in image and speech recognition. In particular deep learning algorithms outperform other computing approaches where large amounts of data are available. In the field of medical instrumentation, photonic time stretch based instruments have established record real-time measurement throughput in spectroscopy, optical coherence tomography, and imaging flow cytometry. These real-time instruments produce well above 1 terabits of continuous measurement data per second and hence, have propelled the discovery of rare phenomena in nonlinear and complex systems as well as new types of biomedical instruments. Owing to the abundance of data they generate, time-stretch instruments are a natural fit to deep learning classification. It has been demonstrated in literature that high-throughput label-free cell classification with high accuracy can be achieved through a combination of time-stretch microscopy, image classification and feature extraction, followed by deep learning to detect cancer cells in the blood. Such a technology holds promise for early detection of primary cancer or metastasis. In this work, we present a new deep learning pipeline which completely avoids the slow and computationally costly signal processing and feature extraction steps. Its convolutional neural network operates directly on the measured signals. The proposed AI framework takes less than a few milliseconds to classify the cells, fast enough to provide a decision to a cell sorter for real-time separation of individual target cells.

# ABSTRACTS: POSTER PRESENTATIONS

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## HEALTH DISPARITIES

### Poster #62:

#### **Southern California Health Volunteers Double the Number of Refugees Receiving Health Services in Tijuana via Consultation and Integrated Care**

Philip Cañete

Jaideep Chakladar

Mikaela Mizuno

Summer Khan

Patty Medina

Mojdeh Motamedi, PhD

**Background:** The refugee population in Tijuana, MX has grown more than 3,500% since 2014 (UNHCR, 2021). Many refugees have significant health problems exacerbated by COVID-19 stressors, systemic discrimination, lacking accessible/affordable health services, and crowded shelters they do not leave for fear of getting hurt. This case study examines how health providers, including from the UCs and Rady, use integrated care, task shifting, and consultations to address these refugee needs.

**Methods/Interventions:** Founded by UCSD medical students and local clinicians, the volunteer-run nonprofit Refugee Health Alliance (RHA) provides the majority of medical care for Tijuana's refugees via our clinics and Saturday shelter visits. In 2021, we had 8 paid and 0-3 rotating volunteer providers in our clinics plus a core team of ~20 remote volunteer clinicians consulting with and training our staff/interns. RHA has hundreds of other volunteers and a network of specialists for everything from a few hours of remote consultation to Saturday shelter visits. We also address social determinants of health by providing water, food, bathrooms, and showers.

**Results:** In 2021, RHA saw ~13,000 patients: 70% were Haitian, one of the most discriminated against groups in Tijuana, and 42% were children, many of which we could only see by consulting with RHA volunteer specialists, including pediatricians, child psychologists, psychiatrists, neurologists, perinatologist, dermatologists, etc. Through consulting, RHA saw ~35% more patients. Comparing our model to the market value of hiring Tijuana specialists for a similar patient volume, our cost savings is over 50% - doubling how many patients we could see with our budget.

**Conclusions:** The poster will highlight success stories, how Rady and other hospitals' work have informed RHA's integrated care approaches, how providers and medical students have learned from locals to provide more culturally informed care in the US, and ways to support this initiative.

## HEMATOLOGY & ONCOLOGY

### Poster #63:

#### Parental Informed Consent Comprehension in Cancer Clinical Trials and Associations with Social Determinants of Health

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**Background:** Informed consent comprehension is an ethical right prior to participation in clinical trials. Research investigating informed consent comprehension and associations with social determinants of health (SDoH) is lacking. We assessed whether SDoH and related contextual factors were associated with parental informed consent comprehension in therapeutic childhood cancer clinical trials.

**Methods:** We prospectively enrolled parents of children diagnosed with cancer. Univariable and multivariable regression were conducted to assess if informed consent comprehension and related domains (*Purpose/Procedures/Randomization, Risks/Benefits, Alternatives, and Voluntariness*) were associated with SDoH (ethnicity, marital status, language, education attainment, employment, insurance, socio-economic status, health literacy and contextual factors (cancer type, voluntariness, satisfaction).

**Results:** Of 223 parents enrolled, 112 (50%) were Hispanic and of those 38% preferred Spanish for written and verbal medical information. In multivariable analysis, limited health literacy was significantly associated with lower comprehension of informed consent ( $\beta = -7.22$ ; 95%CI, -10.9, -3.59;  $P < 0.001$ ) and of *Purpose/Procedures/Randomization* ( $P < 0.011$ ), *Risks/Benefits* ( $P = 0.031$ ), and *Alternatives* ( $P = 0.013$ ) domains. Spanish as the preferred language of written and verbal medical information was associated with lower comprehension of *Purpose/Procedures/Randomization* ( $P = 0.012$ ) and *Voluntariness* ( $P = 0.008$ ).

**Conclusions:** Among parents of children with newly-diagnosed cancer who had consented for their child's participation in a therapeutic clinical trial, limited health literacy was consistently associated with lower comprehension of informed consent of most domains analyzed. Spanish as the preferred language of written and verbal medical information was also associated with lower comprehension. Our findings suggest that parents with limited health literacy or limited English-proficiency may not fully comprehend the informed consent and thereby not truly make informed decisions. Our findings highlight the potential role of interventions tailored to the participant's language and health literacy level to improve informed consent comprehension in underserved populations.

### HEMATOLOGY & ONCOLOGY

#### Poster #64:

#### Social Determinants of Health and Mistrust in Children with Sickle Cell Disease Prescribed Hydroxyurea

Shreya Banerjee, MD<sup>1</sup>; Bianca Perdomo, MA<sup>2-3</sup>; Courtney Thornburg, MD<sup>2-3</sup>; Paula Aristizabal, MD, MAS<sup>2-4</sup>

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**Background:** Hydroxyurea reduces the occurrence of complications and hospitalizations in children with sickle cell disease (SCD). However, adherence to long-term medications can be difficult for patients and caregivers. Given the complexity, mistrust and social determinants of health (SDoH; race, socio-economic status, education level, insurance type, health literacy, social support, and food security) may impact adherence to hydroxyurea as well as disease knowledge and health care utilization.

**Methods:** Our objective was to determine associations between mistrust and SDoH and adherence with hydroxyurea. We also evaluated associations between mistrust and SDoH on disease knowledge and health care utilization. We included parents of children with SCD prescribed hydroxyurea and followed within the comprehensive SCD center at Rady Children's Hospital-San Diego. Clinical characteristics and socio-demographics were collected. Patient-reported adherence to hydroxyurea was assessed using the Modified Morisky Scale. Health literacy was assessed with the New Vital Sign, and food insecurity was assessed via the USDA Food Security Module. To assess mistrust and social support, we used the Pediatric Trust Scale and the Duke-UNC Social Support Scale, respectively. Disease knowledge was assessed using the Georgia Department of Public Health SCD Knowledge Quiz, and calls/visits regarding SCD-related complications were assessed via chart review. Descriptive statistics were used to characterize the population. We assessed significant associations using regression models.

**Results:** Forty-eight parents were enrolled. We did not find any associations with adherence, likely due to the small sample. Limited health literacy was associated with lower disease knowledge ( $p = 0.006$ ). Higher mistrust and food insecurity were associated with more calls/visits for SCD-related care ( $p = 0.036$  and  $<0.001$ , respectively).

**Conclusions:** Health literacy clearly impacts disease knowledge. Further research of SDoH in a larger sample can help elucidate factors contributing to lower adherence and inform interventions aimed at improving adherence and reducing complications in children with SCD.

## HEMATOLOGY & ONCOLOGY

### Poster #65:

#### **Health Literacy in Parents of Children Newly-Diagnosed with Cancer: Social Determinants of Health and a Comparison of Health Literacy Measurements**

Victoria Bird, BA, MDc1; Shilpa Nataraj, MD1,2; Nikhil Kumar, MD1,3; Bianca P. Perdomo, MA4,5; Paula Aristizabal, MD, MAS4,5

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**Background:** Health literacy (HL) is the ability to understand and make decisions based on health-related information to function effectively in a healthcare environment. Limited HL correlates with higher healthcare utilization and worse health outcomes. Our objectives were 1) to assess Social Determinants of Healths associated with HL levels among caregivers of children newly-diagnosed with cancer and 2) to determine correlations among established measures of adult HL.

**Methods:** Caregivers of children (0-17yo) with newly-diagnosed cancer (n=199) were recruited between June 2017 and December 2021 at Rady Children's Hospital-San Diego. Socio-demographics (race/ethnicity, language, insurance type, marital status, education level) were collected. HL was measured using the Newest Vital Sign (NVS), Short-form of the Test of Functional Health Literacy (s-TOFHLA), Parental Health Literacy Activities Tests (PHLAT), Rapid Estimate of Adult Literacy in Medicine (REALM), Short Assessment of Health Literacy for Spanish Adults (SAHLSA-50), and Brief Health Literacy Screen (BHLS). We used linear regression models to assess for associations.

**Results:** Lower HL levels (measured by NVS) were positively correlated with Hispanic ethnicity ( $p<0.001$ ), Spanish as primary language ( $p<0.001$ ), public insurance ( $p<0.001$ ), unmarried status ( $p<0.006$ ), and a high school or less education ( $p<0.001$ ). Among HL surveys, s-TOFHLA was significantly correlated with NVS ( $p<0.001$ ), PHLAT ( $p<0.001$ ), REALM ( $p=0.009$ ), BHLS ( $p<0.001$ ), and SAHLSA-50 ( $p=0.025$ ).

**Conclusions:** Among caregivers of children newly-diagnosed with cancer, lower HL was significantly correlated with Hispanic ethnicity, Spanish language, public insurance, unmarried status, and lower education level. s-TOFHLA, considered the gold standard for measurement of HL, was correlated with NVS and other measurements. The NVS takes only 3-5 minutes to administer and is validated in English and Spanish. Its efficient administration and simplicity make it an attractive option to integrate into clinical care. By identifying caregivers with limited HL, we can help them navigate complex cancer care more efficiently.

### Poster #66:

#### **Getretinib is an Effective Treatment Against Neuroblastoma *In Vitro***

Breanna Breeding, MD and Peter Zage, MD

**Background:** Neuroblastoma is the most common extracranial solid tumor in children and has a poor prognosis despite intensive upfront therapy. Therefore, new therapeutic options are needed. Rearranged during transfection (RET) is a tyrosine kinase receptor that is important in normal neural differentiation. Inhibition of RET has been previously shown to be effective against neuroblastoma cell lines in vitro. Previous RET inhibitors tested in neuroblastoma have been non-specific tyrosine kinase inhibitors, which can increase side effects. Getretinib is a novel RET inhibitor that utilizes atropisomerism to specifically bind to and inhibit RET. Efficacy against neuroblastoma cell lines has not previously been tested.

**Methods:** Established neuroblastoma cell lines were grown in culture and treated with various doses of getretinib. Cell confluence was measured via continued image monitoring. Western blots were used to show RET and downstream inhibition as well as to show effect on viability.

**Results:** There was a dose-dependent decrease in confluence in cells treated with getretinib versus control. Western blot revealed decreased levels of phosphorylated RET in treated cells compared to controls.

**Conclusions:** Getretinib is effective against neuroblastoma cell lines in vitro via RET inhibition. Further preclinical studies are required, but getretinib is a promising potential drug for neuroblastoma.

## HEMATOLOGY & ONCOLOGY

### Poster #67:

#### **A World Health Organization Framework Approach to Building Sustainable Leukemia Care in Northwestern Mexico**

Andrew Chang, MD<sup>1</sup>; Rebeca Rivera-Gomez, MD<sup>2</sup>; Mario Ornelas, MD<sup>2</sup>; Maribel Ramirez, MD<sup>2</sup>; Gabriela Tamayo, MD<sup>2</sup>; Angelica Martinez, MD<sup>2</sup>; William Roberts, MD<sup>3,4</sup>; Paula Aristizabal, MD, MAS<sup>3,4,6</sup>

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**Background:** Pediatric leukemia outcomes are poor in many low-and middle-income countries (LMIC) and are exacerbated by healthcare systems ill-equipped to manage cancer. Effective leukemia management in LMIC involves a multi-step approach. It involves curating epidemiologic data; providing healthcare workforce specialty training; developing evidence-based treatments and supportive care programs; safeguarding access to medications/equipment; providing patient/family psychosocial, financial, and nutritional support; partnering with non-governmental organizations; and ensuring treatment adherence.

**Methods:** In 2013, in a partnership between North-American and Mexican institutions, we used the World Health Organization (WHO) health systems strengthening strategy "Framework for Action" with six domains in Services delivery, Workforce, Information systems, Access to essential medicines, Financing, and Leadership/Governance to implement a leukemia care program aimed at improving acute lymphoblastic leukemia (ALL) outcomes at a public hospital in Mexico that previously did not have an established pediatric oncology department. We prospectively assessed clinical features, risk classification, and survival outcomes in children with ALL at Hospital General-Tijuana from 2008-2012 (pre-implementation) and from 2013-2017 (post-implementation). We also evaluated program sustainability indicators.

**Results:** Our approach led to a fully staffed leukemia service, sustainable training programs, evidence-based projects to improve clinical outcomes, and funding for medications, supplies and personnel through local partnerships. Pre-implementation and post-implementation 5-year overall survival for children with standard-risk and high-risk ALL improved from 52% to 82% ( $P=0.023$ ) and from 46% to 76% ( $P=0.031$ ), respectively. Additionally, all sustainability indicators improved between 2013 and 2017.

**Conclusions:** By using the WHO framework, we improved leukemia care and survival in a public hospital in Mexico and established a foundation for continued program sustainability. We provide a multi-tiered framework for the development of similar programs in LMIC to sustainably improve leukemia outcomes.

## HEMATOLOGY & ONCOLOGY

### Poster #68:

#### **Shared decision-making for hemophilia gene therapy: patient perspectives and expectations**

Jacqueline Limjoco (jlimjoco1@rchsd.org)<sup>1</sup> ; Hannah Reyes (hreyes@rchsd.org)<sup>1</sup> ; Jennifer Han (jhan3@rchsd.org) <sup>1, 2</sup>; and Courtney Thornburg (cthornburg@rchsd.org) <sup>1, 2</sup>

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**Background:** The goal of shared decision-making (SDM) is for patients to understand available treatment options and choose the best option in the context of their values and preferences. Gene therapy is an emerging therapeutic option for hemophilia, and SDM tools may facilitate patient decision-making. This study was designed to inform the development of SDM tools for gene therapy.

**Methods:** Men with severe hemophilia received a study invitation email from the National Hemophilia Foundation Community Voices in Research and contacted the study team if interested in participation. Semi-structured interviews were conducted via telephone or videoconference. The interviews were transcribed verbatim. This analysis focuses on education needs and expectations, key stakeholders in decision-making, and perceived utility of a SDM tool.

**Results:** Twenty-five men with severe hemophilia A participated. When asked their opinion about gene therapy, 10 (40%) indicated that they are excited about gene therapy, 12 (48%) indicated that they are hopeful about gene therapy, one (4%) indicated that they are worried or scared about gene therapy, and one (4%) indicated that they don't have strong feelings about gene therapy. Participants most reported engaging the Hemophilia Treatment Center (HTC), family, and the hemophilia community in decision-making. The most reported information needs are efficacy, safety, cost/insurance, mechanism of action, and follow-up. In addition, key information themes that emerged were patient testimonials, hard data and statistics, and comparison to other products. Twenty-two (88%) indicated that a SDM tool would be useful when discussing gene therapy with their hemophilia team.

**Conclusions:** These data inform the development of SDM tools. Most participants identified the utility of a tool. Key information should be provided along with patient testimonials in non-biased format and allow comparison to other treatment options. In addition to the patient, stakeholders in the decision-making process are the HTC, family, and community members.

## HEMATOLOGY & ONCOLOGY

### Poster #69:

#### **Social Determinants of Health and their association with household material hardship and food insecurity in children with newly diagnosed cancer**

Carolyn Rocha, BS, MDc1; Shilpa Nataraj, MD2; Nikhil Kumar, MD3; Bianca P. Perdomo, MA4; Euyhyun Lee5; Matthew Banegas6; Corinne McDaniels-Davidson7; Paula Aristizabal, MD, MAS4,8,9

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**Background:** Poverty is associated with poorer health outcomes. Research on association of household material hardship (HMH) and food security with social determinants of health (SDoH) in diverse populations is lacking in pediatric cancer. To fill this gap, we conducted cross-sectional and longitudinal assessments of HMH and food security in families of children with cancer.

**Methods:** We prospectively enrolled parents of children with newly-diagnosed cancer at Rady Children's Hospital-San Diego, a large children's hospital with high representation of Hispanics. Assessments of HMH (food, housing, energy insecurity), food security, and SDoH (health literacy, acculturation (if Hispanic), socio-demographics) were conducted at 0, 3, 6, 12, and 24 months after diagnosis. Univariate and multivariate analyses were used to determine associations at each timepoint and longitudinally.

**Results:** Of 107 parent respondents, 55% were Hispanic and 74% were married. At baseline, 52% reported HMH and 24% reported food insecurity. In univariable analysis, public insurance was associated with HMH ( $p=0.007$ ) and food insecurity ( $p<0.001$ ); associations remained in multivariable analysis of HMH ( $p=0.046$ ) and food insecurity ( $p=0.008$ ). In univariable analysis, unmarried status was associated with HMH ( $p<0.001$ ) and food insecurity ( $p<0.001$ ); in multivariable analysis, associations with HMH ( $p=0.004$ ) and food insecurity ( $p=0.001$ ) remained.

Longitudinally, unmarried individuals and those with public insurance had higher odds of HMH (OR 3.40,  $p<0.001$ ; OR 2.71,  $p=0.014$ ) and food insecurity (OR 5.42,  $p<0.001$ ; OR 4.09,  $p=0.011$ ).

**Conclusions:** HMH and food insecurity were highly prevalent in our sample and associated with unmarried status and public insurance. These associations persisted over time. Our findings contribute to the scant literature in diverse populations, emphasizing the importance of financial hardship screening and resources, particularly to underserved individuals. Future directions include systematic assessments of HMH and food insecurity in children with cancer, including those enrolled in clinical trials, and development and implementation of effective interventions targeting HMH and food insecurity.

## HEMATOLOGY & ONCOLOGY

### Poster #70:

#### **Targeting Syk reprograms tumor-associated macrophages and enhances responses to immune checkpoint blockade and radiation therapy in high-risk neuroblastoma**

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**Background:** Immune checkpoint inhibition using anti-PD1/PDL1 antibodies has improved clinical outcomes in some adult cancers, while neuroblastoma (NB) patients received minimal clinical benefit from this therapy. Emerging evidence indicates that tumor-associated macrophages (TAMs) promote tumor growth and immunosuppression, leading to immune escape and resistance to checkpoint inhibitor therapy in NB. Our group has recently identified that spleen tyrosine kinase (Syk) regulates immunosuppressive transcriptional programming of macrophages in solid tumors. The role of Syk in NB and its correlation with the tumor immune microenvironment is unclear.

**Methods:** Immunohistochemistry was performed to determine the presence of Syk in human NB tumors. To elucidate the effect of myeloid Syk deficiency on NB tumor microenvironment, syngeneic MYCN-amplified (NB9464) and non-MYCN amplified (NBT3L) cell lines were used. The effect of Syk inhibitor, R788, in antitumor immunity alone or in combination with anti-PDL1 mAb and radiation was also determined in vivo. Tumor growth was monitored three times a week, and immune cell populations from tumors were analyzed by flow cytometry. RNA-seq and gene expression analysis were performed to define underlying mechanisms.

**Results:** We found that Syk is abundantly present in TAMs infiltrated in MYCN and non-MYCN amplified human NB tumors. Targeting Syk either by genetic deletion or pharmacological inhibition markedly impaired neuroblastoma tumor growth. This effect was facilitated by macrophages that became immunostimulatory in the absence of Syk, thereby recruiting CD8<sup>+</sup> T cells and activating anti-tumor immune responses. Moreover, combining R788 with anti-PDL1 mAb and radiation provided a synergistic effect leading to complete tumor regression and durable anti-tumor immunity in MYCN-driven murine neuroblastoma tumor model.

**Conclusions:** Collectively, these findings describe the role of Syk in controlling macrophage-mediated immunosuppression in NB tumors and support the clinical evaluation of R788 with anti-PDL1 mAb and radiation as a novel treatment strategy to increase anti-tumor immunity in neuroblastoma.

### Poster #71:

#### **Outcome of targeted therapy with PIK3CA-inhibitor alpelisib for patients with severe or life-threatening PIK3CA-related overgrowth spectrum (PROS)**

Deborah Schiff, Neera Gundrania, Hilda Ding, and John Naheedy

**Background:** PIK3CA-related overgrowth spectrum (PROS) includes various disorders that involve vascular malformations and overgrowth of different tissues caused by somatic gain-of-function mutations in the PIK3CA gene. PIK3CA inhibitor alpelisib, an FDA-approved treatment for metastatic breast cancer, has shown promising results for treatment of PROS in preclinical models and in patients.

**Methods:** We administered alpelisib to a cohort of patients with serious or life-threatening PROS who were enrolled on the Novartis alpelisib managed access program (MAP) for PROS. We retrospectively reviewed treatment outcomes for our alpelisib MAP cohort. Eligibility criteria included a diagnosis of PROS, age >2 years, patient's condition was severe or life-threatening, treatment was necessary, and there were no alternative treatments for the patient. Written consent was obtained prior to start of treatment. The dose of alpelisib for alpelisib MAP subjects was 250 mg PO daily for subjects >18 years of age and 50 mg PO daily for subjects <18 years of age. Baseline and surveillance labs were performed according to standard of care.

**Results:** Seven patients enrolled and were treated on alpelisib MAP for PROS. Five patients had a history of previous sirolimus therapy. Patient's ages ranged from 2-24 years. Diagnoses included PROS, LM, KTS, CLOVES, and FAVA. The genomic diagnosis was made from blood samples in 2 cases and from affected tissue in 5 cases. All patients had a beneficial response to alpelisib. Responses included decreased pain, improved mobility, decreased fatigue, decreased girth, and decreased port wine stains and lymphatic malformations. Two of 7 patients had alpelisib-related adverse effects: 1 had stomatitis but no dose modification was needed; 1 had diarrhea which improved with dose reduction. No patients discontinued therapy. Median duration of Alpelisib treatment was 468 days (range 245-626).

**Conclusions:** Alpelisib was effective and well-tolerated by a cohort of children and young adults with PROS.

### HEMATOLOGY & ONCOLOGY

**Poster #72:**

**Investigating intra-tumoral heterogeneity of extrachromosomal DNA in SHH medulloblastoma**

Sunita Sridhar, Owen Chapman, Robert J Wechsler-Reya, Jill P Mesirov, Lukas Chavez

Extrachromosomal circular DNA (ecDNA) is an important driver of aggressive cancers, including medulloblastoma (MB), the most common malignant pediatric brain tumor. Our study's aim is to better understand how ecDNA containing cells can potentiate malignant growth. EcDNA's role in the development of treatment resistance and association with poor outcomes is hypothesized to arise from its contribution to intra-tumoral heterogeneity and its potential to promote oncogene dependency switching. To analyze the intra-tumoral distribution of ecDNA, we have now simultaneously analyzed the accessible chromatin and gene expression in single cells of a SHH medulloblastoma (MB) patient using multiome single-cell ATAC-seq and gene expression (10X Genomics). Whole genome sequencing (WGS) of this tumor previously revealed a heterozygous somatic TP53 mutation and two distinct ecDNAs: a 3.2Mbp amplicon comprising 3 regions of chr1 and another 4.5Mbp amplicon comprising 23 segments originating from chr7 and chr17. We then used multimodal analysis to describe the tumor cell types, gene expression, variant signatures and estimate ecDNA copy number in the medulloblastoma tumor sample. We identified 12 distinct clusters in the human tumor, 5 of which were determined to be normal non-tumor cells, as identified by specific cell type markers, and 7 of which were determined to be tumor cells. One of the tumor clusters was found to be highly enriched for ecDNA. In addition, we also performed the same multiome single-cell analyses in an orthotopic xenograft model derived from this SHH MB patient tumor. In the PDX, 17 clusters were identified, all of which were determined to be tumor cells and enriched for ecDNA. Our preliminary results indicate that tumor cells with ecDNA in the human tumor (particularly the ecDNA enriched cluster) almost exclusively account for the cells in the corresponding PDX, emphasizing the aggressiveness of ecDNA containing cells.

## HEMATOLOGY & ONCOLOGY

### Poster #73:

#### **Theory-guided Assessment of Barriers and Facilitators to Adequate Informed Consent for Childhood Cancer Clinical Trials: Using the Exploration, Preparation, Implementation, Sustainment (EPIS) Framework**

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**Background:** To participate in childhood cancer clinical trials, parents/legal guardians must provide informed consent, which is a fundamental ethical right. However, barriers to achieving valid informed consent include: use of medical jargon, misunderstanding about clinical trials procedures, tremendous emotional distress surrounding the initial cancer diagnosis, and the complexity and length of the informed consent forms. There are scarce data on using theory to assess perspectives of parents of children with cancer on barriers and facilitators for adequate informed consent in diverse populations.

**Objective:** Using implementation science theory and methods, we assessed parent-reported barriers and facilitators to adequate informed consent, in a convenience sample that included a significant number of Hispanic parents.

**Methods:** Twelve qualitative semi-structured interviews and 224 open-ended surveys were conducted with 236 parents of children with newly-diagnosed cancer at Rady Children's Hospital-San Diego, a large quaternary children's hospital in California. Fifty-three percent of participants were Hispanic and 38% of Hispanics were monolingual Spanish-speakers. We utilized the Exploration, Preparation, Implementation, Sustainment (EPIS) Framework, specifically domains of outer context, inner context, bridging and innovation factors. Four main codes (informed consent concepts and delivery; desired clinical trial information; motivations and emotions related to clinical trial enrollment; and potential areas for interventions) were used as a coding guide for analysis. Interviews and surveys were transcribed and coded for thematic analysis by three independent coders to identify key barriers and facilitators.

**Results:** Four main themes were identified as barriers: 1) Complexity of the informed consent forms and discussion (lengthy, confusing, not available in Spanish, and use of medical jargon);

2) parents feeling emotionally overwhelmed, anxious and pressured around the informed consent;

3) parents viewing the clinical trial as the only treatment option; and 4) mistrust and fear of clinical trial procedures. Four informed consent facilitators were identified: 1) simpler explanations of study procedures; 2) provider training and flexibility for accommodations when delivering the informed consent, including additional time for decision-making and psychosocial support; 3) active promotion of voluntariness and trust; and 4) supplemental education in lay language, including request for peer-education, decision aids, and navigation to "bridge the provider-patient gap."

**Conclusions:** Our implementation science approach identified multiple barriers and facilitators to adequate informed consent in a diverse sample of parents. Findings can inform potential interventions to enhance informed consent for childhood cancer clinical trials, including the use of decision aids, peer-navigation, and interventions tailored to the language and culture of the individual.

### HEMATOLOGY & ONCOLOGY

**Poster #74:**

**OUTCOMES IN A PREDOMINANTLY HISPANIC/LATINO PATIENT COHORT WITH PHILADELPHIA-LIKE B-ALL**

Helena Yu, MD and Victor Wong, MD

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**Background:** Philadelphia (Ph)-like B-ALL presents a therapeutic challenge due to high rates of relapse. Common genetic pathways involved include the JAK-STAT pathway and ABL class fusions. Recent clinical trials incorporated the JAK-STAT inhibitor ruxolitinib and tyrosine kinase inhibitor dasatinib into treatment for Ph-like B-ALL. In addition, the National Comprehensive Cancer Network recommends enrolling Ph-like B-ALL patients on clinical trials which include ruxolitinib and dasatinib in front-line therapy.

**Methods:** We conducted a case series of 13 patients at Rady Children's Hospital with Ph-like B-ALL treated from 2015 to present, including a subset who received targeted agents, to investigate their treatment outcomes.

**Results:** Eight patients identified as Hispanic/Latino. Median age at diagnosis was 15 years. Of the Ph-like fusions identified, IGH-CRLF2 was most common, occurring in five patients. For upfront therapy, patients were predominantly treated on or following COG protocols. Eight patients received additional targeted agents, with 5 receiving ruxolitinib, 2 receiving dasatinib, and 1 receiving imatinib. One patient who received dasatinib then switched to ponatinib upon second relapse, which was stopped after molecular testing did not identify the EBF1-PDGFRB fusion present at diagnosis. Patients had poor outcomes, with seven patients relapsing at a median of 21 months (range 19-61 months). All patients receiving targeted agents relapsed. All relapsed patients received re-induction chemotherapy and/or blinatumomab. Five then underwent hematopoietic stem cell transplant (HSCT), and two multiply relapsed patients underwent both HSCT and CAR-T. Three relapsed patients died of infectious complications.

**Conclusions:** Our series of Ph-like B-ALL cases includes predominantly Hispanic/Latino patients with IGH-CRLF2 fusions, consistent with prior demographics for the Ph-like B-ALL population. Despite most patients receiving targeted agents with upfront therapy, they frequently relapsed. Further analysis of recent clinical trials incorporating targeted agents will characterize the utility of these treatment options for patients with Ph-like B-ALL.

## HOSPITAL MEDICINE

### Poster #75:

#### Impact of Cell-Free Next-Generation Sequencing on Management of Pediatric Complicated Pneumonia

Zephyr D. Dworsky, MD,\* Begem Lee, MD,\* Nanda Ramchandar, MD, MPH, Tiranun Rungvivatjarus, MD, Nicole G. Coufal, MD, PhD, and John S. Bradley, MD

**Background:** Community acquired pneumonia (CAP) is a common disease in pediatrics. Complicated pneumonia (cCAP) requires broad-spectrum therapy, but targeted therapy for a specific pathogen is preferred. Cell-free plasma next-generation sequencing (cfNGS) has the potential to guide therapy.

**Methods:** We conducted a retrospective review of children aged 3 months - 18 years admitted with cCAP over 3 years. We compared the positivity rate of conventional microbiologic diagnostic testing with that of cfNGS and the impact of cfNGS on clinical management. We performed chart review to determine if and how cfNGS results changed management as assessed by the documented impression and plan of the clinical team at the time the cfNGS result returned.

**Results:** We identified 46 children with cCAP who met our inclusion criteria and in whom cfNGS was sent. Of the 34 children with blood cultures, one (3%) was positive. Of the 37 children with pleural fluid cultures, 14 (27%) were positive from 10 children. cfNGS was positive in 45 out of 46 children (98%) and deemed likely to be pathogenic by the treating team in 41 of 46 children (89%). In 32 out of the 46 children (70%), cfNGS was the only means of pathogen identification. The results of cfNGS changed management in 36 of 46 cases (78%); antibiotics were narrowed in 29 of these cases (81%). In 6 of the 29 cases, antibiotics were changed, and in one of these, the duration of antibiotic treatment was also shortened. In one child, the cfNGS result led to broadening of antibiotic therapy.

**Conclusions:** In this retrospective series of 46 children with cCAP, cfNGS identified a pathogen in 41 children (89%) and impacted management in 36 (78%). While this uncontrolled data is promising, well-designed prospective studies are needed to best characterize the clinical use of cfNGS in children with cCAP.

### Poster #76:

#### Pharmacokinetics of Oral Dexamethasone in Children with Asthma and Obesity

Manaswitha Khare<sup>1</sup>, Jeremiah Momper<sup>2</sup>, Marlon Liyanage<sup>2</sup>, Vanessa Tamas<sup>3</sup>, Maria Huang<sup>1</sup>, Adriana Tremoulet<sup>4</sup>, Kyung Rhee<sup>1</sup>

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**Introduction:** Children with obesity are at twofold increased risk of developing asthma compared to normal weight children, and obesity related asthma has been associated with decreased medication responsiveness [2]. The altered body composition in children with obesity may also affect drug pharmacokinetics (PK) including drug absorption, distribution, metabolism, and excretion [7]. Therefore, children with obesity-related asthma are often sub-optimally treated, which can lead to poor disease control [2, 3]. Since most medication dosing in children is weight-based, this practice results in high doses of dexamethasone (DEX) in children with obesity experiencing asthma exacerbations. However, no data are available on DEX PK in children with obesity to guide dosing. Therefore, providers often "max out" at the adult dose which may place children at increased risk of toxicity or reduced therapeutic effect of DEX.

**Objective:** To characterize the pharmacokinetics of a single oral dose of DEX in overweight and obese (BMI  $\geq$  85th percentile) children with asthma (age 4-17 years old) and compare to historical data.

**Methods:** Pediatric patients with asthma and obesity receiving oral DEX for acute asthma exacerbation were enrolled. DEX was dosed at 0.6 mg/kg up to a maximum of 16 mg. Blood samples were collected between 0 and 39.4 hours post-dose using dried matrix microsampling via a fingerstick using the Mitra Microsampling Device. DEX concentrations were determined using a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method. PK data were pooled and analyzed with noncompartmental methods using Phoenix WinNonlin (Cary, NC).

**Results:** A total of 18 patients were enrolled. The median (interquartile range; IQR) age and body weight were 7 (4-13) and 34.5 kg (23.8 - 36.7), respectively. The median (range) number of samples per patient was 2 (1 - 4). DEX PK data are displayed in Table 1. Compared to previously reported DEX PK data in healthy adults, C<sub>max</sub> and AUC were 5% lower and 12% lower, respectively, in overweight and obese pediatric patients.

**Conclusions:** DEX exposures in overweight and obese pediatric patients receiving 0.6 mg/kg doses (up to a maximum of 16 mg) were overall similar to those in healthy adults. Additional data are needed to confirm this observation and support dosing recommendations. This study also illustrates the utility to perform microsampling to facilitate PK studies in children.

## HOSPITAL MEDICINE

### Poster #77:

#### Self-Service Reporting in Pediatrics

Tiranun Rungvivatjarus MD, Mario Bialostozky MD, Aarti Patel MD, Med, Cynthia Kuelbs, MD, Amy Chong MD

**Background:** Many EHRs provide physicians with user-friendly self-service reporting tools that enable extraction of patient data directly from the medical record for use in scholarly work. However, physician training on how to use these tools has been limited and, to our knowledge, not been reported in the literature. Our objective was to develop a curriculum for physicians to enhance understanding and empower them to utilize these tools in hospital operations and scholarly work.

**Methods:** In 2019, physician informaticists developed 2 interactive sessions to train physicians on self-service reporting tools available in our EHR: Epic® SlicerDicer and Reporting Workbench (RWB). Sessions were conducted virtually over Zoom. We assessed participants' knowledge, confidence and application of reporting tools before, immediately after, and 3-month post session using a REDCap® survey.

**Results:** Virtual training sessions occurred between April and August 2021. Thirty-six participants participated in the study. Sixteen surveys were collected after training sessions. Twenty-two surveys were collected at 3-month post assessment. Regarding data literacy knowledge, the pre-test average score was 62%, which then increased to 93% ( $p < 0.05$ ) immediately post-session, and was 74% at 3-month post assessment ( $p = 0.05$ ). Our surveys did not find statistical significance increase in tool utilization (Figure 1). Participants reported increased confidence in performing certain SlicerDicer-specific tasks such as model selection, criteria selection, and data visualization ( $p < 0.05$ ). Similar increase in confidence was observed in RWB-specific tasks ( $p < 0.05$ ) (Figure 2). Eighty-five percent of participants expressed that they would be interested in attending a follow-up, more advanced workshop on this same topic in the future.

**Conclusions:** Virtual physician training on self-service reporting tools such as Epic® SlicerDicer and Reporting Workbench are effective in increasing data literacy knowledge, tool utilization, and confidence. Physicians expressed interest in similar, more advanced self-service reporting training in the future.

### Poster #78:

#### Safety of Oral Feeding on High-Flow Nasal Cannula in Children Hospitalized with Bronchiolitis

Sarah Schneidera,b, MD; Begem Leea,b, MD; Michael Levya,b, MD; Tiranun Rungvivatjarusa,b, MD; Aarti Patela,b, MD, MEd; Elizabeth Mannino Avilaa,b, MD; Erin Fishera,b, MD, MHM; Kyung E. Rheeab, MD, MSc, MA

aUniversity of California San Diego; and bRady Children's Hospital San Diego

**Background:** Oral feeding on high-flow nasal cannula (HFNC) in patients hospitalized with bronchiolitis is questioned due to concerns for safety, swallowing dysfunction, and aspiration, resulting in high practice variability. Our objective was to determine the incidence of adverse feeding events and aspiration pneumonia in children with bronchiolitis who fed orally while on HFNC.

**Methods:** We conducted a single-center, retrospective chart review from March 2017-May 2020. We included children up to age 2 admitted for bronchiolitis and treated with HFNC (2L/kg, up to max 12L) on the pediatric ward. We excluded patients with chronic medical conditions, chronic lung disease, congenital heart disease, and bacterial pneumonia. Primary outcomes: incidence of adverse feeding events and aspiration pneumonia. Secondary outcomes: escalation to nCPAP, PICU transfer, NPO status and duration, LOS, and 7-day readmission. Frequencies, means (SD), or medians (IQR) were used to describe the sample.

**Results:** Of the 876 patients with bronchiolitis on HFNC, 676 met inclusion criteria (Table 1). Adverse feeding events (e.g., choking with feeds) occurred in 11 patients (1.6%). Of those 11 patients, 3 had concern for possible micro-aspiration leading to increased respiratory support or LOS, but none were diagnosed with or treated for aspiration pneumonia. All patients fed orally with a median time to first feed of 2 hrs. Average max HFNC flow rate was 8L/min or 1L/kg/min. Escalation to nCPAP occurred in 64 patients (9.4%), and 35 patients (5.2%) transferred to the PICU. Patients were made NPO while on HFNC ( $n = 55$ , 8.1%) primarily due to worsening respiratory distress with a median time NPO of 4 hrs.

**Conclusions:** We identified a low incidence of adverse feeding events in children with bronchiolitis on HFNC who received oral nutrition. No patients were diagnosed with aspiration pneumonia. These results suggest that adverse feeding events are rare, and oral nutrition is well tolerated on HFNC.

## *HOST-MICROBE SYSTEMS AND THERAPEUTICS*

### **Poster #79:**

#### **Context-aware deconvolution of cell-cell communication with Tensor-cell2cell**

Erick Armingol<sup>1,2,7</sup>, Hratch M. Baghdassarian<sup>1,2,7</sup>, Cameron Martino<sup>1,2,3</sup>, Araceli Perez-Lopez<sup>4</sup>, Caitlin Aamodt<sup>2</sup>, Rob Knight<sup>2,3,5,6</sup>, Nathan E. Lewis<sup>2,6\*</sup>

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**Background:** Cell-cell communication coordinates biological functions occurring at an organismal level. However, cellular contexts such as disease state, organismal life stage and tissue microenvironment are the conditions that shape intercellular communication, and ultimately affect an organism's phenotypes. Molecules mediating cell-cell communication are measured through single-cell technologies, and emerging computational tools can exploit these data to decipher intercellular communication. A major limitation of current methods is that they disregard cellular contexts or rely on simple pairwise comparisons between samples, which limits the analysis of how cell-cell communication is shaped by, for example, multiple time points, levels of disease severity, or spatial contexts.

**Methods:** Here we present Tensor-cell2cell, an unsupervised method using tensor decomposition, which is the first strategy to decipher context-driven intercellular communication by simultaneously accounting for multiple stages, states, or locations of the cells. Tensor-cell2cell uses single-cell data to extract multiple modules of intercellular communication based on ligand-receptor interactions while linking them with variations in the cellular contexts, helping to gain insights on how these contexts shape the communication at the cellular and molecular levels.

**Results:** We further demonstrate how Tensor-cell2cell can identify multiple modules associated with distinct communication processes (e.g., participating cell-cell and ligand receptor pairs) in both simulated and real datasets. We also show how cell-cell communication is linked to Autism Spectrum Disorder in a patient-wise manner.

**Conclusions:** Thus, we introduce an effective and easy-to-use strategy for understanding complex communication patterns across diverse conditions, and for identifying molecular and cellular mechanisms that could be used for biotherapeutic applications.

# ABSTRACTS: POSTER PRESENTATIONS

## HOST-MICROBE SYSTEMS AND THERAPEUTICS

### Poster #80:

#### Nanoparticle Vaccine Protects Against *A. baumannii* Sepsis and Pneumonia

Elisabet Bjanes, Jiarong Zhou, Liangfang Zhang, Victor Nizet

**Background:** Multidrug-resistant (MDR) bacterial infections kill 1.3 million people globally each year. The Gram-negative opportunistic pathogen *Acinetobacter baumannii* is the top priority by the WHO and CDC for new therapeutics development. MDR prevalence in *A. baumannii* strains is as high as 80%, contributing to hospital-acquired infections including ventilator associated pneumonia and sepsis. Immunosuppression, prolonged antimicrobial therapy, COVID19 infection, and mechanical ventilation increase susceptibility to *A. baumannii* infection. Vaccines are an alternative strategy to provide immunity while limiting opportunities for antimicrobial resistance.

**Methods:** Our strategy utilizes outer membranes vesicles (OMVs) as highly immunogenic vaccine antigens; however, OMV heterogeneity renders them undesirable for large-scale clinical development. Studies have employed nanoparticles as vaccine delivery platforms, providing improved stability, delivery efficiency, and immune cell activation. Combining nanotechnology with OMVs may overcome the limitations of OMV-only vaccines. I developed a candidate vaccine platform where gold nanoparticles are coated with OMVs from the hypervirulent clinical isolate *A. baumannii* Lac-4.

**Results:** My Ab-NP vaccine completely protects mice from disseminated sepsis and pneumonia. Vaccination generates robust *A. baumannii*-specific IgG antibody responses and induces increased antigen presenting cells recruitment to draining lymph nodes. Ab-NP vaccination enables rapid control of inflammation, bacterial dissemination, and hypothermia in systemic infection models. Additional analysis shows that Ab-NP vaccination is protective by inducing synergy between the innate and adaptive immune systems, as immune serum significantly enhances the recruitment and killing capacity of neutrophils, and passive vaccination with immune serum completely protects naive mice against lethal sepsis.

**Conclusions:** My work has generated a protective vaccine candidate against *A. baumannii*. My ongoing studies seek to ensure the NP vaccine platform is broadly cross-protective against the most common clinical *A. baumannii* isolates, protects in the context of host immunosuppression such as neutropenia or corticosteroid therapy, and may be extended to other high-priority MDR pathogens.

### Poster #81:

#### Characterizing *Candida auris* Virulence Using Markerless CRISPR/Cas9 to Delete *pra1* and *pmt1*

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*Candida auris* is a highly multidrug-resistant (MDR) fungal pathogen that is becoming a global concern. The ability of this pathogen to produce serious human infections implies virulence mechanisms to avoid efficient clearance by the host innate immune system. The virulence factors involved in *C. auris* disease development remain understudied compared to the common fungal pathogen *Candida albicans* where the genes *pmt1* and *pra1* are known to contribute to immune evasion. *Pmt1*, or protein O-mannosyltransferase 1, affects fungal cell wall composition, where deletion of the *C. albicans* *pmt1* gene reduces mannoprotein and increases  $\beta$ 1,3-glucan. Since  $\beta$ 1,3-glucan is the primary ligand for the pattern recognition receptor dectin-1 on immune cells, a *C. albicans*  $\Delta$ *pmt1* mutant activates the host innate immune response more strongly. *C. albicans* *Pra1* is a strong immune deactivator that recruits inhibitory complement components Factor H and C4B binding protein to reduce innate immune cell interaction. In this work, I have used a markerless CRISPR/Cas9 system to successfully delete the *pmt1* and *pra1* homologues of *C. auris* and used the resulting mutants to study their contribution to fungal interactions with the complement system, dectin-1 and other elements of innate immunity. Overall, these new *C. auris* mutants will help characterize two potential virulence factor targets that could inspire novel approaches to better treatment of this MDR fungal pathogen.

## HOST-MICROBE SYSTEMS AND THERAPEUTICS

### Poster #82:

#### Macrophage biomimetic nanoparticles as a cytoprotective anti-inflammatory therapy in bacterial sepsis

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**Background:** Bacterial sepsis is a deadly dysregulation of the host response to invading pathogens. More than 75,000 children develop sepsis every year in the United States, and it accounts for 1 in 3 hospital deaths. During sepsis, both bacterial products and the host's response produce systemic damage and multiorgan failure. Despite the well-documented role of hyperinflammation in sepsis, current therapies rely on supportive care and rapid administration of antibiotics. In fact, simple anti-inflammatory therapies are notoriously ineffective at improving outcomes in such a multifaceted condition. Macrophages, an innate immune cell, contribute to sepsis both as a target of bacterial damage and as an instigator/propagator of hyperinflammation. We propose exploiting their key role in sepsis by using macrophage biomimetic nanoparticles (MF-NP) as decoys for both bacterial products and host-derived cytokines.

**Methods:** Here we use a combination of in vitro and ex vivo techniques to quantify the ability of MF-NP to prevent cytotoxicity and immune activation by sequestering bacterial pore forming toxins (PFTs) and endotoxins as well as host-derived cytokines.

**Results:** We found MF-NP prevent cytotoxicity in response to the PFTs alpha toxin and streptolysin-O. Furthermore, MF-NP reduce immune activation in response to both gram-negative lipopolysaccharide (LPS) and gram-positive lipoteichoic acid (LTA). Finally, using a novel ex vivo human sepsis model we show MF-NP reduce immune activation by sequestering the inflammatory cytokines interleukin-6 (IL6) and tumor necrosis factor alpha (TNFa).

**Conclusions:** Here we demonstrate MF-NP interrupt both bacterial and host-derived drivers of sepsis. Unlike previous sepsis therapies, they target multiple distinct sources of cytotoxicity and inflammation. Thus, in a field in need of effective sepsis therapies, MF-NP have promising in vitro and ex vivo potential.

### Poster #83:

#### Multisystem Inflammatory Syndrome Therapies in Children (MISTIC) Trial

Sonia Jain, PhD; Feng He; Kiana Brown; Samantha Roberts; Nipha Sivilay; Jane C. Burns, MD; Adriana Tremoulet, MD, MAS

**Background:** Multisystem Inflammatory Syndrome in Children (MIS-C), occurring 2-6 weeks after initial exposure to SARS-CoV-2 and for which there has been no clinical trial to determine the most effective treatment, was first identified in early 2020. The primary aim of this randomized comparative effectiveness study is to determine the anti-inflammatory treatment from first randomization that has the lowest rate of second randomization in the treatment of MIS-C.

**Methods:** Patients at Rady Children's Hospital San Diego are eligible to participate if they meet the CDC criteria for MIS-C (fever, +IgG to SARS-CoV-2 nucleocapsid, at least two body systems involved, predominantly cardiovascular, mucocutaneous or gastrointestinal, and have no other leading diagnosis). Patients are excluded if they have an immunodeficiency, a medical condition that prevents them from receiving one or more of the study drugs, or received any of the study drugs prior to enrollment. All participants are treated with IVIG and then randomized to either infliximab, steroids or anakinra. Serial blood samples are collected for molecular studies of treatment effect. Target enrollment using a Small n SMART design is 108 evaluable patients.

**Results:** We have screened 87 patients and enrolled 67 participants (46 completed the study, 19 active, and two patients discontinued early due to study protocols deviation). The median age of participants is 7.6 years, 63% are male, 74.6% are Hispanic/Latino and 10.5% are African American. There have been no serious adverse events attributable to study drugs or deaths during this study. One third of participants experienced an adverse event, including bradycardia, hallucinations, GI bleeding, or elevation of hepatic enzymes.

**Conclusions:** This study continues to enroll eligible patients to determine the most effective treatment regimen for MIS-C, and will soon expand to include more study sites.

## HOST-MICROBE SYSTEMS AND THERAPEUTICS

### Poster #84:

#### **BRIDGING THE DIAGNOSTIC KAWASAKI DISEASE GENE EXPRESSION PROFILING CLASSIFIER FROM MICROARRAY TO A CLINICALLY APPLICABLE MULTIPLEX QRT-PCR ASSAY (KIDS-GEP)**

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<sup>5</sup>These authors contributed equally

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Kawasaki disease (KD) is a systemic vasculitis that is most prevalent in children under 5 years of age and can result in the development of coronary artery abnormalities (CAA). Early treatment with intravenous immunoglobulin is effective, but diagnosing KD can be challenging. Timely diagnosis of KD may become more straightforward with the recent discovery of a microarray-based host response classifier that discriminates KD patients from patients with other febrile conditions. As a microarray is not suited for the acute clinical care setting, we bridged this microarray-based classifier to a clinically applicable One-step multiplex qRT-PCR assay: the Kawasaki Disease Gene Expression Profiling (KiDs-GEP) classifier.

A qRT-PCR assay was designed and optimized, and subsequently applied to RNA isolated from whole blood samples of KD patients and febrile controls. The results were used to reweight the original classifier.

The performance of the bridged KiDs-GEP classifier was comparable to the original classifier with a cross-validated area under the ROC curve (AUC) of 0.964 [95%CI: 0.924-1.00] vs 0.992 [95%CI: 0.978-1.00] respectively. Both classifiers demonstrated similar trends over various disease conditions, with the clearest distinction between individuals diagnosed with KD and viral infections.

In conclusion, we successfully bridged the microarray-based classifier into the qRT-PCR KiDs-GEP classifier: a more rapid and less costly assay that brings the host response clinical test for KD closer to the hospital clinical laboratory, enabling earlier diagnosis, treatment and better prevention against CAA.

### Poster #85:

#### **The group B Streptococcus virulence factor C5a peptidase role in complement cleavage and vaccine protection**

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Infection by the bacterial pathogen group B Streptococcus (GBS) causes significant morbidity and mortality in pregnant women and neonates, especially in resource-poor countries where universal screening programs and intrapartum prophylaxis remain challenging. In addition, concern about the impact of antibiotic treatment on the developing neonatal microbiome is gaining increased attention. For these reasons, a vaccine to prevent GBS infection is an important public health priority. Our laboratory is collaborating with Vaxcyte, Inc. (Foster City, CA) in advanced preclinical development of the multivalent vaccine VAX-A1, for prevention of infections by the related pathogen group A Streptococcus (GAS). Due to high sequence homology (98%) between a key VAX-A1 component, the surface anchored C5a peptidase (ScpA) and its GBS homolog (ScpB), we predicted that VAX-A1 could also be effective at protecting against GBS infection. In addition, the functional role of ScpB in GBS virulence remains unclear. We generated a GBS ScpB deletion mutant and performed heterologous expression of ScpB gene in nonvirulent Lactococcus lactis to explore the role of C5a peptidase in both GBS virulence and vaccine efficacy. Mice immunized with VAX-A1 were protected against lethal infection with three GBS strains of different serotypes prevalent in human newborn infection. Serum from mice immunized with GAS C5a peptidase present in VAX-A1 cross-react with L. lactis expressing GBS ScpB, suggesting it was the target antigen responsible for cross protection. C5a peptidase in both GAS and GBS cleaves human C5a, a major component of the complement cascade, to evade host immunity. Ongoing studies use our loss and gain of function GBS bacterial reagents to study the contribution of ScpB to GBS immune evasion and virulence. Ultimately this research will show the potential effectiveness of VAX-A1 in preventing GBS infection which would represent a major added benefit of its adoption into the routine immunization schedule

## INFECTIOUS DISEASES

### Poster #86:

#### **Predictive modeling of human *Staphylococcus aureus* vaccine efficacy identifies approach to overcome pervasive vaccine failure**

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**Background:** As a critical pathobiont, *Staphylococcus aureus* (SA) has been the focus of tremendous efforts towards developing a vaccine. Despite producing many promising candidates in pre-clinical animal models, however, all clinical trials have failed to replicate the same efficacy in humans. In our previous investigation that focused on the failed IsdB vaccine trial, we demonstrated that anti-IsdB antibodies from prior SA exposure are non-protective, and interfered with subsequent IsdB vaccination to result in total loss of efficacy.

**Methods:** We utilized a model of SA pre-exposure that mimics ubiquitous human-SA interaction to assess vaccine efficacy in SA-experienced host.

**Results:** We demonstrate that total antibodies from SA-experienced mouse and human serum donors are largely non-protective against SA infections; individually, antitoxin antibodies are neutralizing, while anti-cell wall-anchored antibodies are not opsonic. Consequently, we show in an animal model that the presence of the latter non-protective antibodies against IsdA, MntC, and SpA render their corresponding vaccines non-efficacious. Further, we determined that despite seemingly effective vaccination against LukE and Hla toxins, the inferior neutralizing efficiency of SA-induced antitoxin antibodies compared to vaccine none-the-less quells the maximum protection of the vaccine alone. Importantly, we identified that selection of naturally immune-subdominant targets, like ClfA, SdrE and EsxAB, which minimally elicit obstructive antibodies from prior SA exposure, can circumvent vaccine interference to produce protection in SA-experienced host.

**Conclusions:** Our study demonstrates adverse interaction between pre-existing SA-induced immunity with subsequent vaccination to result in diminished efficacy. Collectively, our findings present an innovative framework to understand the longstanding challenges in staphylococcal vaccinology and provides a tool to discover viable solutions.

### Poster #87:

#### **Pacritinib inhibition of IRAK1 blocks aberrant TLR8 signaling by SARS-CoV-2 and HIV-1 derived RNA**

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**Background:** Toll-like receptors (TLR) recognize specific pathogen-associated molecular patterns and are critical in regulating innate immune responses. Recent studies suggest a role for aberrant TLR8 and NLRP3 inflammasome activation during both SARS-CoV-2 and HIV-1-infection. We previously identified a GU-rich ssRNA sequence from the spike protein of SARS-CoV-2 that triggers a TLR8-dependent pro inflammatory cytokine response from primary human macrophages in the absence of pyroptosis. As IRAKs are critical for TLR signaling and play direct roles in the TLR mediated activation of the NLRP3 inflammasome and the subsequent generation of IL-1 $\beta$  and other important pro-inflammatory cytokines, we examined the mechanism(s) and impact of IRAK1 inhibition following TLR8 activation by GU-rich ssRNA.

**Methods:** Monocyte-derived macrophages were challenged with GU-rich ssRNA derived from SARS-CoV-2 (RNA649) or HIV-1 (RNA40) in the presence or absence of pacritinib, an ATP-competitive, macrocyclic inhibitor of IRAK1. TLR8 signaling and the production of pro-inflammatory cytokines were assessed using immunoblotting, co immunoprecipitation and ELISA. Data were analyzed using the paired, two-tailed, Student's t test.

**Results:** We demonstrate that pacritinib inhibits the TLR8-dependent pro inflammatory cytokine response in macrophages mediated by RNA649 and RNA40. Specifically, pacritinib inhibits the TLR8-mediated IRAK1 phosphorylation and ubiquitination that is required for the recruitment of TRAF6 and the TAK1 complex to IRAK1 post-TLR8 activation. This results in the ablation of the downstream signaling cascade including MAP kinase and transcription factor (NF- $\kappa$ B and IRF5) activation required for pro-inflammatory cytokine transcription, leading to the inhibition of IL-6, TNF and IL-1 $\beta$  release.

**Conclusions:** Our data demonstrate that pacritinib inhibits the SARS-CoV-2 and HIV-1 derived GU-rich ssRNA induced rapid activation, phosphorylation, and ubiquitination of IRAK1 leading to the inhibition of IL-6, TNF, and IL-1 $\beta$  release from macrophages that does not require active viral infection. These data suggest that IRAK1 may prove to be an excellent therapeutic target to ameliorate COVID-19 and HIV-1- associated chronic inflammation.

## INFECTIOUS DISEASES

### Poster #88:

#### **Pediatric Osteoarticular Infections Caused by Mycobacteria Tuberculosis Complex: A Twenty-Six Year Review of Cases in San Diego, California**

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**Background:** Osteoarticular infections (OAI) account for 10-20% of extrapulmonary Mycobacteria tuberculosis (MTB) complex infections in children, and 1-2% of all pediatric tuberculosis infections. Treatment regimens and durations typically mirror recommendations for other types of extra-pulmonary MTB, but there are significant variations in practice, with some experts suggesting a treatment course of 12 months or longer.

**Methods:** We conducted a retrospective review of children diagnosed with MTB complex OAI and cared for between 31 Dec 1992 to 31 Dec 2018 at a tertiary care pediatric hospital near the United States-Mexico border.

**Results:** We identified 21 children with MTB complex OAI during the study period. Concurrent pulmonary disease (9.5%), meningitis (9.5%), and intra-abdominal involvement (14.3%) were all observed. MTB complex was identified by culture from operative samples in 15/21 children (71.4%); 8/15 (53.3%) cultures were positive for *Mycobacterium bovis*. Open bone biopsy was the most common procedure for procurement of a tissue sample and had the highest culture yield. The median duration of antimicrobial therapy was 52 weeks (IQR 46-58). Successful completion of therapy was documented in 15 children (71.4%). Nine children (42.9%) experienced long term sequelae related to their infection.

**Conclusions:** Our study demonstrates adverse interaction between pre-existing SA-induced immunity with subsequent vaccination to result in diminished efficacy. Collectively, our findings present an innovative framework to understand the longstanding challenges in staphylococcal vaccinology and provides a tool to discover viable solutions.

### Poster #89:

#### **Pathobiont-induced immunosuppressive CD4+T cells underlie failure of a Staphylococcus aureus vaccine**

Irshad A. Hajam<sup>1</sup>, Chih-Ming Tsai<sup>1</sup>, JR Caldera<sup>1,2</sup>, Cesia Gonzalez<sup>1</sup>, Desmond Trieu<sup>1</sup>, George Y. Liu<sup>1,3</sup>

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<sup>3</sup>Division of Infectious Diseases, Rady Children's Hospital; San Diego, CA 92123, USA.

**Background:** All vaccine development efforts against *S. aureus* have been unsuccessful to date. We propose that the lack of consideration of prior host exposure to *S. aureus* is a major factor responsible for the failed vaccines.

**Methods:** Mice were first exposed to *S. aureus* followed by *S. aureus* IsdB vaccination. 7 days post-last vaccination, mice were challenged with *S. aureus* and bacterial burdens in spleen and kidneys were enumerated. Naïve mice vaccinated with IsdB vaccine served as a positive control.

**Results:** We showed in a murine sepsis model that prior exposure to *S. aureus* abrogates protection conferred by staphylococcal IsdB vaccine. *S. aureus* exposure induces an immunosuppressive CD4+T cell response which blunts efficacy of the subsequently administered IsdB vaccine. Vaccine interference is dependent on IL-10 that is primarily secreted by IsdB-specific CD4+T cells. Adoptive transfer of the *S. aureus* exposed CD4+ T cells inhibited vaccine-induced antigen-specific protection in the recipient mice. We showed that IsdB vaccination of naïve and *S. aureus*-exposed mice leads to specific antibodies with different levels of sialylation. Anti-IL-10 treatment reverted the non-protective T cell phenotype and restored antibody sialylation levels. We further demonstrated prior *S. aureus* infection downregulated antigen-specific IL-17+T cell responses, but addition of select 17/IFN-γ boosting adjuvants to IsdB vaccine overcame the lack of vaccine protection against *S. aureus*.

**Conclusions:** We showed that prior staphylococcal exposure leads to development of an antigen-specific immunosuppressive IL-10+CD4+T response that drives vaccine failure. Adjuvants that confer robust IL-17/IFN-γ response can overcome vaccine interference in mice previously exposed to *S. aureus*.

# ABSTRACTS: POSTER PRESENTATIONS

## INFECTIOUS DISEASES

### Poster #90:

#### **Astrocytes Transfer Functional Mitochondria to Neurons to Maintain Neuron Function following Exposure to Human Immunodeficiency Virus type-1 Toxic Proteins**

Carmen Teodorof-Diedrich<sup>1</sup>, Stephen A. Spector<sup>1,2</sup>

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**Background:** In healthy cells, damaged mitochondria are eliminated through a process called mitophagy. We have shown that HIV-1 proteins, gp120 and Tat, induce mitochondrial damage and alter mitophagy in primary human neurons. Here we examine the potential compensatory mechanisms within the central nervous system that replenish healthy mitochondria and promote neuron health following exposure to HIV-1 toxic proteins.

**Methods:** Human neurons treated with 100 ng/ml HIV-1 gp120 or Tat proteins were co-cultured with astrocytes, or incubated with astrocyte condition media (ACM)/ $\Delta$ Mtc ACM to determine the effect of astrocyte-derived mitochondria (ADM) on the recovery of mitochondrial function and neuronal network. Confocal, TEM, and immunoblotting analyses were used to identify ADM. Mitochondrial membrane potential was assessed using MitoTrackerCMXRos and the dendritic network was measured using Simple Neurite Tracer (Fiji).

**Results:** We show that mitochondria released by astrocytes either as free organelles or within vesicles are taken up by neurons, and neurons exposed to HIV-1 proteins increase internalization of astrocyte-derived mitochondria ( $P < 0.05$ ). The internalized mitochondria are not targeted for lysosomal degradation and result in a significant increase in ATP levels compared to  $\Delta$ MtcACM treatment ( $P < 0.05$  for all comparisons) and recovery of mitochondrial membrane potential ( $P < 0.05$ ). Additionally, the toxic effects of HIV-1 proteins on the dendritic network are abrogated by ACM and the transfer of mitochondria supports dendritic elongation and overall neuron function.

**Conclusions:** Our findings demonstrate that human astrocytes release mitochondria as free organelles or within membrane vesicles, and exposure to HIV-1 toxic proteins results in enhanced uptake of healthy mitochondria by exposed neurons with subsequent reversal of oxidative stress and recovery of neurite morphology. Thus, we have identified a compensatory mechanism for the maintenance of mitochondrial health that can potentially be utilized to improve neuron function during HIV-associated disorders and other conditions within the CNS that affect mitochondria.

### Poster #91:

#### **Non-protective immune imprint underlies failure of *S. aureus* IsdB vaccine**

Chih-Ming Tsai, JR Caldera, Irshad A. Hajam, Austin W.T. Chiang, Chih-Hsiung Tsai, Haining Li, María Lázaro Díez, Cesia Gonzalez, Desmond Trieu, Gislaine A. Martins, David M. Underhill, Moshe Arditi, Nathan E. Lewis, George Liu

The failure of all *S. aureus* (SA) vaccine trials to date prompted us to explore a fundamental difference between humans and laboratory animals - their natural exposure to SA. Recapitulating the failed Phase III IsdB vaccine trial, we showed that mice previously infected with SA do not mount a protective antibody response to vaccination, unlike naïve animals. The non-protective antibodies exhibit increased  $\alpha 2,3$  sialylation that blunts opsonophagocytosis and preferentially target a non-protective domain of IsdB. IsdB vaccination of SA-infected mice recalls the non-neutralizing humoral responses which further reduce vaccine efficacy through direct antibody competition. Application of human serum antibodies against IsdB and ClfA, target of another failed vaccine, blunted protection conferred by anti-SA passive immunizations. Significantly, IsdB vaccine interference can be overcome by immunization against the IsdB heme-binding domain. Our study demonstrates that failure of anti-SA active and passive immunizations could be explained by non-protective imprint of prior host-SA interaction.

## INFORMATICS

### Poster #92:

#### **Development and Implementation of a Machine Learning Algorithm for Diagnosing Multisystem Inflammatory Syndrome in Children and Kawasaki Disease**

Jonathan Y. Lam<sup>1</sup>, Andrew C. Richardson<sup>2</sup>, Chisato Shimizu<sup>2</sup>, Emelia Bainto<sup>2</sup>, Samantha C. Roberts<sup>2</sup>, Nipha Sivilyay<sup>2</sup>, Adriana H. Tremoulet<sup>2</sup>, Michael A. Gardiner<sup>2</sup>, John T. Kanegaye<sup>2</sup>, Shamim Nemat<sup>1</sup>, Jane C. Burns<sup>2</sup>

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<sup>2</sup>Department of Pediatrics, Rady Children's Hospital and University of California San Diego, San Diego, CA, USA

**Background:** Multisystem inflammatory syndrome in children (MIS-C) is a novel disease identified during the COVID-19 pandemic characterized by systemic inflammation following SARS-CoV-2 infection. Most pediatric patients recover fully with anti-inflammatory treatments, but early detection of MIS-C remains a challenge given its clinical similarities to Kawasaki disease (KD) and other acute childhood illnesses. The goal of this study was to develop an artificial intelligence algorithm that can distinguish between MIS-C, KD, and other similar febrile illnesses and aid in the diagnosis of suspected patients in the emergency department.

**Methods:** We developed a deep learning algorithm called KIDMATCH (Kawasaki Disease vs Multisystem Inflammatory syndrome in Children) using patient age, the five classical clinical KD signs, and 17 laboratory measurements. We trained a two-stage model consisting of feedforward neural networks to distinguish between MIS-C and non-MIS-C patients and then KD and other febrile illness (FC) using 673 FC, 775 KD, and 131 MIS-C patients from 3 hospitals. KIDMATCH was internally validated using stratified 10-fold cross validation and externally validated on 175 MIS-C patients from 16 hospitals across the United States.

**Results:** KIDMATCH achieved a high median area under the curve during internal validation of 0.988 [IQR: 0.980-0.993] in the first stage and 0.960 [IQR: 0.956-0.972] in the second stage using thresholds set at 95% sensitivity to detect positive MIS-C and KD cases respectively. External validation of KIDMATCH achieved over 90% accuracy in 175 MIS-C patients from 16 sites. KIDMATCH was implemented as a web calculator within Rady Children's Hospital and has resolved confusing cases following its deployment in January 2022.

**Conclusions:** KIDMATCH has clinical utility in aiding frontline clinicians at the time of initial evaluation within the hospital setting to distinguish between MIS-C, KD, and similar febrile illnesses to enable prompt treatment and prevent severe complications.

## INFORMATICS

### Poster #93:

#### Single IRB Workforce and Resources Survey

Anthony Magit, MD, MPH

Victor De Oliviera

**Abstract:** An anonymous survey of Institutional Review Boards (IRB) affiliated with medical schools in the United States was conducted to evaluate the impact of the single IRB process on institutional resources, including the use of commercial IRBs. The survey indicated that IRBs have altered the composition of their staffs and have increased the use of commercial IRBs in response to increased use of sIRB review.

**Background:** Implementation of single Institutional Review Board (sIRB) review for multisite human subjects research is intended to reduce time to study initiation and maintain uniformity of studies across multiple sites. The National Institutes of Health (NIH) has mandated sIRB review for all multisite studies. This mandate has altered the approach to IRB review and identified opportunities to standardize IRB review, resulting in reduced heterogeneity of study data. Evaluating the impact of sIRB processes on institutions will assist with planning for staffing and budgets with the goal of optimizing resources committed to ethical and regulatory review of human subjects research.

**Methods:** An anonymous survey was sent to publicly available email addresses identified as the contact email for Institutional Review Boards associated with Medical Schools in the United States. The survey addressed changes in IRB staffing and workflows related to single IRB review. The REDCap application was used to distribute the survey and collect responses.

**Results:** Survey responses indicate that the sIRB process has impacted IRB staffing with increased resources devoted to support single IRB review and increased use of commercial IRBs.

**Conclusions:** Implementation of single IRB review has impacted how institutions conduct regulatory and ethical review of research. Future research will be necessary to determine whether single IRB review results in reducing time to study initiation and elevate the quality of research data.

### Poster #94:

#### Comparison of Median Days to Initial Appointment in Integrated Behavioral Health vs Standard of Care

Anjali D. Sapkal, MS, MBBS, Jasmine R. Holt, PsyD, Mario Bialostozky, MD, Andrew Richardson, MS, Devin P. Adams, MPH, Hilary Bowers, MD, FAAP, Anne Bird, MD, Domonique Hensler, MHA, Kathryn A. Hollenbach, PhD, MPH

**Background:** Rady Children's Hospital-San Diego's Mental Health Integration (MHI) program has begun to embed behavioral health (BH) services at Children's Primary Care Medical Group (CPCMG) practices. BH referrals at Integrated Health Therapist (IHT) embedded clinics are routed to the inhouse therapist. CPCMG clinics without IHTs refer patients to external behavioral health services within the community. We compared the two referral systems.

**Methods:** Data were collected from patient charts 14 days post BH referral. Patients without a scheduled initial BH appointment at embedded sites and all external referrals received phone calls from the MHI research team. Parents were asked questions such as date of scheduled BH appointment, waitlist placement, or reasons why an appointment had not been scheduled. Data were summarized for referrals made from 1/17/2022 to 2/21/2022.

**Results:** Out of the 122 IHT referral orders, 115 (94%) patients had received first contact with IHT within 14 days of the referral. 58 patients were either discharged/referred to MHI HUB clinics or care coordination. 57 patients were eligible for scheduling an initial evaluation with IHT after the first contact. Out of the eligible patients, 45 (79%) patients had a scheduled IHT initial appointment date by 14 days post referral, 12 (21%) had no initial appointment scheduled. Median time to initial IHT scheduled appointment was 21 days (15, 26).

21 external BH referrals were placed, and we contacted 17 (81%) patients. No patients had a scheduled external BH appointment. 9 (53%) parents did not call external resources to schedule, 8 (47%) parents tried to schedule: 3 (37.5%) were waitlisted, and 5 (62.5%) parents were not able to schedule appointments or waitlist their child. Parents were overwhelmingly frustrated as appointments were unavailable without extended waits.

**Conclusions:** Integrated BH demonstrated significantly higher success of accessing and obtaining behavioral health care compared to current care standards.

## MENTAL HEALTH

### Poster #95:

#### High School Athlete Depression Scores since the Onset of the COVID-19 Pandemic

Devin P. Adams MPH, Jasmine R. Holt PsyD, Jenna A. Martin MPH, Domonique J. Hensler, MHA, and Kathryn A. Hollenbach PhD, MPH

**Background:** Adolescent behavioral health was in crisis before the onset of the COVID-19 pandemic. The shutdown and subsequent reopening of in-person learning and extracurricular activities may have worsened this crisis. We evaluated the change in depression rates among high school athletes before and during the COVID-19 pandemic.

**Methods:** Data were collected as part of a pilot program providing depression screening to high school athletes during sport physicals at 4 time periods: once before the COVID-19 lockdown in March 2020 (baseline) and at 3 timepoints after the pandemic began. All students in attendance received a Patient Health Questionnaire-2 (PHQ-2) screening. Those with a score  $>3$  were also administered the PHQ-9. Statistical comparisons between the 4 cohorts were made using Fisher's exact tests and odds ratios with associated 95% confidence intervals (CIs) (STATA 16, College Station, TX).

**Results:** To address repeated measure concerns, randomly selected scores were selected for each student. 927 individual student scores were analyzed: 385 in spring 2020; 145 in fall 2020; 163 in fall 2021; and 234 in spring 2022. Fall 2020 students were 2.6 times more likely to have elevated PHQ2 scores than spring 2020 (95% CI = 1.3, 5.2). Fall 2021 and spring 2022 scores did not differ significantly from baseline, although they were slightly higher than baseline (OR = 1.6; 95% CI = 0.7, 3.3, and OR = 1.7; 95% CI = 0.8, 3.2, respectively). A significant difference in PHQ-9 diagnosis categories was detected over time ( $p = 0.01$ ).

**Conclusions:** A statistically significant increase in PHQ scores was detected after the onset of the COVID-19 pandemic. After an initial peak in PHQ scores in fall 2020, scores decreased but did not reach pre-pandemic levels.

### Poster #96:

#### Primary Care Providers' Beliefs and Attitudes toward a Newly Implemented Integrated Behavioral Health Program: A Preliminary Look at Providers' Responses

Jasmine R. Holt, PsyD, Anjali D. Sapkal, MBBS, MS, Hilary M. Bowers, MD, FAAP, Domonique Hensler, MHA, Kathryn A. Hollenbach, PhD, MPH

**Background:** Primary Care Providers (PCPs) often bear the weight of being the first line of defense for youth with early signs of mental health distress. Rady Children's Hospital recently implemented an innovative integrated behavioral health (BH) program with embedded integrated health therapists (IHTs) in pediatric primary care clinics throughout San Diego. We assessed PCPs' beliefs and attitudes about mental health integration before and after an IHT was embedded in their clinic to understand how an integrated BH program impacted their work.

**Methods:** PCPs at clinics receiving the new integrated BH program completed surveys containing likert scale, multiple choice, and open-ended questions. A 5-point likert scale was used (1 = Strongly Disagree to 5 = Strongly Agree). PCPs received a pre-survey 2-4 weeks prior to the IHT starting at their clinics and again at 4 months and 8 months post IHT integration. Data were collected in SurveyMonkey, and descriptive analyses and repeated measures comparisons were completed.

**Results:** Thirty PCPs completed the pre-survey, 23 completed the 4-month post survey, and 12 completed the 8-month post survey. On questions related to beliefs about quick patient access to BH evaluations, BH therapy, and psychiatric medication consultation, median ratings increased from 2, 1, 2 to 4, 4, and 4 at the 8-month post survey, respectively. In response to open-ended questions, PCPs reported initial concerns at pre-survey about IHT availability and added workload for PCPs. However, in post surveys, PCPs reported good IHT availability, smooth warm hand-offs, and easy access for patients scheduling follow-up appointments.

**Conclusions:** Although PCPs expressed some initial concerns about a new integrated BH program, having an IHT in the primary care setting was appreciated by PCPs and many believed it increased patient access to BH care, which highlights the supportive partnership that can occur within an integrated BH program.

## NEONATOLOGY

### Poster #97:

#### **Growth Trends of Almost 7000 Preterm Infants from Birth to Seventeen Years Does Size at Birth Predict BMI Later?**

Jennifer Barnard, Andrew Defante, Julie Ryu

**Introduction:** Many preterm infants (PI), especially those small for gestational age (SGA) struggle with growth postnatally, but there is no consensus on expected “catch-up” growth rates. In addition to correcting for GA over the first two years, there may be a need to account for growth restriction.

**Methods:** This retrospective study of 6916 followed infants born between 23-32 weeks over 17 years seen at specialist and pediatric visits within Rady Children’s Hospital electronic medical record system. Infants were categorized as SGA, AGA and LGA based on the WHO Fetal Growth Charts. Their weights and BMIs at ages two through 17 years were categorized as below the tenth percentile (small), between the tenth and ninetieth percentiles (appropriate) and above the ninetieth percentile (large) by CDC standards.

**Results:** Using a Chi Squared test, results showed statistically significant differences (p-values <0.001) in the counts of PI who were small, appropriate and large by weight and BMI at ages two through 17 years based on whether they were born SGA, AGA, or LGA. Those born SGA had more infants remain small by weight than those born AGA or LGA (p-values <0.001). But for all groups, we observed significantly more PI stay small than expected.

**Conclusions:** As more extremely premature infants are surviving, there is a need for further assessment of this subpopulation’s expected postnatal growth. Infants born SGA may continue below the tenth percentile for weight for several years and this may not be “abnormal” growth for them. These infants may be seen by various specialists for failure to thrive but might just need different standards. This study validates the need for further investigation of growth for infants born growth-restricted and very premature.

### Poster #98:

#### **Communication in the Neonatal ICU for Spanish Speaking Parents: A Qualitative Interview Study**

Emily Batton, MD1, Samantha Hurst, PhD, MA2, Carlos Ramos, MD1, Leslie Catalan, RRT1, Michele Freeman, LCSW 1, Krishelle Marc-Aurele, MD1

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**Background and Objectives:** Little is known about the communication experience of parents with limited English proficiency (LEP) in the NICU. Our objective was to explore how Spanish speaking parents with LEP receive information in the NICU and to assess their satisfaction with communication.

**Methods:** A certified bilingual provider conducted seventeen in-person interviews of 17 mothers and 4 fathers who identified Spanish as their preferred language and whose newborn was admitted to the NICU for > 1 week. Interviews were conducted August 2020 – December 2021. The average gestational age at birth was 33 weeks, 2 days and 50% of newborns were female. Eighty-five percent of the Scores for Neonatal Acute Physiology-Perinatal Extension II, a predictor of neonatal mortality, at 12 hours of life were between 0 and 20 (low). The average length of stay was 41 days and all newborns survived to discharge. Conventional content analysis of the interviews utilizing an open coding process was performed to distinguish patterns and themes that made up the final results.

**Results:** Four main themes emerged from the analysis demonstrating that Spanish speaking parents with LEP in the NICU experienced 1) difficulty obtaining information 2) delays in communication 3) challenges with interpreters and 4) negative emotional consequences.

**Conclusions:** Parents with LEP face unique challenges communicating in the NICU. Our findings can inform neonatal quality initiatives to decrease delays and burdens for families with LEP to receive timely and good communication.

## NEONATOLOGY

### Poster #99:

#### Placental Pathology and Fetal Growth in Pregnancies Complicated By Obesity

Samantha Hietalati, Donna Pham, Harneet Arora, Marina Mochizuki, Gisselle Santiago, Jordan Vaught, Erika Lin, Karen Mestan, Mana Parast, Marni Jacobs. University of California - San Diego, La Jolla, CA, United States.

**Introduction:** Obesity has been described as an inflammatory condition with resulting systemic effects. In combination with pregnancy, obesity is associated with several comorbidities and pregnancy complications, but specific effects of obesity on the placenta and the potential downstream effects on fetal growth have not been well-studied. We sought to explore the relationship between obesity, placental pathology, and fetal growth.

**Methods:** A cohort of 1467 women with singleton pregnancies from 2011-2020 was identified from an ongoing obstetric registry, with available placental pathology data, as well as demographic, obstetric, and neonatal variables. Maternal weight categories were defined as: normal weight (BMI <25) and obese (BMI ≥30) based on earliest weight recorded during gestation; the overweight category (BMI 25-29.9) was excluded for the purposes of this analysis. Associations between obesity, placental pathology, and fetal growth were assessed with Chi-square and ANOVA tests.

**Results:** Pregnancies from 573 normal weight and 536 obese women were included. Maternal obesity was associated with large-for-gestation (LGA) placental disc (12% vs. 6%), increased incidence of decidual vasculopathy (DV; 37% vs. 11%), accelerated villous maturation (AVM; 19% vs. 14%), intervillous thrombi (IVT; 15% vs. 7%), chronic villitis (CV; 19% vs. 13%), and normoblastemia (40% vs. 25%). Of these, AVM, DV, and normoblastemia were associated with small for gestational age (SGA) infants, irrespective of obesity. In the setting of obesity, however, AVM appeared to have a more significant effect on fetal growth, decreasing mean birthweight percentiles from 37.6 to 27.0 in normal weight mothers, but from 54.3 to 31.9 in obese mothers (p=0.01).

**Conclusions:** Maternal obesity is associated not only with placental inflammation (CV), but also with evidence of maternal vascular disease (DV), abnormal placental development (AVM), abnormal maternal blood flow in the placenta (IVT), and intrauterine hypoxic stress (normoblastemia). Our analysis suggests that while obese patients are more likely to have LGA babies, in the presence of specific patterns of placental injury (namely AVM), there could be a more severe blunting of fetal growth. Future analyses will focus on the effects of placental pathology on neonatal outcomes, beyond birthweight.

### Poster #100:

#### Implementing Screening for Neonatal Delirium in the Rady NICU

Meghana Karmarkar, MD\*, Mark Speziale, MD, PhD, Willough Jenkins, MD, Elle Heath, M.Ed, Jane Kang, RN, Julia Suvak, BSN, RN, RNC-NIC, Peggy Grimm, MS, NP, CNS, RNC-NIC, Rose Manrique, BSN, RN, RNC-NIC, Laurel Moyer, MD, MPH

**Background:** Delirium is defined as fluctuating changes in awareness and cognition occurring in the setting of a medical illness. Although delirium is recognized in pediatric ICUs, it is not commonly diagnosed in the neonatal population. The NICU at Rady Children's Hospital is comprised of medically complex patients with prolonged hospital courses who are often on multiple medications for pain and sedation. We conducted a QI project to implement screening for neonatal delirium in high-risk patients. Our objective is to increase delirium screening (RASS/CAPD scores) from 0% to 85% in eligible NICU patients by 03/2022.

**Methods:** Multiple interdisciplinary meetings were initiated with key stakeholders to develop an algorithm for the evaluation of neonatal delirium. Completion of the RASS (Richmond Agitation and Sedation Scale) and age-adjusted CAPD (Cornell Assessment of Pediatric Delirium) scores were used as the objective tool for delirium screening. Weekly nursing compliance with RASS & CAPD score documentation is the primary process measure. Initial inclusion criteria at the start of the project was defined as NICU patients > or = 38 weeks corrected gestational age who were mechanically ventilated > 7 days and who were receiving any benzodiazepines or opiates. Inclusion criteria was then expanded to include all infants > or = 38 weeks corrected gestational age. Multiple PDSA's were conducted to optimize screening through increasing the reliability of the process. This included creation of an order set, documentation flowsheets, and a required documentation checklist in the EMR.

**Results:** Implementation of screening and data collection began in October 2020. After implementation, data from 10/2020 through 2/2021 showed an average weekly screening compliance of 76%. Expansion of the inclusion criteria on 8/2021 resulted in a sharp decrease in compliance. Subsequently, addition of the documentation checklist in the EMR resulted in a center line shift in the data, with a current average weekly screening compliance of 77%, close to our goal of 85% compliance (Figure 1).

**Conclusions:** Through this QI project, we have increased awareness of neonatal delirium as a diagnosis in our NICU. Our expectation of this project is that early recognition of delirium in our chronic patients will lead to more timely management of symptoms and decreased use of narcotic and sedative medications.

## NEONATOLOGY

### Poster #101:

#### Surfactant Protein B in Respiratory Viral Infections

Sandra Leibel, Ben Croker, Rachael McVicar, Elizabeth Kwong, Rabi Murad, Evan Snyder

**Background:** COVID pneumonia caused by SARS-CoV-2 can result in a depletion of surfactant & lung injury, which resembles neonatal respiratory distress syndrome. Exogenous surfactant has shown promise as a therapeutic option in hospitalized patients. Our preliminary data in human lung organoids showed an increase in surfactant protein B (SP-B) expression after infection with SARS-CoV-2 & human lung organoids with a deficiency of SP-B showed increased viral load. Single cell RNA sequencing (scRNAseq) revealed that SP-B-deficient cells showed increased viral entry genes (ACE2 receptor) & alterations in the IL-17 signaling pathway (STAT3, IL-6) emanating from the lung cells themselves. Our objective is to determine: (1) cell-specific transcriptional differences between normal & SP-B deficient human lung cells after infection with SARS-CoV-2; (2) a therapeutic role of SP-B protein & surfactant in COVID-19 pneumonia.

**Methods:** We used normal and SP-B mutant (homozygous, frameshift, loss of function mutation p.Pro133GlnfsTer95, previously known as 121ins2) human induced pluripotent stem cells (hiPSC) and differentiated them into 3D proximal lung organoids. The organoids were infected with the delta variant of SARS-CoV-2 for 24 hours at an MOI of 1. Infected and uninfected organoids were fixed in trizol in triplicate and underwent processing for bulk RNA sequencing. We tested for differentially expressed genes using the program DESeq. We also plated normal iPSC derived lung organoids as a monolayer and pre-treated them with 1mg/ml of Poractant alfa or 5 uM of recombinant SP-B protein. The delta strain of SARS-CoV-2 was added to the 96 wells at an MOI of 0.1 for one hour with shaking, then an overlay with DMEM/CMC/FBS was added and left on for 23 hours. The plate was fixed and stained for nucleocapsid (NC) protein.

**Results:** Bioinformatic analysis of the bulk RNA sequencing data showed an increase in the viral entry genes ACE2 and TMPRSS2 and an increase in SFTPB. We processed the data through Ingenuity Pathway Analysis (IPA) which showed gene sets involved in IL-17 signaling & IL-6 signaling pathways in the mutant lung organoids. In the exogenous surfactant experiments, there was a decrease in total expression of viral NC in the Poractant alfa & rSP-B-treated cells compared to SARS-CoV-2 infection alone ( $p < 0.001$ ).

**Conclusions:** Surfactant modulates the viral load of SARS-CoV-2 infection in the human lung. Deficiency in SP-B may result in the dysregulation of the IL-17 signaling pathway resulting in worsening infections.

### Poster #102:

#### Determining Whether Starting Intravenous Fluids Affects Rates of Infant Formula Exposure in Healthy Asymptomatic Neonates Admitted to the NICU for Suspected Sepsis.

Charles Sauer DO, Neonatologist, Rady Children's Hospital San Diego and UCSD School of Medicine, Euyhyun Lee MS, Biostatistician Altman Clinical and Translational Research Institute, UCSD School of Medicine

**Background:** Human milk is the optimal form of nutrition for infants. Interventions associated with a decreased rate of exposure to infant formula can contribute to a higher rate of breastfeeding success. During the study period, infants born to a mother with chorioamnionitis were separated from the mother and transferred to the NICU for intravenous antibiotic administration. Some of these infants also received intravenous (IV) fluids. Our hypothesis was that use of IV fluids could be associated with a reduction of infant formula exposure by possibly decreasing the urgency and necessity to give a bottle of formula when the mother is unable to breastfeed the infant.

**Methods:** A retrospective chart review of all healthy term infants admitted to Rady Children's Hospital Satellite NICUs between 1/1/2014 to 8/31/2016 for possible sepsis who received treatment but did not ultimately develop sepsis. Data collected included demographics, IV fluid exposure, breastmilk exposure, formula exposure, delivery type and length of stay. We used a logistic regression model with exposure to infant formula as the binary outcome variable. P-values less than 0.05 were considered significant.

**Results:** 628 infants met the inclusion criteria. 161(25.6%) did receive IV fluids and 467(74.4%) did not receive IV fluids. An infant who received IV fluids was 0.694 times less likely to receive any infant formula during the stay compared to an infant who did not receive IV fluids and this was found to be significant. 95% Confidence interval (0.484, 0.993) p-value 0.046.

**Conclusions:** This retrospective chart review found that infants transferred to the NICU due to chorioamnionitis exposure who received IV fluids were significantly less likely to receive any infant formula. Interventions that increase human milk exposure have important implications and further prospective studies are warranted.

### NEONATOLOGY

**Poster #103:**

**Wee Nuzzle: A Quality Initiative to Promote Non-Nutritive Breast Feeding in Order to Increase Breastmilk at Discharge for Preterm Infants in the Neonatal Intensive Care Unit**

Keriann Schulkers Escalante & Jennifer Barnard, Erika Clemens, Ruth Hammer, Cindy Ritter, Jamie Ko, Jackie Wood, Stephanie Freeman, Julie Cooke, Katherine Weiss, Sandra Leibel

**Background:** Non-nutritive breast feeding (NNBF) is breast/chest feeding on a breast after it has been pumped. Reduced opportunities for infants to practice direct latching may discourage parents, impact breastmilk supply, and reduce breastmilk feeding at discharge. Our level III NICU has seen NNBF attempts delayed due to: 1) varying comfort levels among staff, 2) lack of formal guidelines, and 3) NNBF frequently not being integrated into medical team's daily discussions or documentation. The objective of this Quality Improvement (QI) project is to decrease the time to first NNBF attempt by one week from a baseline of two weeks among infants <34 weeks, between May 2021 to May 2022. The global aim is to support and encourage breastfeeding, promote maternal-infant bonding, and facilitate early positive oral experiences.

**Methods:** A multidisciplinary team developed the "Wee Nuzzle" pathway, which is a pre-feeding developmental pathway to incorporate Skin-to-Skin, Milk Drops, & NNBF. Premature infants  $\geq 30$  weeks are eligible if they are receiving any amount of enteral breast milk, are on room air or NRS, and the parent desires to do NNBF. Infants are excluded if they were intubated within the prior week, have an umbilical arterial catheter, and/or have significant congenital or neurological abnormalities making it unsafe to attempt NNBF.

**Results:** Thus far 3 PDSA cycles have been completed. The control chart in Figure 1 shows a shift in the mean number of days to first NNBF attempt from 13.9 to 5.2 days. As a balancing measure, only one of the 113 infants included had an increase in respiratory support after the first NNBF attempt. As a process measure, 90% of infants had the smart phrase incorporated into their daily progress note.

**Conclusions:** This QI initiative led to a decrease in the mean number of days to first NNBF attempt by over one week. Additional PDSA cycles are planned to identify interventions for maintenance and/or further improvements.

## NEPHROLOGY

### Poster #104:

#### **Uncovering the clinical phenotype and underlying genotype of hospitalized children with both kidney anomalies and congenital heart defects at a single center**

Erika T. Allred MD, Elliot Perens MD PhD, Nicole G. Coufal MD PhD, Erica Sanford Kobayashi MD, Stephen F. Kingsmore MB ChB DSc, David P. Dimmock MD

**Background:** Congenital heart defects (CHD) and congenital anomalies of the kidney and urinary tract (CAKUT) account for significant morbidity and mortality in childhood. Dozens of monogenic causes of each have been identified, but with no reported overlap in prior literature. The interdependent function of these organ systems is well known. Cardiorenal syndrome is associated with increased morbidity and mortality. These adverse effects are magnified and more likely to occur in children that possess congenital anomalies. Identifying a clinical phenotype and genetic risk for this population will allow for early identification and improved prognostication, leading to superior outcomes.

**Methods:** Retrospective review identifying patients with both CAKUT and CHD and either whole genome sequencing (WGS) or whole exome sequencing (WES), admitted to Rady Children's Hospital between January 2015 and July 2020. Demographic information, presenting phenotype, and genetic results were collected, along with the mother's pregnancy history. WGS results were reanalyzed using the CAKUT and CHD phenotype as a primary filter. Genetic results were reviewed to identify causative, candidate, and novel genes for the CAKUT and CHD phenotype. Associated additional structural malformations were identified and categorized.

**Results:** 32 patients were identified. Eight patients had causative variants, 3 patients had candidate variants, and 3 patients had potential novel variants. Five patients had variants in genes not associated with the CAKUT/CHD phenotype, and 13 patients had no variant identified. Of these 8 patients were identified as having possible alternative causes for their CHD/CAKUT phenotype. 88% of all CAKUT/CHD patients had at least one additional organ system with a structural malformation.

**Conclusions:** Our study provided valuable information on approaching acutely ill patients with CAKUT and CHD, including expected phenotypes and appropriate additional diagnostic work up, as well as novel insights into the genetics of CAKUT/CHD overlap syndromes. Our diagnostic rate was 44% in this population.

### Poster #105:

#### **osr1 couples intermediate mesoderm cell fate with temporal dynamics of vessel progenitor cell differentiation**

Elliot Perens, Jessyka Diaz, Agathe Quesnel, Amjad Askary, J. Gage Crump, Deborah Yelon

**Background:** Transcriptional regulatory networks refine gene expression boundaries to define the dimensions of organ progenitor territories. Kidney progenitors originate within the intermediate mesoderm (IM), but the genetic pathways that establish the boundary between the IM and neighboring vessel progenitors are poorly understood.

**Results:** Here, we delineate roles for the zinc-finger transcription factor *Osr1* in kidney and vessel progenitor development. Zebrafish *osr1* mutants display decreased IM formation and premature emergence of lateral vessel progenitors (LVPs). These phenotypes contrast with the increased IM and absent LVPs observed with loss of the bHLH transcription factor *Hand2*, and loss of *hand2* partially suppresses *osr1* mutant phenotypes. *hand2* and *osr1* are expressed together in the posterior mesoderm, but *osr1* expression decreases dramatically prior to LVP emergence. Overexpressing *osr1* during this timeframe inhibits LVP development while enhancing IM formation, and can rescue the *osr1* mutant phenotype.

**Conclusions:** Together, our data demonstrate that *osr1* modulates the extent of IM formation and the temporal dynamics of LVP development, suggesting that a balance between levels of *osr1* and *hand2* expression is essential to demarcate the kidney and vessel progenitor territories.

### NEPHROLOGY

**Poster #106:**

**redictors of successful discontinuation of continuous renal replacement therapy in children**

Elizabeth Y. Wei, Kim T. Vuong, Elizabeth Ingulli, and Nicole G. Coufal

**Background:** 1.5% of pediatric patients with severe acute kidney injury require continuous renal replacement therapy (CRRT). Optimal timing for CRRT discontinuation is unknown. Adult data posits urine output to be the most robust parameter for predicting CRRT liberation. The objective of this study is to determine factors predictive of successful CRRT discontinuation in pediatric patients.

**Methods:** A retrospective single center cohort study of all patients <21 years of age who received CRRT from January 2011 to March 2021 was performed. Those who remained off CRRT for at least 7 days (success) were compared with those requiring re-initiation (failure). Biochemical and physiologic parameters, including urine output (UO), diuretic administration, vasoactive inotropic scores (VIS), and serum creatinine, were obtained at CRRT initiation, discontinuation and in the 12 hours after discontinuation. The predictive ability of urine output was further analyzed using receiver operative characteristic (ROC) curves.

**Results:** Of the 99 patients trialed off CRRT, 76 patients remained off CRRT (success); 23 required reinitiation (failure). The success group demonstrated significantly higher UO in the 6-hour (0.833 vs 0.06 ml/kg/hr,  $p=0.0007$ ) and 24-hour periods (0.83 vs 0.18 ml/kg/hr,  $p=0.0059$ ) prior to CRRT discontinuation, as well as in the 6-hourss (1.8 vs 0.1 ml/kg/hr,  $p=0.001$ ) and 12 hours (2.4 vs 0.09 ml/kg/hr,  $p<0.0001$ ) after discontinuation. The area under the ROC curve for UO in the 6 hours prior was 0.72 (95% CI 0.60-0.84,  $p=0.0009$ ). UO of 0.51 ml/kg/hr in the 6 hours prior to discontinuation had the highest combined sensitivity and specificity (77% and 62%, respectively). UO in the 6 hours after CRRT discontinuation demonstrated similar area under ROC curve, sensitivity and specificity.

**Conclusions:** Patients who successfully liberated from CRRT demonstrated significantly higher urine output prior to CRRT discontinuation. Urine output of 0.5 ml/kg/hr in the 6 hours prior to CRRT discontinuation was predictive of renal recovery.

### NEUROLOGY

**Poster #107:**

**A systematic review and quantitative synthesis of the long-term psychiatric sequelae of pediatric autoimmune encephalitis**

Linda Nguyen, MD, PhD, Jennifer H. Yang, MD, Sajan Goyal, Najin Irani, BS, Annalise Miner, BS, and Jennifer S. Graves, MD, PhD, MAS

**Background:** Long-term neuropsychiatric sequelae of autoimmune encephalitis (AE) remain understudied, particularly in pediatric-onset AE. We aimed to synthesize the published data on ongoing psychiatric symptoms in pediatric-onset AE.

**Methods:** The Pubmed, PyscINFO, Web of Science databases were searched from their inception years to August 23, 2021, and 29 studies were identified and analyzed. We also performed a quantitative synthesis of available patient data from the 29 studies combined with a cohort of anti-NMDA receptor (NMDAR) AE from our institution to examine the associations between acute treatment course and long-term psychiatric outcome.

**Results:** At long-term follow up, 52.3% of the cases with pediatric-onset AE had any persistent symptoms and 36.0% had at least one psychiatric symptom. Pooled data found that 37% of pediatric-onset anti-NMDAR AE had ongoing psychiatric symptoms. Using a univariate logistic regression analysis, we found that abnormal initial EEG, use of certain immunotherapies, and persistent cognitive impairments were associated with ongoing psychiatric symptoms.

**Conclusions:** Chronic psychiatric and behavioral problems remain present in one-third of children months to years after onset of AE. Limitations included a significant paucity of outcomes measured using consistent, objective methods. Larger scaled prospective observational studies with a consistent standardized battery of testing are needed to examine impact of specific clinical features and immunotherapies on long-term mental health outcomes.

### NURSING

**Poster #108:**

**Child Life Specialists “Play” an Innovative Role in Health Enhancement and Wellbeing**

Erin Dale, MSN, RN, FNP-C, Erin Carpenter, CCLS, Drisana Moss, BSN, RN, Karen Anaya, RN, BS, CHTP, Keri Carstairs, MD, MBA, FACEP, FAAP

**Background:** Pandemic-related isolation and anxiety impacted our youth. A mental and behavioral health crisis has been declared. Friendships, connections, and social groups were some social supports that were greatly restricted. As needs grew, resources became scarce, with long wait times to connect to mental health services. Families expressed frustration and helplessness to their healthcare team. As children struggled to cope, child life specialists were in a unique position to be of help.

**Methods:** Child life services for mental and behavioral health were piloted with a subset of Medical eligible children with a chronic diagnosis. Nursing Care Navigators and the Specialty Care Team identified patients who would benefit. The Child Life Specialist (CLS) performed phone outreach, intake, and set up initial telemedicine visits. Patients received on average 3- 4 follow up visits for therapeutic art therapy, normalization of disease, coping techniques, routine building, shared care planning, and connection to resources such as peer support groups.

**Results:** Over two years the pilot enrolled 49 children with 1 Child Life Specialist. 47% of children referred had a positive depression screening and after the intervention 100% showed statistically significant improvement in depression scores upon rescreening (p value < .001). Following the intervention, 78% did not need additional mental health services during the pilot period. 35% were proactively identified early and would otherwise not have been offered services.

**Conclusions:** Child life Specialists have proved to be an asset to help meet the unique needs of children with complex chronic health conditions and mental health concern. They can serve as a bridge for mental health services while families navigate access issues and long wait times, and may even eliminate the need for more complex intervention.

## OTOLARYNGOLOGY

### Poster #109:

#### Cross Collaborative Airway Management in the Cardiac Catheterization Laboratory

Matthew T. Brigger MD, MPH; Nikita Mittal; Aparna Rao MD, John Nigro MD, Howaida El-Said, MD, PhD

**Introduction:** The augmented imaging available in the cardiac catheterization lab uniquely provides enhanced diagnostic and therapeutic tools in the management of complex airway disease.

**Methods:** We conducted a retrospective review of children with complex airway disease evaluated and treated in the cardiac catheterization lab over the course of 4 years. A multi-disciplinary complex airway team (otolaryngology, interventional cardiology, pulmonology and cardiothoracic surgery) evaluated patients using laryngoscopy, bronchoscopy, X-Ray fluoroscopy, and contrast bronchography.

**Results:** Evaluation and treatment of 15 children in the cardiac catheterization lab was successful in all patients attempted. There were no procedural adverse events and there were no complications at most recent follow up (mean 13 months, range 1-44 months). Airway stent implantation was performed in 9/15 cases; airway balloon dilation was performed in 4/11 cases; diagnostic fluoroscopy and bronchograms only (no intervention indicated) were performed in 2/11 cases. Cases included severe infant bronchomalacia, postoperative tracheomalacia, airway stenosis, a symptomatic tracheal diverticulum and an acquired tracheoesophageal fistula that required palliation. Nine bare metal stents were placed for severe malacic airway segments, one self expanding covered stent was used to palliate an acquired tracheoesophageal fistula. Balloon dilation was used in patients that presented with complex anatomy limiting distal visualization as well to treat a symptomatic tracheal diverticulum.

**Conclusions:** The cardiac catheterization lab serves as a unique resource that allows cross collaboration between specialties to improve management of complex airway problems. This approach can likely serve as a model for other institutions in the management of complex airway problems.

### Poster #110:

#### Development of a Medical Complexity Score for Pediatric Aerodigestive Patients

Henry M Horita BS, Gabrielle Cahill MPH, Hailey Brigger, Tzyynong L Friesen MD, Aparna Rao MD, Soma Kumar MD, Kimberly Morris CCC-SLP, BCS-S, Lisa Horvay OTR/L, Virginia Floco PA-C, Matthew T Brigger MD MPH

**Objectives:** This study aimed to develop a complexity scoring system to characterize the diverse population served in pediatric aerodigestive clinics and help predict their treatment outcomes.

**Study Design:** Retrospective chart review

**Setting:** Rady Children's Hospital San Diego, Aerodigestive Clinic

**Subjects and Methods:** A 7-point medical complexity score was developed through an iterative group consensus of relative stakeholders to capture the spectrum of comorbidities among the aerodigestive population. One point was assigned if a diagnosis was present for each of the following comorbidities: airway anomaly, neurological, cardiac, respiratory, gastrointestinal, genetic diagnoses, and prematurity. A score of 7 indicated the highest medical complexity. Then a retrospective chart review was conducted of all patients seen in the aerodigestive clinic of a single institution who had at least two visits and a complete data set between 2017-2021. Selected outcomes were analyzed with univariate and multivariate logistic regression.

**Results:** 234 patients were analyzed with complexity scores assigned, showing a normal distribution (Shapiro Wilk  $p = 0.406$ ) of the scores from 1 to 7 (median=4; mean=3.50; SD=1.47). The complexity score was predictive of clinical metrics as described below. Among children with dysphagia, there was waning success in the progression of oral feeding with increasing scores (OR=0.733; 95%CI 0.59,0.92;  $p=0.006$ ). Children with higher complexity scores were less likely to meet the criteria for discharge from the aerodigestive clinic (OR = 0.720; 95% CI 0.60,0.87;  $p=0.001$ ).

**Conclusions:** We propose a novel complexity score for the pediatric aerodigestive population that is easy to use, successfully stratifies the diverse presentations, and shows promise as a predictive tool to assist in counseling and resource utilization.

## OTOLARYNGOLOGY

### Poster #111:

#### **Near Infrared Spectroscopy as a Guide for Multidisciplinary Feeding Therapy in Infants with Congenital Heart Disease**

Kimberly Morris (1), Rohit Rao (2), John Nigro (3), Srujan Ganta (4), Kastley Marvin (2), Matthew Brigger (2), Kimberly Morris (5)

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**Objective:** Near Infrared Spectroscopy (NIRS) is commonly used to monitor real time regional tissue oxygenation in infants and has found particular utility in cardiac intensive care units. These commonly used non-invasive measures provide a marker to evaluate the balance between oxygen delivery and consumption by the tissue. When combined with arterial saturation, the regional oximetry can assess the flow across an organ bed by measuring the AVDO<sub>2</sub> and using the modified Fick Principle. Cerebral and renal NIRS have been shown to be predictive of neurodevelopmental outcomes in children with congenital heart disease. Infants with congenital heart disease have well described challenges with oral feeding that require a multidisciplinary approach. The ability to objectively assess feeding skills and energy expenditure is critical when optimizing growth and nutrition pre and post operatively. The application of NIRS is an enticing adjunct in directing feeding therapy and offers the medical team unique insight when determining timing of cardiac repair.

**Methods:** Case series of infants admitted to the cardiovascular intensive care unit experiencing feeding difficulty. Variations in NIRS values are reported and feeding strategies described that aim to prevent hypoperfusion (descending values), which indicates a low circulatory blood flow. In addition, pre-operative and post-operative CTICU data for 20 infants will be described that supports how the use of NIRS guided feeding optimizes physiologic stability in the setting of heart disease.

**Results:** NIRS guided feeding utilized in 20 patients pre and post-operatively with 80% of patient reaching full oral intake by discharge, 10% of patients PO/NG fed which was related to ineffectiveness of feeding strategies to stabilize NIRS values, 10% of patients PO/NG fed due to oropharyngeal swallowing dysfunction in the presence of stable NIRS. Three specific cases using NIRS guided feeding to facilitate differential diagnosis will be described.

**Conclusions:** NIRS as a real time physiologic blood flow monitor to measure the effectiveness of various approaches to feeding provides objective physiologic data to guide therapeutic strategies. Knowledge of individual baselines prior to feeding and variations during feeding can be utilized to guide overall feeding efficiency, endurance, and skill for infants. Further, attention to NIRS aids in determining the etiology of feeding difficulties including differentiation between poor endurance versus oropharyngeal dysfunction and guide optimal timing of instrumental swallowing -assessments. Increased utilization of NIRS during feeding assessments and treatments facilitates establishment, maintenance, and optimization of oral feeding in the setting of complex cardiopulmonary conditions both pre and post operatively.

## *PEDIATRIC CRITICAL CARE/PICU*

### **Poster #112:**

#### **Pediatric Resident Critical Care Curriculum: Providing Consistent Education in a Dynamic Environment**

Emily Foreman MD, Helen Harvey MD, Christopher Cannavino MD

**Background:** Pediatric residents rotate through the pediatric critical care unit (PICU) for 2 months over the course of their 3 year residency. It is typically one of the more arduous rotations as a resident due to patient volume and acuity, new emotional experiences, and long clinical hours. Our goal was to create a PICU resident curriculum that would provide consistent, structured and multi-modal education highlighting the American Board of Pediatrics critical care content topics.

**Methods:** A research study was conducted in a tertiary PICU from September 2020 to July 2021 with pediatric residents. Based upon the results of a needs assessment survey, a four-week curriculum was developed with an educational theme for each week: cardiac arrest, respiratory failure, shock, and neurocritical care. Instructional strategies included: journal articles and online resources for self-directed learning, hands on sessions, in person didactics, and discussion of current PICU patients. Pediatric residents completed a knowledge pre-test and post-test survey at the beginning and end of the PICU rotation. A post assessment survey evaluated resident confidence level using Likert scale, evaluating their ability to manage PICU core concepts and skills learned during the rotation.

**Results:** 27 residents completed a pre-assessment and 18 of these residents completed the post-assessment (67%). The mean confidence level for taking care of critically ill pediatric patients pre intervention was 2.91 and significantly improved ( $p < 0.001$ ) post intervention to a mean confidence level of 3.93. The mean correct score on the pre intervention knowledge assessment was 61% and increased to 74%.

**Conclusions:** The curriculum fulfilled our goal of developing diverse instructional strategies to provide consistent educational opportunities. The residents reported both improvements in confidence and knowledge after completing the curriculum. These results confirm that pediatric residents can benefit from a structured and multi-modal education curriculum in the PICU.

### **Poster #113:**

#### **Impact of Rapid Whole Genome Sequencing in the PICU**

Katherine Rodriguez<sup>1, 2</sup>, Erica Sanford<sup>2,3</sup>, David Dimmock<sup>2</sup>, Stephen Kingsmore<sup>2</sup>, Nicole G. Coufal<sup>1</sup>

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**Introduction:** Genetic disorders are a significant contributor to morbidity and mortality in pediatric critical care. Recently, rapid whole genome sequencing (rWGS) has drastically impacted the care provided in neonatal intensive care units. There remains a population of undiagnosed patients with rare genetic diseases who present critically ill to the pediatric intensive care unit (PICU) and the application of rWGS in this setting is not yet fully described. This study evaluates the utility of rWGS in the PICU.

**Methods:** This is a retrospective cohort study conducted at a single tertiary children's hospital from August 2016 to July 2021. Children were nominated for rWGS by the care team when etiology of illness was unclear, a priori suspicion of a genetic disorder was not required. Children who received rWGS in the PICU age 1 month to 18 years were eligible for inclusion. rWGS with targeted phenotype-driven analysis was performed. Clinical diagnostic utility was assessed via provider surveys of PICU physicians and electronic health record review.

**Results:** Sixty cases were identified to meet the inclusion criteria making this the largest cohort of rWGS in the PICU in the United States. Diagnostic sensitivity was 42% (25 of 60). The molecular diagnosis was considered to completely describe the phenotypic presentation in 80% of diagnosed cases. Over the 5-year study period, test turnaround time improved from 13.6 to 3.3 days. The majority of patients with diagnostic genomes (64%) had no known dysmorphic features or developmental delay. rWGS molecular diagnosis was responsible for changes in management in 76% of diagnosed cases. PICU provider surveys for a subset of patients identified clinical utility specifically in diagnosis, medical decision making, referrals to palliative care, and changes in code status.

**Conclusions:** In this cohort, most of the diagnosed patients did not have features classically associated with genetic disorders, making them difficult to identify. Molecular diagnosis of genetic disorders in the PICU population frequently results in changes in care during hospitalization, making rapid case identification and testing imperative. Increasing availability of rWGS can significantly impact patient care and assist families in making difficult decisions during times of critical illness.

### *PEDIATRIC CRITICAL CARE/PICU*

**Poster #114:**

**Impact of Hyperchloremia on Clinical Outcomes in Pediatric Patients with TBI Treated with Continuous Hypertonic Saline Infusion**  
**Hyperchloremia and AKI in Pediatric Patients with TBI Treated with Hypertonic Saline Infusion**

Austin Weiss, MD; Jennifer Foley, RN, BSN; Nicole G. Coufal MD, PhD; Helen Harvey, MD, MS1

**Background:** Hyperchloremia is associated with acute kidney injury (AKI) and increased mortality among in critically ill adults, but it is unknown if a similar association exists among critically ill children. The aim of this study is to determine the prevalence incidence of hyperchloremia and its association with AKI and mortality in pediatric patients with traumatic brain injury (TBI) receiving continuous infusion of hypertonic saline (HTS).

**Methods:** We conducted a single center retrospective review at a tertiary pediatric hospital from January 2014 to 2020. We reviewed 190 pediatric patients with met inclusion criteria; all patients with TBI who received continuous infusions of HTS met inclusion criteria hypertonic saline. The development of AKI was defined by the Kidney Disease Improving Global Outcomes (KDIGO) consensus criteria. Hyperchloremia was defined as a serum concentration  $\geq 110$  mmol/L. Outcomes included incidence and severity of AKI, 28-day mortality, complicated course, and length of stay.

**Results:** The average duration of HTS hypertonic saline infusion was 4.54 days (IQR: 2-7). The average GCS at presentation was 9.5 (IQR: 5-14). 110. 54. patients, (put the number here) 82 patients (43.2%) had an EVD or ICP monitor placed. 75 patients (40.1%) were remained intubated on day 7 of admission. 53 patients (28.3%) had a vasoactive requirement on day 7 of admission. 164 patients (86.3%) developed hyperchloremia with  $[Cl^-]_{max} \geq 110$  mmol/L. 138 patients (72.6%) were persistently hyperchloremic with  $[Cl^-]_{mean} \geq 110$  mmol/L. 15 patients (7.9%) developed AKI per KDIGO criteria, with only 5 patients (2.6%) Stage 2 or higher. One patient (0.5%) required hemodialysis, with recovery of renal function[NC1] . No patients developed liver failure[HH2] . Overall 28-day Mortality within 28 days of admission occurred in 7 patients was 7.4%.

[NC1]Yes? Or persistent HD requirement

[HH2]Do you mean persistent renal failure? (do not include this sentence if commenting on liver failure.

**Conclusions:** The curriculum fulfilled our goal of developing diverse instructional strategies to provide consistent educational opportunities. The residents reported both improvements in confidence and knowledge after completing the curriculum. These results confirm that pediatric residents can benefit from a structured and multi-modal education curriculum in the PICU.

## PSYCHIATRY

### Poster #115:

#### **Adoption and Acceptability of an Autism Friendly Health System Initiative among Providers within the Emergency Department of a Regional Children's Hospital.**

Trent DesChamps, M.S1., Themba Carr, Ph.D., Nicole Stadnick, Ph.D., Abbey Hye, BCBA., Dayna Stout, Kristin Gist, M.S., & Lauren Brookman-Frazee, Ph.D.2

**Background:** Youth with autism spectrum disorder (ASD) have unique clinical concerns, and utilize health services, including emergency departments (ED), more frequently than neurotypical youth (Lytle et al., 2018). Since health settings may be especially stressful for autistic youth (Nicholas et al., 2016), institutions are increasingly creating "ASD-friendly" clinical environments. Here, we report ED provider perceptions of the Autism Friendly Healthcare System Initiative (AFHSI) at Rady Children's Hospital-San Diego.

**Methods:** A core component of the AFHSI is the Autism Friendly Questionnaire (AFQ; adapted from Boston Medical Center), a caregiver-report measure of child communication, sensory needs, behavioral supports, and provider interaction preferences. ED providers were trained to incorporate AFQ information to provide supports for patients with ASD. Providers completed a survey before training and after ~1 year to assess their perspectives on aspects of the initiative. Between January 2020-January 2022, 135 provider surveys were completed. Year 1 and Year 2 responses were compared.

**Results:** Compared to providers who completed the survey in 2020 (Y1), a greater proportion of 2021 (Y2) providers indicated that they knew about the AFQ,  $X^2(1, n=134)=10.54$ ,  $p=.001$ ,  $j=.28$ ; could locate the AFQ in the patient's chart,  $X^2(1, n=130)=12.54$ ,  $p=.001$ ,  $j=.31$ ; and had used the AFQ during patient encounters,  $X^2(1, n=131)=15.54$ ,  $p<.001$ ,  $j=.34$ . The median score for provider perceptions of the helpfulness of the AFQ during ASD patient encounters was higher among Y2 providers ( $Mdn=3$ ) compared to Y1 providers ( $Mdn=2$ ),  $U=810.50$ ,  $p<.001$ ,  $r=.47$ . The median score for provider perceptions that the ED is ASD-friendly was higher among Y2 providers ( $Mdn=4$ ) compared to Y1 providers ( $Mdn=3$ ),  $U=1213.5$ ,  $p=.001$ ,  $r=.28$ .

**Conclusions:** Results revealed increased adoption and acceptability of AFHSI among ED providers, suggesting early success of AFHSI implementation despite unprecedented challenges to health systems during the pandemic (e.g., staff turnover). As such, these results support continued efforts to implement and evaluate ASD-friendly programs in health settings.

### Poster #116:

#### **Patient and Parent Satisfaction for a Newly Implemented Integrated Behavioral Health Program**

Caleen Chalhoub, BS, Anjali D. Sapkal, MS, MBBS, Jasmine R. Holt, PsyD, Devin P. Adams, MPH, Domonique Hensler, MHA, Anne Bird, MD, Kathryn A. Hollenbach, PhD, MPH

**Background:** Rady Children's Hospital-San Diego launched the Mental Health Initiative (MHI) in June 2020 which embeds Integrated health therapists (IHT) within primary care (PC) clinics to provide short-term behavioral health therapy, and IHTs and psychiatrists for children needing longer treatment at Hub sites. Satisfaction surveys began July 2021 for our initial PC and Hub integrated sites.

**Methods:** Parent and patient paper surveys (English and Spanish) were created to measure satisfaction at the IHT and Hub sites. Respondents rate aspects of care, using 5- or 10-point likert scales, including office staff, appointment scheduling, care convenience, communication between treatment teams, tools learned, patient progress (5-point scales) and overall IHT help (10-point scale). Open ended questions for recommendations are included. HUB surveys include additional questions regarding psychiatry services. Surveys are distributed at follow-up visits and are collected from locked collection boxes at each site.

**Results:** Cumulative median (25th, 75th percentile) were calculated for surveys collected between July 2021 and February 2022 using STATA 16.1. Patient ( $n=90$ ) and parent ( $n=94$ ) PC sites surveys had high overall satisfaction ratings, ranging from 4 to 5 on all questions. Overall help (10-point scale) was 8 (7, 9) for patients and 9 (7, 10) for parents. Hub sites median satisfaction ranged from 4 to 5 for both therapy and psychiatry among patients ( $n=18$ ) and parents ( $n=19$ ). Overall HUB therapist help was 8 (6.5, 8.5) for patients ( $n=16$ ) and 8 (6, 10) among parents ( $n=16$ ). HUB psychiatrists were rated highly by patients (9 (8.5, 9)  $n=4$ ) and parents (9 (7, 10),  $n=6$ ).

**Conclusions:** Satisfaction for the newly implemented IHT program in pediatric PC clinics is high and consistent with the goals of MHI. Data will guide program modifications to better serve patients and their needs.

## RESIDENT

### Poster #117:

#### Comparison of sonographic characteristics of neck masses in Kawasaki disease (KD) and other febrile illnesses

Andrew Bowman, MD, Caleen Chalhoub, BS, Michael Gardiner, MD, Nipha Sivilay, BS, John H. Naheedy, MD, Brian S. Pugmire, MD, Adriana H. Tremoulet, MD, Jane C. Burns, MD, John T. Kanegaye, MD

Department of Pediatrics and Radiology, University of California San Diego School of Medicine, La Jolla, California; Rady Children's Hospital San Diego, San Diego, California

**Background:** The published sonographic characteristics of cervical lymphadenopathy in Kawasaki disease (KD) are based on limited data and have not been compared to febrile neck masses (FNMs) from a wide range of etiologies. We sought to describe and compare sonographic characteristics of cervical lymphadenopathy in KD and other FNM, including Multisystem Inflammatory Syndrome in Children (MIS-C), to identify ultrasound (US) findings that distinguish these illnesses.

**Methods:** We identified subjects <18 years old with temperature  $\geq 38^{\circ}\text{C}$  who underwent US to evaluate acute cervical masses, excluding those with midline masses and masses of known congenital, traumatic, vascular, malignant, or lymphatic origin. We abstracted clinical, laboratory, and sonographic characteristics and compared continuous variables using rank sum test and categorical variables using chi square and Fisher's exact tests.

**Results:** The 53 subjects with KD, 110 with FNM, and 7 with MIS-C had median ages of 4.3, 5.1, and 13.3 years, respectively (Table). Most common diagnoses of FNM were adenitis (64), abscess (14), and specific viruses (10). Neck masses were more frequently multiple, distinct nodes in KD than in FNM (88.7% vs. 60.0%), less frequently conglomerations of matted nodes (1.9% vs. 14.5%), and less frequently submandibular in location (3.3% vs. 27.3%). Sonographic characteristics did not differ significantly between KD presenting first with only fever and lymphadenopathy (41 pts, 77%) and more complete KD. Nodes in MIS-C were less often enlarged but did not differ from KD in presence of multiple, distinct nodes. Irrespective of final diagnosis, most patients received antibiotics after initial evaluation (KD, 64%; FNM, 80%; MIS-C, 57%).

**Conclusions:** Subjects with KD more often had multiple, distinct nodes confined to the anterior cervical region than those with FNM. US may be a useful diagnostic adjunct in the early diagnosis of KD, especially before the appearance of other KD clinical criteria.

### Poster #118:

#### Change in weight status among children who do and do not participate in an obesity treatment program

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**Background:** It is unclear what happens to BMI trajectories of children with overweight/obesity (OW/OB) who express interest in pediatric weight management programs, but do not enroll. We compared the weight status of children who participated in the Guided self-help Obesity Treatment in the Doctor's office (GOTDoc) study (randomized to Guided Self-Help (GSH) or family-based behavioral therapy (FBT)) to those who consented but did not complete enrollment procedures and were therefore not randomized to treatment.

**Methods:** Longitudinal anthropometric data for children who consented but not randomized were extracted from EPIC. Receipt of weight management counseling by the pediatrician was determined via medical record review. Children were divided into four groups: 1) GOTDoc treatment with high attendance (  $\geq 50\%$  of sessions), 2) GOTDoc treatment with low attendance ( $<50\%$  of sessions), 3) no-treatment but received pediatrician counseling, 4) no-treatment and did not receive pediatrician counseling. Main outcomes were change in child BMI z-score, %BMIp95, BMIDiff95 at the end of treatment (month 6) and 6-month follow-up (month 12).

**Results:** Of the 234 participants who consented, 164 were randomized to receive GSH or FBT and 70 were not randomized. There were no demographic differences between those who were and were not randomized to treatment. Group 1 had significant decreases in BMI z-score, %BMIp95, and BMIDiff95 at the end of treatment ( $p<0.01$ ) (Figure 1). Weight status was relatively unchanged in Groups 2, 3, and 4 during the 12-month period; Groups 3 and 4 had slight, but non-significant, increases in weight status.

**Conclusions:** Attendance at an obesity treatment program can have a significant impact on weight status. However, discussing treatment opportunities with families was associated with weight stabilization. At a population level, weight stabilization may help stave off excessive medical burdens associated with obesity. Future studies should evaluate the effects of weight stabilization on clinical outcomes.

## RESIDENT

### Poster #119:

#### **Pediatrics Educational Module on Care of Transgender and Non-Binary Youth: Analysis of Efficacy and Knowledge Retention**

Eileen Chen, MD, Bixby Marino-Kibbee, LCSW, Ron S. Newfield, MD, David Inwards-Breland, MD, MPH, and Maja Marinkovic, MD

**Background:** There are striking healthcare disparities for transgender and non-binary (TGNB) individuals. One major barrier to care is lack of familiarity with gender affirming care (GAC): care supporting medical, social, and legal transition. Pediatrics residents often lack opportunities to train in specialized GAC centers, and other education modalities must be considered.

**Methods:** We developed an online, self-directed, and interactive learning module on the basics of GAC. Pediatrics residents completed the module as part of protected didactic time. Residents completed 3 assessments: before, immediately after, and 2 months after completing the module. Assessments involved knowledge-based questions as well as self-evaluation of 9 clinical skills competencies on a Likert scale. Responses were compared using the student's t-test. Subgroup analysis was additionally performed for residents who had previously received training in GAC.

**Results:** Roughly 60% of Pediatrics residents had prior training on GAC, although 100% had provided care to TGNB youth prior to the study. There were significant improvements in knowledge-based question scores ( $p < 0.001$ ), and in self-efficacy scores ( $p < 0.05$ ) for 8 out of 9 clinical skills competencies. There were high post-module self-efficacy scores (an average score of  $>4.0/5.0$ ) for 7 out of 9 clinical skills competencies. Residents with prior training on GAC also improved in several clinical skills competencies. At the 2 month follow up, there were retained improvements in knowledge base and in self-efficacy of some, but not all, clinical skills competencies.

**Conclusions:** Our online learning module was effective at increasing Pediatric residents' knowledge base and clinical self-efficacy in GAC. Residents with prior training on GAC still benefitted from receiving this education at the residency level. Some improvements in self-efficacy were lost at the 2 month follow up, suggesting that residents may need on-going educational measures in order to maintain certain skillsets.

### Poster #120:

#### **A RARE CASE OF SECONDARY HLH DUE TO VACCINE-STRAIN MEASLES IN A YOUNG CHILD WITH HEPATOBLASTOMA**

Art Kulatti, MD; Navid Djassemi, MD; Helena Yu, MD; Alice Pong, MD; Sun Choo, MD; Megan Paul, MD

**Background:** Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening disorder characterized by systemic hyperinflammation that can cause multi-organ failure and death. Rarely, secondary HLH has been associated with reactivation of viral infections during immunosuppressive therapy. We report a case of HLH secondary to vaccine-strain measles in a young boy undergoing treatment for hepatoblastoma.

**Methods:** Case Report

**Results:** A 19-month-old male was diagnosed with hepatoblastoma at 14 months and treated with chemotherapy per AHEP1531, 11 days after receiving MMR and varicella vaccines. After two cycles of treatment, he developed skin lesions with vaccine-strain varicella, treated with acyclovir. The subsequent three months of chemotherapy were complicated by fevers and progressive cryptogenic lung infiltrates. Despite broad coverage and chemotherapy being withheld, progression of his nodules led to an extensive evaluation for infectious causes. A lung biopsy showed nodular histiocytic infiltrates with reactive multinucleate cells. PCR testing and histopathology were negative for TB, VZV, adenovirus, HSV and CMV. Eventually, next-generation sequencing of a BAL sample revealed measles, later confirmed as vaccine-strain. He developed persistent fevers with worsening anemia, thrombocytopenia, coagulopathy, hepatosplenomegaly, and cardiogenic shock. Ferritin and sIL-2R were elevated. He was diagnosed with HLH per HLH-2004 criteria. Whole-genome sequencing was negative for primary HLH and other inborn errors of immunity. He began immunosuppressive therapy for secondary HLH. Measles-directed therapy (ribavirin + IVIG + vitamin A) was initiated once measles was confirmed. Despite these interventions, he succumbed to complications from measles and secondary HLH two weeks after starting HLH-directed therapy.

**Conclusions:** Although there are rare reports of HLH secondary to primary measles infection, to our knowledge this is the first report of HLH secondary to vaccine-strain measles [1]. This case highlights an exceptionally rare complication of immunosuppressive therapy in a patient with recent live vaccination. We hope greater awareness can lead to earlier recognition and improved outcomes.

### RESIDENT

#### Poster #121:

#### A Descriptive Study of Patient Profiles and Treatment Response at Severe Asthma Clinic (SAC) at a Tertiary Hospital

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**Background:** Rady Children's Hospital in San Diego has a prevalence of asthma of 8.6% compared to 8.1% nationally. Severe Asthma Clinic (SAC), a multidisciplinary clinic for patients with 2 or more ED visits in the past 6 months or 2 or more hospitalizations in the previous year, was started in 2015. The objective of this study is to 1) describe the SAC patient demographics 2) assess frequency of healthcare utilization after SAC visit 3) investigate changes in asthma control with each SAC visit.

**Methods:** Retrospective analysis was performed on patients seen at SAC at RCHSD from January 2015 to December 2020 three years prior to (pre-SAC) and one year after (post-SAC) the visit. Measures were compared using paired Wilcoxon Signed-Rank tests and a linear mixed effects model was used to analyze change over time. Results are reported in median and quartile (Q1-Q3) format.

**Results:** Of the 153 patients that were included (median age of 9.85 years) twenty-one percent (21.7%) were obese, 50% (76 patients) were white, 67.3% had Medicaid/Medical insurance coverage, and 43.8% had a diagnosis of allergic rhinitis (Table 1). The median household income was \$64,940 based on zip code. There was a statistically significant difference ( $p < 0.001$ ) for all treatment and hospital related outcomes from pre-SAC and post-SAC, including decrease in ED visits, hospitalizations, ICU admissions, number of systemic steroid courses, and inhaled corticosteroid potency scores (Table 2). With increase in time by 1-month post-SAC there was improved asthma control (decrease in ATAQ score by -0.050) and improved lung function (increase in FEV1 by 0.015 and increase in FVC by 0.020) (Figure 1).

**Conclusions:** Multidisciplinary care at the SAC has led to a significant decrease in healthcare utilization and improved asthma control for patients with severe asthma.

### RESIDENT

#### Poster #122:

##### **Characterization of Fractures and Their Etiology in Pre- and Early Ambulatory Children**

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**Background:** As children become ambulatory, the incomplete development of motor and balance skills may predispose them to injury. Given that there is no universally accepted approach to evaluation of young children who present with fractures, this allows for the potential for unrecognized or delayed diagnosis of non-accidental trauma, a genetic condition, or a metabolic disorder. The purpose of this study was to determine the incidence of metabolic and genetic disorders that predispose to fracture in young children.

**Methods:** A retrospective chart review was completed of a population-based sample from a regional pediatric health care facility. All encounters for fractures in Epic between July 2011 and December 2012 for children 18 months and younger were analyzed by a team of reviewers and revised with specialty faculty if required. Etiologies were classified as Accidental, Inflicted, Genetic/Metabolic Disorder, Other Predisposing Factor, Undetermined, and Birth Trauma. Exclusion criteria included dental fractures, imaging without evidence of fracture, or imaging not associated with an encounter. Statistical analysis was completed using Stata 16 (College Station, TX). Fisher's Exact Test was used for comparisons of demographic and clinical factors among etiologic groups. Cases of Undetermined etiology were excluded from group-wise comparisons.

**Results:** 754 encounters were analyzed. Etiologies of fractures by research team review were as follows: 640 (84.8%) cases of Accidental injury; 39 (5.2%) of Inflicted Injury; 6 (0.8%) due to a Genetic disorder known to predispose to fracturing; 2 (0.26%) due to a Predisposing Factor; 54 (7.2%) of Undetermined cause; and 13 (1.7%) due to Birth-related Trauma. Interestingly, in 196 cases (25.9%), there was discrepancy between the initial clinical impression and the research team review of fracture etiology.

**Conclusions:** A significant number of children with metabolic and genetic disorders presented with fractures in early age. The discrepancy between initial and review team etiologies requires further analysis into factors that may have affected these conditions.

## RESPIRATORY

### Poster #123:

#### **Adaptive role of ARID1B as an erythropoietic suppressor at high altitude**

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**Background:** At high altitude Andean region, hypoxia-induced excessive erythrocytosis (EE) is the defining feature of Monge's disease or chronic mountain sickness (CMS). At the same altitude, resides a population that has developed adaptive mechanism(s) to constrain this hypoxic response (non-CMS). Interestingly, children and women (until menopause) are protected from this condition. The molecular basis underlying pathology helps in deciphering mechanism(s) leading to the sensitivity or protection of the disease.

**Methods:** In this study, we have utilized an in vitro induced pluripotent stem cell as well as native CD34+ve derived model systems combined with genomic (Whole Genome Analysis) and molecular approaches (in-vitro functional assays, ATAC-seq, q-PCR) to understand the mechanism(s) regulating erythropoietic response under hypoxia in both CMS patients and adapted non-CMS subjects.

**Results:** Our whole genome analysis of the two groups identified differential SNPs between the CMS and non-CMS subjects in the ARID1B region. Under hypoxia, the expression levels of ARID1B significantly increased in the non-CMS cells but decreased in the CMS cells. At the molecular level, ARID1B knockdown (KD) in non-CMS cells increased the levels of the transcriptional regulator GATA1 by 3-fold and RBC levels by 100-fold under hypoxia. ARID1B KD in non-CMS cells led to increased proliferation and EPO sensitivity by lowering p53 levels and decreasing apoptosis through GATA1 mediation. Interestingly, under hypoxia ARID1B showed an epigenetic role, altering the chromatin states of erythroid genes. Indeed, combined Real-time PCR and ATAC-Seq results showed that ARID1B modulates the expression of GATA1 and p53 and chromatin accessibility at GATA1/p53 target genes.

**Conclusions:** We conclude that ARID1B is a novel erythroid regulator under hypoxia that controls various aspects of erythropoiesis in high-altitude dwellers. At the molecular level, it mediates an adaptive response of curbing excessive red blood production in the non-CMS group through its effect on GATA1 and p53 levels.

### RESPIRATORY

#### Poster #125:

#### **Methadone disrupts early synaptic development in human cortical organoids**

Ila Dwivedi, Dan Zhou, Andrew Caldwell, Shankar Subramaniam, Gabriel G. Haddad

In the last decade, the national opioid epidemic has yielded a 131% increase in pregnant women diagnosed with opioid use disorder (OUD), which is characterized by opioid abuse and dependence. Pharmacological treatments for OUD involve methadone, a synthetic opioid analgesic that attenuates withdrawal symptoms. However, its ability to readily enter fetal circulation, accumulate in neural tissue, and cause long-term neurocognitive sequelae, has led to concerns regarding the drug's effect on fetal brain development. Since little is known about how methadone impacts human fetal brain development, we took advantage of the in vitro induced pluripotent stem cell (iPSC)-derived human cortical organoid (hCO) technology to probe its effects on the earliest developmental stages. Our lab demonstrated that exposure to 1-10  $\mu$ M doses of methadone suppresses neuronal and neural network function in 2-to 3-month-old hCOs. Therefore, we hypothesized that chronic exposure to methadone from the earliest stages of cortical differentiation would alter the molecular mechanisms underlying synapse formation. To test this, we conducted bulk mRNA sequencing of 2-month-old hCOs derived from two cell lines chronically treated with 1  $\mu$ M methadone for 50 days. Differential expression analyses revealed a robust transcriptional response to methadone, with 2124 genes significantly differentially expressed independently of baseline differences between the cell lines ( $|\text{Confect}| \geq \text{Log2}(1.5)$  at FDR < 0.05). Gene set enrichment (GSEA) and gene ontology (GO) analyses revealed significant alterations in genes associated with pre- and post-synaptic structure and function, as well as cilia and the extracellular matrix (ECM). Unsupervised co-expression network analysis and predictive protein-protein interaction analysis revealed that methadone alters a highly correlated and interconnected network of regulatory synaptic, ECM, and ciliary genes. During brain development, primary cilia regulate the integrity and composition of the ECM, influencing synapse formation, differentiation, maturation, and refinement. Our results indicate that chronic methadone fundamentally alters synapse formation, potentially leading to the observed alterations in synaptic transmission.

## RESPIRATORY

### Poster #126:

#### Non-invasive Ventilation Usage and Adherence in Children and Adults with Duchenne Muscular Dystrophy: A Multicenter Analysis

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**Background:** Non-invasive ventilation (NIV) is routinely prescribed to support the respiratory system in individuals with Duchenne muscular dystrophy (DMD); however, factors promoting optimal NIV usage in this population is unclear.

**Methods:** Multicenter retrospective analysis of DMD patients who were prescribed NIV and followed at The Hospital for Sick Children (SickKids), Canada, Rady Children's Hospital (RCHSD), and University of California San Diego Health (UCSD), USA between February 2016 to October 2020 was performed. The primary study outcome was NIV adherence from 90-day period data downloads reporting on the percentage of nights used and average nightly usage in hours. The secondary study outcomes were the clinical and socioeconomic predictors of NIV adherence.

**Results:** Fifty-nine individuals with DMD prescribed NIV (mean  $\pm$ SD age = 20.1 $\pm$ 6.7 years) were identified. Overall, percentage of nights used, and average nightly usage was 79.9  $\pm$  31.1% and 7.23  $\pm$  4.12 hours, respectively. Compared with children, adults had higher percentage of nights used (92.9  $\pm$  16.9% versus 70.4  $\pm$  36.9%;  $p < 0.05$ ), and average nightly usage (9.5  $\pm$  4.7 hours versus 5.3  $\pm$  3.7 hours;  $p < 0.05$ ). Primary language ( $p = 0.01$ ), and deflazacort prescription ( $p = 0.02$ ) were significantly associated with percentage of nights used while ethnicity ( $p = 0.01$ ), household income ( $p = 0.02$ ), and deflazacort prescription ( $p = 0.02$ ) were significantly associated with nightly usage. Based on univariable analysis, older age and declining forced vital capacity were associated with increased percentage of nights used and increased average nightly usage.

**Conclusions:** Adults with DMD had greater average NIV usage adherence compared to children. Clinical and socioeconomic determinants have an impact on NIV adherence. Future longitudinal interventional prospective studies are needed to improve NIV adherence.

## RESPIRATORY

### Poster #127:

#### Functional profiling of CFTR-directed therapeutics in pediatric CF patients with rare genotypes

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**Background:** The first description of the chloride impermeability in the reabsorbing sweat glands of cystic fibrosis (CF) patients (Quinton, 1986) has paved the way for CFTR-directed therapeutics to treat the underlying chloride and HCO<sub>3</sub><sup>-</sup> channel defect in CF. Presently, a total of 2,109 CFTR mutations have been reported (genet.sickkids.on.ca). Of these 382 CFTR mutations cause CF (CFTR2.org). Individual responses to FDA-approved CFTR drugs show the potential of providing significant benefits, however, the development of 2D airway epithelial cell models for drug assessment remains a central task.

**Methods:** Airway epithelial cells were obtained from five pediatric CF patients by performing a simple nasal swab with a sterile cytology brush and expanded using EpiXTM cell culture media. CF genotypes were F508del/R117H-7T (male, 6 yr), F508del/F508del (male, 17 yr), R334W/406-1G>A (female, 3 yr), F508del/c.850dupA (female, 20 yr), and CFTRdele2,3(21 kb)/CFTRdele2,3(21 kb) (female, 4 yr).

**Results:** An initial harvest of as few as 20,000 cells was sufficient to expand within 31 days up to 50 million cells that were used to generate air-liquid interface cultures for ion transport studies in Ussing chambers. Short-circuit current measurements discriminated CFTR function between healthy control subjects (wild type, WT) and CF patients with intermediate (F508del/R117H-7T: 56% WT) and severe mutations (F508del/F508del: 12% WT). CFTR activity for R334W/406-1G>A was 24% WT, F508del/c.850dupA was 12% WT, and CFTRdele2,3(21 kb)/CFTRdele2,3(21 kb) was 9% WT. The CFTR correctors, VX-809 (lumacaftor) and VX-661 (tezacaftor), significantly increased CFTR currents for F508del/R117H to 73% WT and 67% WT, respectively. Cultures with the large deletion mutation CFTRdele2,3(21 kb) unexpectedly responded to VX-661 treatment (20% WT). Amiloride-sensitive sodium currents were robust and ranged between 20–80  $\mu$ A/cm<sup>2</sup> depending on the subject.

**Conclusions:** The EpiXTM technology provides a valid cell propagation technique for in vitro CF diagnostic analyses of mutant CFTR function. Future studies in our lab will use the “patient-in-a-dish model” to assess CFTR mRNA-based strategies in patients with CFTR nonfunction mutations including CFTRdele2,3(21kb).

### Poster #128:

#### Leveraging electronic health records for Evidence-Based Asthma Documentation

Landeo-Gutierrez J, Defante A, Ryu J, Tantisira K

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**Background:** Electronic health records (EHR) have the potential to record key clinical data systematically at a large scale, however significant variability in documentation persists. Standardized asthma clinical guidelines rely on thorough and systematic history taking for accurate diagnosis and management. We hypothesize that the use of a specific structured asthma template is associated with a significant increase in evidence-based documentation when compared to using non-structured templates.

**Methods:** Retrospective case-control study, comparing the use of asthma structured templates versus non-structured templates among pulmonologists at Rady Children’s Hospital. We included new patient encounters between 2016 and 2020 that had a first ever entry of an Asthma ICD-10 code associated with them, and one return encounter within a year. The asthma specific template available in our EHR was adherent to the history items recommended by asthma guidelines, summarized in 29 items for initial encounters (table) and 21 items for follow ups. Asthma history completeness was obtained by calculating the proportion of items included in each document. Statistical analyses included chi square tests for categorical variables, two sample t tests for binary and continuous variables and linear regression for bivariate analyses of history completeness and template use.

**Results:** 546 patient initial encounters met the inclusion criteria, in 450 of them a structured template was used (table). Using a structured template was associated with significantly higher documentation of asthma items in both initial and follow up encounters (figure). Linear regression analysis showed that the use of structured templates was associated to a 28.2% and 39.65% increase in asthma history completeness (in initial and follow up encounters, respectively), when compared to using non-structured templates (panel B).

**Conclusions:** The use of asthma structured templates significantly increases evidence-based asthma documentation. Leveraging the EHR as a clinical and research tool has the potential to improve clinical practice.

## RESPIRATORY

### Poster #129:

#### **“What I Would Do to Take Away Your Pain:” A Photovoice Project Conducted by Mothers of Children**

Daniel Lesser, M.D., Jesse Van Leeuwen, Darlene Abrams, Brittany Jarmin, Rachel Marquadt, Sara Taitingfong, Riahannon Valdez, Melanie Sonsteng-Person, M.S.W.

**Background:** Children with medical complexities face high service needs. Existing research focuses on how mothers of these children identify themselves, define their role in coordinating care, and how they view their own mental and physical health. This study aims to provide an understanding of how mothers navigate the day-to-day realities of having a child with medical complexities.

**Methods:** Photovoice is a qualitative research method rooted in participatory action principles incorporating photography, analysis, group discussions, and action. Participants photography of their children to discuss identity, advocacy, health, voice, and daily life. Sessions were recorded, transcribed, and analyzed using thematic analysis. Coding consisted of descriptive, In Vivo, and emotion. Codes were moved into categories by discussing the commonalities and differences, compared and grouped to identify themes.

**Results:** Six mothers of children with medical complexities ages 0-6 years in the San Diego area participated in eight weekly sessions via Zoom. One theme and three sub themes were identified that provide a better understanding of how mothers navigate the day-to-day psychological, social, and physical realities of having a child with medical complexities. There was an overarching theme of The Repetitive Nature of Trauma that can be found throughout each of the three sub themes. These sub themes are Light in the Darkness, Finding and Creating Space, and Motherhood vs. Caregiver.

**Conclusions:** This study seeks to move beyond the current deficit conceptualizations of parenting children with medical complexities. By documenting their day-to-day lives, these mothers share the most sacred pieces of themselves and their family with the hopes of advancing family centered care. While mothers affirmed previous research, which has identified the negative impact on their physical and mental health, they conveyed a message of hope. Implications provide recommendations for hospitals working with mothers of children with medical complexities.

### Poster #130:

#### **Ion channel trafficking is coordinated with dendrite morphogenesis and proper Golgi localization in sensory neuron**

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\*Presenter

An organism's ability to perceive stimuli, such as pain, from its surrounding environment is essential to survival. The perception of an external stimulus and its transformation into a cellular response depends on ion channels that are distributed throughout the dendritic arbor of peripheral sensory neurons. However, it is not well understood how the trafficking of ion channels to their sites of function in the dendritic membrane is regulated and whether or how their localization is coordinated with dendrite morphogenesis. We investigated how ion channel localization is regulated using the fruit fly class IV dendritic arborization neurons. In fruit fly larvae, painful mechanical stimuli are sensed in part by pickpocket 1 (ppk1) and pickpocket 26 (ppk26), which are members of the degenerin/epithelial Na<sup>+</sup> channel/acid sensing ion channel (DEG/ENaC/ASIC) family. Ppk1 and ppk26 form a heterotrimeric channel in the class IV sensory dendrites. To study the regulation of pickpocket ion channel trafficking, we used CRISPR-Cas9 genome engineering to fluorescently tag endogenous ppk1. We found that ppk1 localizes robustly and uniformly throughout the dendritic membrane and is present in actively growing dendrite tips. This indicates that ppk1 localization is coordinated with dendrite growth and that ppk1 is likely delivered to dendrites with the membrane that fuels dendrite growth. While investigating how ppk1 localization is regulated, we also discovered that the mis-localization of Golgi to axons correlates with an increase in axonal ppk1 levels. This suggests the dendrite-specific localization of Golgi is important to the enrichment of ppk1 in dendrites.