

12th Annual Southeastern Pediatric Research Conference



**OPTIMIZING HEALTH ACROSS THE
LIFESPAN THROUGH
INNOVATION, DISCOVERY, AND EQUITY**

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**ABSTRACT
BOOK**



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Oral Presentation Abstracts

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The Relationship Between Child Opportunity Index and Mortality in Pediatric Patients With Intracranial Firearm Injuries

Presenting Author: Ruhika Aguru, B.S.; Georgia State University

Aguru, Ruhika; Mulugeta, Makda; Bailey, Gabrielle; Reisner, Andrew; and Blackwell, Laura S.

Background: Gunshot wounds (GSW) are one of the leading causes of death for children in the US, with the most lethal being a GSW to the head (GSWH). Although all patients with GSWH are at risk for poor outcomes, disparities based on social determinants of health (SDH) exist. A multidimensional measure of SDH, the Child Opportunity Index (COI), has been developed to analyze census tract opportunities for children. However, it has yet to explore the relationship between SDH and disparity in health outcomes of pediatric patients with GSW.

Objective: This study aims to analyze the relationship between the COI and clinical outcomes of pediatric GSWH patients: mortality rates, GCS, Injury Severity Scores (ISS), and disposition post-emergency department (ED; surgery, ICU, home). We expect patients with lower COI scores to have worse clinical outcomes.

Methods: This is a retrospective cohort study of patients presenting to the EDs at Children's Healthcare of Atlanta with an intracranial GSWH from 2014 to 2022. Forty-two patients are included and range from 0-16 years old ($\bar{x} \pm s = 7.88 \pm 4.769$). The majority are male (64.3%) and Black (61.9%).

Results: In our sample, 11.9% of patients had high/very high COI scores, indicating better opportunities, 9.5% had moderate COI scores, and 52.4% had low/very low COI scores. Contrary to our hypotheses, results revealed patients who died were more likely to have higher COI scores (OR: 1.03, $p < .05$, $\bar{x} = 43.07$ vs. 26.31). Upon further analysis, results revealed patients with intentional injuries (i.e., suicide) were more likely to have higher COI scores (OR: 1.03, $p < .05$, $\bar{x} = 41.13$ vs. 28.41), and a trend was found with the relationship between intentional injury and mortality ($\chi^2: 4.33$, $p < .05$). GCS and ISS as well as post-ED disposition were not related with COI.

Conclusions: Findings reveal that children living in areas of high opportunity may be at higher risk for mortality due to more lethal mechanisms of injury (e.g., suicide). Further research should explore the relationship between mechanisms of GSW injury and access to weapons, in addition to demographic variables (e.g., race). This research is critically important to establish preventative measures and target interventions in specific areas of need.

The Use of AI to Address Pediatric Mental Health Crisis

Presenting Author: Yared Alemu, Ph.D.; TQIntelligence and Morehouse School of Medicine

Yared Alemu, Ph.D





Background: There is a mental health crisis for Children and adolescents from low-income communities; COVID and the lack of trained mental health providers have exacerbated this crisis. The high rate of mental health issues for children and adolescents in low-income communities is partly driven by multiple trauma incidents. Exposure to trauma has a pernicious impact on the development of children and adolescents, including signs of attention span dysregulation, distractibility, and disorganized attachment.

Method: Among the multitude of digital innovations to identify a biomarker for psychiatric diseases currently, as part of the macro-level digital health transformation, speech stands out as an attractive candidate with features such as affordability, non-invasive, and non-intrusive. TQI has developed a unique methodology, establishing a link between trauma, stress, and voice types partly related to the automatic nervous system changes, including disrupting speech-based characteristics.

We have a unique downstream model for each emotion type to determine the severity of that particular emotion. This downstream model involves a series of convolutional neural networks (CNN) since they've proven effective for learning the underlying structures of speech and the temporal evolution of those emotions. We couple the CNN structures with an attention mechanism. For example, in a 15-second audio sample, a particular emotion might be most prevalent in 10 seconds out of those 60 seconds. Inspired by a human's ability to concentrate on one or a few things while ignoring others selectively, we developed deep neural models that incorporate an attention mechanism to mimic human brain actions in a simplified manner.

Results: We have yet to analyze the 6872 15-second (split sample) and compare predictive accuracy with the original, longer voice samples, and we are working on it and should have the results in a few weeks. Currently, we correctly identified emotional distress at 75% and improving.

Conclusion: Addressing this crisis requires a technology-enabled augmented clinical intelligence to support providers and patients. Voice biomarker technology could provide a suite of mental health assessment, decision support, and triaging solutions focused on the unique needs of kids, teens, and adolescents.

A comparison of health care transition among children with cerebral palsy, developmental disabilities, and typically developing children

Presenting Author: Sarah Creveling, M.S. Kinesiology; Georgia Southern University

Creveling, Sarah; Keko, Mario; Rochani, Haresh; Vova, Joshua; Modlesky, Christopher; and Colquitt, Gavin

Background and Objective(s):

Children with developmental disabilities (DD) are in need of supports to transition from pediatric to adult care. Due to the potential complexities of care, it is crucial that children with cerebral palsy (CP) receive support from providers for this transition. The purpose of this study was to examine transition services among children with CP, children with DD and typically developing children (TDC).





Methods:

Participants included parent respondents to the 2018-2020 (3 years combined) National Survey of Children's Health (NSCH). Of the 174,551 respondents, 263 parents reported having a child with CP, 9,620 reported having a child with DD, and 21,404 TDC between the ages of 12 and 17. The variable of interest is receiving services necessary for transition to adult health care. Binary logistic regression analyses which adjusted for age, income, sex, and race were employed after performing multiple imputations to address missing data.

Results:

The proportion of children who received services necessary for transition to adult health care was lower among children with CP (9.69%) compared to children with DD (19.42%) and TDC

(20.82%). Compared to TDC, children with CP were 61% less likely ($p < 0.0001$) to receive

services necessary for transition to adult health care and children with DD were 13% less likely ($p < 0.00001$) to receive necessary services compared to TDC. Among all children, 24.11% of children with CP, 46.91% of children with DD, and 46.59% of TDC had time alone with the provider ($p < 0.0001$). Providers worked with 56.97% of children with CP, 64.15% of children with DD, and 68.83% of TDC to gain skills to manage health/health care or understand health care changes at age 18 ($p < 0.0001$). The health care provider discussed the shift to adult health care providers for 25.0% of children with CP, 22.8% of children with DD, and 22.82% of TDC ($p = 0.76$).

Conclusions:

Most adolescents, especially those with CP or DD, are not receiving the necessary preparation and support needed to transition to adult health care. It is imperative that pediatric health care providers be proactive in discussing and planning for transition to adult health care for their

patients.

High-Resolution Ensemble Prediction: Percentage of Children with Blood Lead Levels $\geq 5\mu\text{g}/\text{dL}$ and $2-5\mu\text{g}/\text{dL}$ in the Metro Atlanta Region

Presenting Author: Carmen Dickinson-Copeland, MSCR, Ph.D.; Morehouse School of Medicine

Frndak, Seth; Yan, Fengxia; Edelson, Mike; Immergluck, Lilly Cheng; Kordas, Katarzyna; Idris, Muhammed Y; and Dickinson-Copeland, Carmen M

Background: Current lead exposure prevention efforts, including county and state-wide policies and programs, target large geographic areas for intervention. Primary prevention of low-level lead exposure in children might be supported using a geographically high-resolution predictive modeling approach. **Methods:** A sample of 92,792 urban and suburban children ≥ 5 years of age from the metro Atlanta region was curated from the Georgia Department of Public Health Healthy Homes and Lead Prevention Program database for lead exposure between 2010 and 2018. A raster stack with $\sim 1 \text{ km}^2$ cells was created, including the number of children with venous blood lead levels (BLLs) ≥ 2 to $< 5\mu\text{g}/\text{dL}$ (sub-





clinical) and $\geq 5\mu\text{g}/\text{dL}$ (clinical) in each cell and 12 predictors. An ensemble machine learning approach, including a generalized linear model, a gradient-boosted machine, and a deep neural network, was used to predict the number of children within each BLL category, sub-clinical and clinical, in each raster cell. Permutation-based predictor importance and partial dependence plots were used to interpret the final ensembles for sub-clinical and clinical BLLs. Maps of predicted vs. observed raster cell values are presented to visually compare model performance. Results: Most important predictors for predicting sub-clinical and clinical BLLs were similar, including an Environmental Protection Agency Toxic Release Inventory for air-based toxic release facility density (positive association), percent of the population below the poverty threshold (positive association), percent of the population that is White (negative association), a crime index (positive association) and road network density (positive association). The predictive values for sub-clinical and clinical BLLs generally matched the observed values; nevertheless, cells with a high number of lead-exposed children were underestimated. Conclusions: High-resolution geographic prediction of lead-exposed children using ensemble machine learning is a promising approach to support lead prevention efforts. Model transportability for communities outside of the Atlanta Metro area will require further development and validation.

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

Presenting Author: Venkata Viswanadh Edara, M.S, Ph.D.; Emory University

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

Background: Vertical transmission of Zika virus (ZIKV) can result in birth defects including microcephaly and additional adverse neurologic outcomes have been reported following ZIKV infection in the first year of life. While intense research has focused on the neuropathogenesis of prenatal ZIKV infection, there is an incomplete understanding of the consequences of postnatal ZIKV infection in infants and children. We have previously shown abnormal brain structure and function that is predictive of behavior in infant rhesus macaques infected with ZIKV postnatally. Here, we explored the brain regions, cells, and pathways impacted by postnatal ZIKV infection to suggest mechanisms of injury and neuropathogenesis.

Methods: To understand the effect of acute postnatal ZIKV infection on Central Nervous System (CNS), infant rhesus macaques (RMs) were infected with ZIKV at one month of age and euthanized 14 days after infection for single cell transcriptomic analyses of the hippocampus, amygdala, and striatum. ZIKV-infected infant RMs were compared to age and sex-matched uninfected controls. Bioinformatic approaches using R (V4) and Seurat (V4) were utilized and, after quality control, 105,421 cells from controls and 94,975 cells from ZIKV-infected animals were analyzed. Principal-component analysis (PCA) and dimensional reduction were conducted to identify various clusters of cells and their neighbors.

Results: Overall, 25 clusters representing all CNS major cell types were identified and annotated. We identified unique transcriptional phenotypes in the CNS between uninfected and ZIKV-infected RMs, including nervous system development, glial cell differentiation, neuron differentiation, activation of



innate immune response and regulation of myelination. As expected, we found a signature of activated microglia along with upregulation of transcription factors involved in interferon signaling and downstream activation of interferon stimulated genes (ISGs) such as IRF1, IRF9, MX1, MX2 and ADAR in ZIKV-infected RMs. Furthermore, ZIKV infection significantly reduced the expression of several genes involved in myelination processes in both mature and newly formed oligodendrocytes.

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

Pro-Inflammatory SIRPα-Expressing Monocytes and Macrophages Mediate Anti-TNF Refractory Crohn's Disease in Children

Presenting Author: Duke Geem, MD, PhD; Emory University School of Medicine

Geem, Duke; Maddipatla, Sushma; Pelia, Ranjit; Chinnadurai, Raghavan; Venkateswaran, Suresh; Matthews, Jason; Anbazhagan, Murugas; Kolachala, Vasantha; Dodd, Anne; and Kugathan, Subra

Background: Crohn's disease (CD) is a chronic inflammatory gastrointestinal disorder with detrimental consequences in children. Anti-tumor necrosis factor (aTNF) therapies are the only FDA-approved biologic therapy for pediatric CD, however, one-third of patients fail anti-TNF induction, and, of those who initially respond, 15% relapse every year. Thus, there is an urgency to elucidate the underlying immunogenetic mechanisms of anti-TNF refractory CD. Methods: A prospective cohort study was employed consisting of treatment-naïve (TN-CD; n= 12), aTNF refractory (REF-CD; n=11), and endoscopic remission CD (REM-CD; n=16) along with non-IBD control (n=13) children. High dimensional flow cytometric analyses (HD-FACS) of the blood along with ileal and rectal biopsies were performed. Further ileal immune characterization was conducted via single-cell RNA sequencing (scRNA-seq) using the 10X Chromium platform and sequenced on Illumina's Novaseq600. The Seurat v4.1 workflow was used for the UMAP cell clustering algorithm. To assess effects of conditioned media (CM) from SIRP α cells on non-IBD ileal organoids, blood SIRP α + cells from REF-CD were enriched via magnetic activated cell-sorting and stimulated with LPS and flagellin (FLG) for 96 hrs. The ileal organoids were treated with CM for 72 hrs followed by viability and intracellular cytokine staining. Descriptive statistics, one-way ANOVA with multiple comparisons testing, and univariate linear regression were applied. Results: A significant enrichment of SIRP α +CD11c+HLA-DR+CD64+ (SIRP α) cells in the ileum, rectum, and blood of REF-CD was observed based on HD-FACS (P< 0.05). In-depth characterization with scRNA-seq indicated a monocyte/macrophage lineage based on expression of transcriptional markers: CD14, FCGR3A, CD68, CD163, FCGR1A, and MRC1. Functionally, SIRP α macrophages expressed the pro-inflammatory cytokines, IL-1 β , IL-6, and TNF α , detected by HD-FACS as well as the pro-fibrotic cytokine, TGF β 1, and the neutrophil chemokine, CXCL8. Univariate regression highlighted significant positive correlation of intestinal SIRP α macrophage proportions with fecal calprotectin (P<0.05) and C-reactive protein (P<0.05). The CM from SIRP α + cells of REF-CD induced significant cell death and increased TNF α and IL-1 β expression from ileal organoids. Conclusion: SIRP α cells are a distinct pro-inflammatory monocyte/macrophage population enriched in REF-CD patients that may mediate resistance to anti-TNF



therapy via dysregulated secretion of pro-inflammatory cytokines and disrupting the intestinal epithelium.

Kinetics of Infant Crawling: Preliminary Results

Presenting Author: Mark Geil, PhD; Kennesaw State University

Geil, Mark; Stockwell, Emma; Grayson, Sarah; Poisal, Micah; Cannoy, Jill; Coulter, Colleen

Background: Approximately 93% of typically developing infants progress through at least one stage of crawling during development of locomotion. Our understanding of crawling in both typically and atypically developing infants has been hindered by the multiple difficulties of applying traditional motion analysis techniques to this form of gait. Consequently, no normative data exist with which to understand atypical development. This study seeks to quantify kinetic and temporospatial aspects of stages of crawling using a novel, noninvasive technique in typically-developing children and children with limb loss.

Methods: Crawling was assessed using a 4.9m (16') x 0.6m (2') Zeno pressure transducer mat. The mat incorporates a distributed array of 1 cm² force sensors that output 16 levels of pressure. PKMAS4 software, originally designed for animal-based studies of quadrupedal gait, is used to capture infant crawling. Following informed parental permission, subjects were placed on the mat and encouraged to crawl. Five primary outcome measures were assessed: crawling speed, cadence, percent limb support, anterior-posterior pressure ratio, and bilateral pressure ratio.

Results: To date, we have collected data for three children in the Limb Loss (LL) and two children in the Typically Developing (TD) cohort. Within the TD cohort, a total of six data collection sessions have taken place. Longitudinal analysis of crawling development was available for one TD child. Crawling speed was significantly correlated with age ($p=0.00013$). These gains were not entirely attributable to increase in limb length, as cadence was also significant ($p=0.0021$). Comparing the groups, children with limb loss showed similarity to TD crawling in several measures. The only metric for which there was a significant statistical difference between the development status groups was for A-P weightbearing ($p=0.03$), indicating that, on average, the LL sample bore more weight on their arms vs. legs than the TD sample.

Conclusions: Even at this preliminary stage, we are gaining new insights into typical and atypical crawling development. Cadence may be an important indicator of development. Weight carriage by the arms might hinder progression toward walking in children with limb loss. Comparisons will provide information for clinicians to improve therapies towards more typical mobility development.

Adipocyte-secreted purines inhibit T-cell function and alter in vitro leukemia cell cycle dynamics in B-cell acute lymphoblastic leukemia

Presenting Author: Delaney Geitgey, B.S.; Emory University

Delaney Geitgey, Uma Obalapuram, Miyoung Lee, Joshua D. Chandler, Curtis J. Henry





Background

B-cell acute lymphoblastic leukemia (B-ALL) is the most common childhood cancer and is a leading cause of pediatric illness-related death. Among children with B-ALL, the survival of patients with obesity is about 30% lower than similar lean patients. Two-thirds of the United States population is overweight or obese with numbers steadily increasing. Oncology researchers must understand how obesity impacts B-ALL pathogenesis to improve outcomes in this growing demographic. Current hypotheses posit that the obesity-mediated effects on B-ALL may occur via direct influence of adipocytes on B-ALL cells and via indirect effects on the anti-cancer response of the immune system.

Methods

Adipocyte-mediated effects were studied in vitro through conditioned media development. Bone marrow mesenchymal stem cells were differentiated into stromal cells or adipocytes, and then media from these cultures was collected after three days. Differences between the stromal cell and adipocyte secretomes were identified using mass spectrometry. Human B-ALL cell lines and primary human T-cells were exposed to adipocyte conditioned media (ACM), stromal cell conditioned media (SCM), cell-inexperienced unconditioned media (UCM), and exogenous forms of the differentially secreted factors.

Results

Mass spectrometry revealed that adipocytes secrete the purine nucleobases adenine and guanine at high levels relative to UCM or SCM. Culturing B-ALL cells with exogenous purines altered cell cycle dynamics as indicated by DNA incorporation of the fluorescent thymidine analog EdU; guanine increased the number of cells in S-phase and decreased the number of cells in growth phases or mitosis relative to controls. These results provide a tentative mechanism for our previous findings: adipocyte-conditioned media (ACM) induced B-ALL senescence and resistance to cell cycle-targeting chemotherapies. Furthermore, adding exogenous purines to primary human T-cells during activation decreased costimulation receptor expression (CD3 and CD28), decreased effector cytokine production (IFN γ and TNF α), and increased oxidative stress (via mitochondrial superoxide) over three days.

Conclusions

These findings demonstrate that adipocyte-secreted purines can modulate both the anti-tumor immune response and the growth dynamics of leukemia in vitro. Findings from these studies will be applied in murine models to validate the potential of purinergic signaling as a therapeutic target in the context of B-ALL and obesity.

Longitudinal Surveillance of SARS-CoV-2 (SARS) IgG Antibodies in Pediatric Healthcare Workers (HCW)

Presenting Author: Dunia Hatabah, MD; Emory University

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



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

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

Methods: Prospective longitudinal cohort conducted from April 2020 to May 2022 in 642 pediatric healthcare workers (HCW) working in a pediatric facility. Serum samples were analyzed using an MSD serology kit testing for IgG antibodies against 4 major SARS antigens and other coronaviruses.

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

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

Melatonin Modulates HCMV Infection at the Maternal-Fetal Interface by Decreasing NLRP3 Expression

Presenting Author: Tyana Joseph, PhD/MSCR Student; Morehouse School of Medicine

Joseph, Tyana T.; Thompson, Nia; Johnson, Erica L.

Background: Human cytomegalovirus (HCMV) is a major cause of pregnancy complications and congenital disabilities due to the virus being the leading cause of prenatal viral infection. In an immunocompetent host, HCMV can establish dormancy in the body, but the viral infection can reactivate during pregnancy and cross the placental barrier to the fetus. Studies suggest that continuous exposure to HCMV during gestation implicates HCMV as a significant contributor to abnormal placenta development and dysfunction due to the inhibition of trophoblast terminal differentiation and invasion coupled with the decreased immunological response and increased oxidative stress. Therefore, HCMV is a potential trigger for NLRP3 inflammasome activation. Melatonin



can reverse the effects of viral-induced infection and oxidative stress due to its potent anti-inflammatory and antioxidant properties. As a result, basal and exogenous melatonin sources can reduce HCMV-mediated inflammation through its anti-inflammatory and antioxidant properties by deactivating NLRP3 inflammasome.

Methods: With written informed consent, placenta from healthy women (>18 years) will be collected from Emory University Midtown Hospital, GA. We isolated decidual mononuclear cells, macrophages, and trophoblast cells from term placenta. We also cultured trophoblast cell lines (JEG-3). Cells were treated with HCMV, LPS, 1mM Melatonin, LPS + 1mM Melatonin, and HCMV + 1mM Melatonin. We determined the expression of NLRP3 inflammasome using RT-qPCR.

Results: Data was collected to determine the role of melatonin during HCMV infection at the maternal-fetal interface. From the data, we found that NLRP3 expression was decreased in HCMV + 1mM Melatonin treated cells in comparison to HCMV-treated cells. This demonstrates that melatonin reduces NLRP3 activation, thus downregulating viral-induced inflammation at the placenta.

Conclusion: This data suggests that melatonin is an essential molecule in regulating HCMV-induced inflammation at the maternal-fetal interface. Understanding melatonin's role at the maternal-fetal interface during HCMV infection is crucial to develop therapeutic strategies to reduce adverse pregnancy outcomes.

Low-cost Microfluidic Device Capable of Producing Rapid Colorimetric Results for Detection of Pediatric Carbapenem Resistant Enterobacteriaceae (CRE) Infections

Presenting Author: Lily Kamat, B.S. Biology - Undergraduate Student; Georgia Institute of Technology

Kamat, Lily; Delgado, Priscilla; Haider, Ali; Waggoner, Jesse; and Myers, David

Background: The mortality rates for pediatric patients with Carbapenem resistant Enterobacteriaceae (CRE) infections are steadily increasing and already as high as 50%. The decreased survival is in large part due to the multi-day long delay in identification of a CRE infection and lack of identification of specific mechanisms. The central barrier to faster testing has been the lack of easy-to-use tests that can be implemented on demand at or near the point-of-care. To that end, we leveraged a recent innovative microfluidic design, self-coalescing microfluidics, which enable multiple colorimetric tests to be run on a single injected sample. Unlike the original self-coalescing microfluidic, our design is simple to make with low cost materials, and requires no external equipment for its operation or use. When a specimen is injected, reagents are reconstituted and 4 colorimetric assays are run simultaneously, including a control and testing for class A, B, and D beta-lactamases.

Methods: The traditional self-coalescing design was scaled up and laser cut onto 0.13mm silicone-adhesive roll-based tape. Reagents for the assay were spotted on the channel via micropipette. A micropipette was used to input 180µL of bacterial sample for a pH-dependent carbapenemase detection assay that output control and test colorimetric signals. The resulting colorimetric signal for carbapenem hydrolysis was interpreted by visual inspection.



Results: An 80% success rate was achieved with preserving the self-coalescing flow pattern on a larger scale using the laser cut device. The colorimetric test output a strong signal that was easily detectable by eye to indicate the presence of CRE.

Conclusion: We pioneered a new highly accessible method for rapid detection of CRE infections. The scaled-up design combines low-cost manufacturing, and reduces the need for costly equipment to run and analyze the assay. Further optimization of the design will be done to achieve a higher success rate. The innovative application of a microfluidic POC diagnostic to CRE infections not only revolutionizes testing for all patient populations, but also the miniscule sample size required makes the device ideal for children and neonates, alike.

Accuracy Deficits During Reaching are Related to Altered Prefrontal Cortex Activity in Children With Cerebral Palsy

Presenting Author: Owais Ahmed Khan, PhD Candidate in Speech and Hearing Science; The University of Georgia

Khan, OA; Singh, T; Barany, DA; and Modlesky, CM

Background: Children with cerebral palsy (CP) exhibit impaired reaching due to central deficits in motor planning. The prefrontal cortex (PFC) mediates action planning within the frontoparietal neural network for reaching, but its role in mediating reaching performance in CP is unexplored. This study combines a robotic task with portable functional neuroimaging to concurrently evaluate reaching accuracy and PFC activity in children with CP.

Methods: Seated participants grasped a robotic arm (KINARM End-Point) to hit targets projected onto a screen. Fourteen children with spastic CP (5–11 y, Manual Ability Classification System levels I-II) and fourteen age-, sex- and arm dominance-matched typically developing controls completed four blocks (10 trials/block) for each arm. Time constraints (high, low) were imposed by varying the time allowed to hit the target in each block. Linear mixed models were used to assess effects of group, arm, time constraint and PFC hemisphere on reaching accuracy and PFC activity. Spearman rho was used to assess relationships between accuracy and PFC activity and Cohen's d (d) was used to assess effect sizes.

Results: Children with CP had lower reaching accuracy than controls, with greater deficits observed in the non-preferred arm ($d = 1.92$, $p < 0.001$) than the preferred arm ($d = 1.03$, $p = 0.011$). Limb differences in accuracy were noted only in children with CP ($d = 0.75$, $p < 0.001$). PFC activity differed across groups during preferred arm reaching under high time constraints, with PFC deactivation observed in children with CP compared to PFC activation in controls ($d = 1.09$, $p = 0.006$). Children with CP exhibited PFC deactivation under high time constraints compared to low time constraints during preferred arm reaching ($d = 0.69$, $p = 0.001$). Reaching accuracy was positively related to PFC activity in each arm and across time constraints in children with CP, but not in controls.

Conclusions: The contrasting patterns of PFC activity observed in children with CP compared to controls provide novel insights into the neurophysiological regulation of goal-directed reaching in CP. This study



supports the feasibility of integrating portable functional neuroimaging with robotic tasks to assess purposeful reaching in CP.

Mother's Voice Intervention Results in Increased Attention in Infants with Neural Insults

Presenting Author: Caitlin Kjeldsen, A.B.; Emory University

Kjeldsen, Caitlin; Neel, Mary Lauren; and Maitre, Nathalie L.

Background

Neural insults in infancy often have severe long-term impacts on neurodevelopmental outcomes including attention and learning. During hospitalization, these infants are often excluded from interventional trials due to concern for confounders. Non-nutritive suck (NNS) training using contingent mother's voice has been shown to promote improved suck-swallow-breathe patterns in preterm infants in the NICU; however, it is unclear whether hospitalized infants with neural insults have the capacity to attend to and engage in this type of intervention.

Objective

To determine whether hospitalized infants with brain injuries have the capacity to engage in a contingent learning intervention leveraging mother's voice as measured by pause time between suck bursts.

Design/Methods

This randomized controlled trial (N=105) included infants with neural insults (hemorrhage, ischemia, thrombosis/infarct) or those with abnormal General Movements Assessment (GMA). Infants were randomized to receive 20 sessions of NNS-contingent mother's voice recording or passive mother's voice. Pause time between suck bursts was used to measure infant attention to the auditory stimulus at pre-/post-assessment, with decreased pause times indicating increased attention. A generalized linear mixed-effect model (GLMM) with Poisson likelihood and log link function was constructed to predict average pause time between suck bursts at final assessment. Fixed effects included baseline average pause time, severity of neural insult, gestational age, group, and number of sessions; subject was treated as a random effect.

Results

There were no demographic differences between groups at baseline. Median gestational age for both groups was 27w (Intervention IQR: 25-29.2w; Control IQR: 25-30w). Infants in the intervention group (n=53) demonstrated 24% decreased average pause time at final assessment compared to the control group (n=52) ($p=.002$) indicating increased attention to the auditory stimulus. Severity of neural insult was not a predictor of pause times ($p=.79$).

Conclusion





In a group of hospitalized infants with neural insults, we showed that those exposed to mother's voice contingent on NNS demonstrated decreased pause time between suck bursts, indicating increased engagement with and attention to the auditory stimulus compared to those who received passive exposure only. Beginning intervention while infants are hospitalized may maximize neuroplasticity and promote establishment of effective neural networks and patterns.

Parent-Caregiver Reports Demonstrate Inconsistencies in Timing of Social Milestone Acquisition in Typical Development vs. Autism Spectrum Disorder

Presenting Author: Alp Koksal, PhD; Marcus Autism Center

Köksal, Alp; Shultz, Sarah; Jones, Warren

Background: Infants' milestone acquisition provide insights into later diagnoses of Autism Spectrum Disorder (Werner et al., 2000). For example, divergences in joint attention and affect were reported at 6 months of age, with increasing severity over childhood (Clifford and Dissanayake, 2008). Many studies rely on retrospective parent reports, where reliability is called into question (Ozonoff et al., 2010). We hypothesize that children with ASD will attain smiling and first words milestones later than typically-developing peers, with no difference in parent consistency by diagnostic group or milestone.

Methods: Infants with (n=25) and without ASD (n=81) were selected from a prospective longitudinal study of infants at low- and elevated-likelihood for ASD. Caregivers completed Parent-Caregiver Questionnaires (PCQ) at 9, 12, and 18 months, asked for their child's age of smiling and first words (in months). Descriptive statistics, intra-class correlation coefficients (ICC), Fleiss' Kappa and linear regressions were used to determine age of emergence and intra-rater reliability.

Results: A total of 318 PCQ responses determined the mean age of smiling (2.04(1.07)months) and first words (7.86(2.05)months). Mean age for TD smiling was earlier than ASD (TD: MAge(SD)=2.00(0.95)months; ASD: MAge(SD)=2.25(1.34)months; p=0.03), as well as first words (TD: MAge(SD)=7.37(1.68)months; ASD: MAge(SD)=8.15(2.2)months; p=0.05). Looking at parent consistency in reports over time indicates great variability in response consistency (ICC=0.54, κ =0.47). Parents of ASD infants were less consistent for smiling (ASD: ICC=0.32, κ =0.45; TD: ICC=0.63, κ =0.48). Their average age responses increased from 9 to 18 months (p=0.05, r=0.22), to become significantly greater than TD at 18 months (p=0.03). For first words, both groups show an increase in mean answer value over time (TD: p<0.01, r=0.309; ASD: p=0.06, r=0.363).

Conclusions: The analysis of retrospective parent reports help establish developmental windows for milestones, yet also demonstrate inconsistencies over time. The trend in reports for smiling in ASD may hint at parents' perception of diagnosis, while the increase of reported age in first words highlight difficulty in measuring prospective milestones without granular data (i.e. in days/weeks rather than months). Increasing sampling frequency or using ecological momentary analysis may draw a higher fidelity picture of divergence in typical development and autism.



Spatial and single cell transcriptomic analysis of Crohn's disease ileal mucosa reveals changes in cellular crosstalk during inflammation

Presenting Author: Vasantha Kolachala, PhD; Emory University

Kolachala, Vasantha; Maddipatia, Sushma C; Murthy, Shanta; Dodd, Anne; Pelia, Ranjit S; Venkateswaran, Suresh; Anbazhagan, Murugadas; Geem, Duke; Joshi, Gaurav N; Jhita, Navdeep; Yin, Hong; Cutler, David; Qiu, Peng; Matthews, Jason; and Kugathasan, Subra

Background: The complex architecture of the intestinal mucosa requires spatial resolution of single cells to better understand the heterogeneous nature of Crohn's disease (CD), especially during active disease with inflammation. Here we examine the impact of inflammation on changes in cellular crosstalk in the intestinal mucosa using single cell and spatial transcriptomics.

Methods: We performed single cell RNA sequencing (scRNA-seq) and spatial transcriptomics (ST) coupled with immunofluorescence and hematoxylin and eosin staining using CD patient samples. Ileal pinch biopsies (7 inflamed, 5 non-inflamed) and resected ileal CD surgical tissue (9 inflamed, 3 non-inflamed) were used. Receptor-ligand (R-L) interactions were measured by CellphoneDB and the composition of the cellular milieu per ST spot was determined by Conditional AutoRegressive-based Deconvolution (CARD) and further studied with pathway analysis using STRING.

Results: Cellular crosstalk was disrupted during inflammation, including differences in subtypes of epithelial-stromal, epithelial-immune, and epithelial-epithelial interactions. Combinatorial use of scRNA-seq and ST data revealed CD74-MIF crosstalk of the epithelium with the immune and stromal compartment as a significant interaction in CD mucosa. CD74-MIF-MHCII signaling was at the center of numerous changes in the cell types communicating within the lamina propria of active CD. Involvement of HSP90AA1, PDAI3 and CALR pathways during active disease with CD74-MIF-MHCII signaling connected cellular ER stress and fibrotic pathways with alterations in epithelial cell antigen presentation.

Conclusion: Our multimodal analytical approach captures the impact of active CD on the cellular networks within the intestinal mucosa and offers new insight into complex molecular interplay, patient heterogeneity, and inflammatory signatures associated with CD revealing potential drug targets.

Steroid-Associated Adverse Events are Dose-Dependent Following Hematopoietic Cell Transplantation for Pediatric Acute Lymphoblastic Leukemia

Presenting Author: Robert Lisac, MD; Emory University

Lisac, Robert; Raghunandan, Sharmila; Gillespie, Scott; Liu, Katie; Williams, Kirsten; Watkins, Benjamin; and Qayed, Muna

Background: Hematopoietic cell transplantation (HCT) is a successful treatment of relapsed acute lymphoblastic leukemia (ALL), but can be associated with high systemic steroid exposure (SSE) due to treatment of graft-versus-host disease (GVHD). Steroids are associated with many late complications



including poor bone health and cataracts. We hypothesized that SSE would increase late bone and eye toxicities in a dose-dependent manner following HCT for pediatric ALL.

Methods: In this retrospective study, pediatric recipients of first HCT for ALL at a single institution between 2011 to 2017 and survived at least 100 days post-HCT were captured. Exclusions from subset analysis included: pre-existing avascular necrosis (AVN), fractures, and cataracts. Patients were censored at relapse and death.

Results: Forty-seven patients were identified with a median age of 12 years old (range 3.2 - 21) at HCT. Thirty-five (74%) patients had post-HCT SSE, 29 (83%) had acute and 23 (66%) had chronic GVHD. Median SSE was 46 mg/kg prednisone equivalents (PE) (IQR 2.2 - 178). Nine (24%) patients experienced bone events, including AVN (n = 3), axial (n = 1) and appendicular (n = 5) fractures. The median time to event was 1.3 years (range 0.4 - 5.3) post-HCT. In those that received ≥ 100 mg/kg PE versus < 100 mg/kg PE, the cumulative incidence rate of bone events was 56.8% (95% CI 25.5% - 79.1%) versus 7.1% (95% CI 0.4% - 28.5%) ($p = 0.002$). Thirteen (30%) patients developed cataracts a median of 5.1 years (range 1.7 - 6.8) post-HCT. Cumulative incidence rate of cataracts was 79.4% (95% CI 31.5% - 95.5%) if exposed to ≥ 100 mg/kg PE versus 43.3% (95% CI 12.8% - 71.2%) if < 100 mg/kg PE ($p = 0.025$). Adjusting for age at transplant and complete remission status, cumulative SSE remained significantly associated with bone events and cataracts.

Conclusion: Our results suggest that adverse bone events and cataracts are common in pediatric patients with ALL following HCT and are increased in patients who received higher SSE following HCT. These results reinforce that patients should be closely followed for late complications of SSE and highlights the need for steroid-sparing approaches to GVHD treatment.

Focused Cardiac Ultrasound in the Pediatric Cardiac ICU: The Modern Physical Exam Using Portable Ultrasound

Presenting Author: Kevin Maher, PT; Children's Healthcare of Atlanta

1998 Society

Marcos Mills, MD; Kevin Maher, MD

Background: Despite a multitude of invasive and non-invasive methods of monitoring patient hemodynamics in the pediatric cardiac intensive care unit (CICU), patients remain at risk for clinical decompensation. It is unknown whether the use of portable focused cardiac ultrasound (FCU) as part of the routine physical exam would result in the discovery of new information in a timely manner that meaningfully adds to the clinical evaluation.

Methods: In this prospective descriptive study at Children's Healthcare of Atlanta's pediatric cardiac intensive care unit, cardiac intensivists with board certification in pediatric cardiology performed FCUs on both post-operative and non-surgical critically ill patients. Successful FCU completion consisted of acquisition of 4 imaging window: parasternal long, parasternal short, apical, and subcostal. Pre and post FCU questionnaires were filled out comparing echocardiographic estimates (pre) to echocardiographic findings (post), along with physician experience and impact on clinical management.





Results: Six cardiac intensivists performed 34 FCUs. 62% of the encounters occurred on patients who had previously undergone cardiac surgery during their hospitalization, which was less than 48 hours prior to FCU in 25 (74%) of these encounters. The majority of FCUs (74%) were completed in less than 3 minutes and with successful acquisition of all imaging windows in 88% of encounters. The median time since their most recent formal echocardiogram was 4 days (IQR 2.25-7). New findings occurred in 59% of FCUs and resulted in changes in clinical management 18% of the time. Physician confidence in their clinical assessments increased in 50% of encounters.

Conclusions: In this novel use of portable ultrasound technology, pediatric cardiac intensivists frequently discovered new information that would not otherwise have been known at that moment and often resulted in changes to clinical management. The technology was easily incorporated and frequently increased overall physician confidence in their clinical assessments. Further investigation regarding the use of portable focused cardiac ultrasound's potential impact on clinically relevant outcomes is warranted.

Hyperoxia During Veno-veno Extracorporeal Life Support Due to Cardiopulmonary Failure is Associated with Mortality in Neonatal and Pediatric Patients

Presenting Author: Paola Rodriguez Morales, BS; Emory University School of Medicine

Paola Rodriguez Morales; Rebecca Shamah; Joshua Qian; Kasey Keane-Lerner; Tawanda Zinyandu; Joel Davis; Joshua Rosenblum; Heather K. Viamonte; Asaad G. Beshish

Introduction:

Patients requiring extracorporeal life support (ECLS) are frequently exposed to supranormal blood oxygen tension, termed hyperoxia. Recent studies suggest that hyperoxia is associated with worse outcomes in patients exposed to extracorporeal technology. Data regarding the effects of hyperoxia in pediatric patients is limited. We sought to evaluate the association of hyperoxia with mortality in a large-volume ECLS center.

Methods:

Retrospective single-center study. All patients 0-18 years who required VV-ECLS between 01/2014 and 12/2019 were included. An internal registry was reviewed for patient characteristics, clinical variables, and average partial arterial pressure of oxygen (PaO₂) during the first 48-hours of ECLS. Analysis was performed using appropriate statistics with a significance level set at $p = 0.05$.

Results:

During the study period, 110 VV-ECLS runs occurred in 107 patients. The median age and weight were 4.9 months (IQR 0.1, 105.4) and 5.4 kg (IQR 3.4, 35.0), respectively. Most runs occurred in neonates ($n=63$, 57.3%). Median time from admission to cannulation was 39 hours (IQR 3,116) and median ECLS duration was 140.5 hours (IQR 98.0, 289.0). Overall mortality was 26.4%. Using an ROC curve, a mean PaO₂ of 122 mmHg in the first 48-hours of ECLS was determined to have optimal discriminatory ability for mortality (sensitivity 41% and specificity 86%). Of the VV-ECLS runs, 68 (61.8%) had a PaO₂>122





mmHg categorized as hyperoxia group. Patients in the hyperoxia group were older (median age 105.4 vs 1.6 months), weighed more (28.3 vs 4.3 kg), had higher rates of hemorrhagic complications while on ECLS (69.6% vs 25.3%), and had higher mortality rates (52.2% vs 19.5%) ($p < 0.05$).

In the logistic regression, patients in the hyperoxia group had higher odds of mortality in the unadjusted analysis. This persisted when adjusting for cofounders (OR 7.97, 95% CI 1.72-36.86, $p = 0.0079$).

Conclusion:

Children exposed to hyperoxia during the first 48-hours of VV-ECLS were 8 times more likely to die than those who were not exposed to hyperoxia. Multicenter and prospective evaluation of this modifiable risk factor is imperative to improve the care of this high-risk cohort.

SNAP Restrictions for Drug Felons: A Recipe for Food Insecurity among US Children

Presenting Author: Fatima Waseem, PhD, MPH; Hubert Department of Global Health

Fatima Waseem, Maha Abu-Salah, Kevin E. Markes, Solveig A. Cunningham, Liliana Aguayo

Background: Approximately 13 million US children experience food insecurity, which negatively impacts their physical and mental health, academic performance, and social outcomes. The Supplemental Nutrition Assistance Program (SNAP) is one of the most efficient tools presented to combat child hunger. However, about 20% of food-insecure children live in households ineligible for SNAP benefits. The Personal Responsibility and Work Opportunity Act imposed a lifetime ban on SNAP for convicted drug felons and their households. After this law was signed in 1996, States adopted the ban, modified the regulations to limit the disqualifications, or opted-out of the disqualifications. We examined the association between State ban-related policies from 2001 to 2016 with county-level rates of food insecurity among children.

Methods: Westlaw, an online legal research database, was used to identify annual changes in SNAP ban-related policies from 2001 to 2016 and categorized States based on whether they adopted 1) no ban, 2) a modified ban, or 3) a full ban each year. The State mode (i.e., the most frequent category between 2001-2016) was used to categorize each counties' SNAP-ban level. Map the Meal Gap data were used to estimate rates of food insecurity among children at the county level. One-way ANOVA tests were used to examine differences in the county rates of food insecurity among children across different levels of SNAP-ban policies.

Results: Between 2001-2016, 12% of US counties had no ban ($n=381$), 38% had a modified ban ($n=1197$), and 50% a full ban ($n=1564$). County-level rates of food insecurity among children significantly differed across SNAP-ban categories ($F(2,3139) = 76.95$, $p < 0.001$). Tukey post-hoc tests revealed that, compared to counties with a full SNAP ban, the prevalence of food insecurity among children was significantly lower in counties that had no ban (1.19 ± 0.26 , $p < 0.001$) or a modified ban (1.75 ± 0.18 , $p < 0.001$).

Conclusion: State-level policies that limit access to SNAP benefits for convicted drug felons and their household members were associated with higher rates of food insecurity among children. As food



insecurity during childhood has adverse long-term health consequences, findings highlight the potential negative impact of restricting SNAP benefits.

Soft Imperceptible Wearable Electronics for Cardiovascular Monitoring of Infants with Single Ventricle Heart Disease

Presenting Author: Lauren Zhou, BS Mechanical Engineering, MS Mechanical Engineering; Georgia Institute of Technology

Imlay Innovation Fund (2021)

Zhou, Lauren; Aljiffry, Alaa; and Yeo, Woon-Hong

Soft Imperceptible Wearable Electronics for Cardiovascular Monitoring of Infants with Single Ventricle Heart Disease

Lauren Zhou, Alaa Aljiffry, MD, and Woon-Hong Yeo, PhD

Background:

Patients with single ventricle heart disease (SVHD) require multiple palliative surgeries. High mortality rates during the interstage period encouraged at-home monitoring practices, significantly improving morbidity and decreasing mortality. Modern-day interstage monitoring includes logging the infant's weight, feeding patterns, and oxygen saturation once a day in a journal to be reviewed by the medical team. Here, we introduce an electronic system for the home monitoring of SVHD patients.

Methods:

We used a flexible, wearable, and wireless electronic system that is ultrathin and allows seamless integration with infants' sensitive and fragile skins. Data from the device will be transferred in real-time into an IoT-compatible, cloud-based computation platform. This will allow AI-powered long-term patient-specific abnormality detection and more comprehensive data sharing between the home and the hospital.

Six patients with SVHD were examined in the CICU to directly compare the gold-standard monitoring used in the hospital environment and the wearable system. Electrocardiogram metrics (heart and respiratory rates) and photoplethysmography metrics (blood oxygen saturation) were compared for accuracy and reliability.

Results:

High signal-quality waveform data was obtained from all the patients with easy data transfer into a cloud-based environment allowing for real-time remote monitoring (Figure A). We are still waiting on waveform data from the hospital to verify accuracy.

Conclusions:





The proposed flexible and wearable system successfully uses real-time health assessments and automated notification of patient-specific abnormalities. The cloud-based processing and storage of data allow for improved communication between the caretaker and clinician and long-term pattern recognition, further improving the patient's healthcare. Following the clinical study, we can compare the ease of use and user preference for at-home interstage monitoring.

Poster Abstracts

Listed in Alphabetical Order by Presenting Author

Investigating the Association Between Proband ASD Affectedness and Younger Sibling Social Visual Engagement Across the First Three Years of Development

Presenting Author: Motunrola Adebogun, B.A.; Emory University

Poster Number: 96

Motunrola Adebogun, Warren Jones, Sarah Shultz, Ami Klin, Cheryl Klaiman, Stormi White

Background: ASD is a highly heritable neurodevelopmental condition. One in 3 to 5 younger siblings of individuals with ASD (probands) also receive an ASD diagnosis by the age of three (McDonald et al., 2020; Ozonoff et al., 2011). A recent study by Girault et al. (2022) linked early brain MRI phenotypes of ASD in younger siblings with proband ASD traits, representing one approach to investigate inherited genetic liability in ASD. Previous research identifies social visual engagement as a neurodevelopmental endophenotype for ASD and suggests patterns of social visual engagement are highly heritable (Constantino et al., 2017). However, social visual engagement has yet to be leveraged in studying the heritability of ASD traits within families.

Methods: With a sample of 167 proband-sibling pairs, the association between proband ASD affectedness—as indicated by scores on the Social Communication Questionnaire (SCQ)—and social visual engagement in younger siblings was examined. Eye percent fixation, calculated using data collected from eye-tracking sessions, was used to index younger siblings' social visual engagement. Linear regressions tested the predictive power of probands' SCQ scores on younger siblings' eye fixation at 2, 3, 4, 5, 6, 9, 12, 15, 18, 21, 24, and 30 months.

Results: Analyses indicate probands' SCQ scores have differential predictability for younger siblings' eye fixation from 9 to 24 months depending on siblings' diagnostic outcome. Probands' SCQ scores negatively predicted eye percent fixation for younger siblings later diagnosed with ASD at months 9 ($r = -.54$, $n=21$, $p=.001$), 15 ($r = -.62$, $n=22$, $p=.004$), 18 ($r = -.82$, $n=13$, $p<.001$), and 24 ($r = -.61$, $n=10$, $p=.04$). In contrast, for siblings who were later diagnosed as unaffected, proband SCQ scores positively predicted their eye percent fixation at months 9 ($r = .88$, $n=12$, $p<.001$), 12 ($r = .56$, $n=17$, $p=.006$), 21 ($r = .66$, $n=5$, $p=.02$), and 24 ($r = .79$, $n=8$, $p=.005$).

Conclusions: Analyses demonstrate that ASD affectedness in probands correlate differentially with eye fixation trajectories between unaffected siblings and younger siblings later diagnosed with ASD. These findings, which further the understanding of familial ASD traits, provide a foundation upon which researchers can build to identify early markers of inherited genetic predisposition to ASD at different time points in development.

Assembly of BSA Nanoparticles for Brain Targeted Delivery of Oxytocin using the Microfluidics system.

Presenting Author: Emmanuel Adediran, B.PHARM, PhD(in view); Mercer University

Poster Number: 1



Emmanuel, Adediran; Sharon, Vijayanand; Akanksha, Kale; Andrew, Escayg; Jennifer, Wong; Kevin, Murnane; and Martin J. D'Souza

Epilepsy is a central nervous system disorder that causes a sudden, uncontrolled electrical disturbance in the brain characterized by a change in behavior, feeling and state of consciousness. Providentially, oxytocin, a form of neuropeptide, has been identified in the treatment and management of seizures. However, its therapeutic potential is limited because it does not readily cross the blood-brain barrier due to its hydrophilic nature, large size, and short half-life. Herein, we hypothesize that encapsulation of oxytocin in polymeric nanoparticles using the microfluidics system should achieve sustained delivery of oxytocin to the brain.

We use an albumin matrix to encapsulate the oxytocin into nanoparticles using a nanoprecipitation method. The nanoparticles are formulated using a 5-input microfluidics chip, cross-linked, and tagged with Rabies virus glycoprotein (RVG) for enabling brain-targeted delivery. The formulation was optimized by investigating the effect of process parameters such as flow rate ratio, total flow rate, and temperature and polymer concentration on the size, and PDI of the nanoparticles. The final nanoparticle formulation was lyophilized and characterized for its size, PDI using a dynamic light scattering (DLS) particle size analyzer. Furthermore, the content analysis and the release profile were assessed using an oxytocin ELISA kit. Next, the cytotoxicity of the nanoparticles was investigated using a cell-based assay.

The sizes of the nanoparticles assembled by this microfluidics system were between 57 nm-75 nm with a PDI of less than 0.3. The optimum flow rate ratio of the aqueous phase to the organic phase was found to be 1:1.5. The smaller the flow rate ratio, the smaller the size. Moreover, the encapsulation efficiency of the oxytocin in the BSA particles was >80% w/w. Interestingly, 50 % w/w of oxytocin was released from the nanoparticles over six days. The sizes of the nanoparticles increase with an increase in polymer concentration. The nanoparticles were also found to be non-cytotoxic to cells.

Conclusively, the polymeric nanoparticles of less than 100 nm were successfully formulated using the microfluidics system in a reliable and reproducible manner. The small size and release profile are desirable for sustained delivery of oxytocin to the brain.

Case Report- Identical Twins with Hiatal Hernias

Presenting Author: Lujain al Omari, MD; University of Texas Medical Branch

Poster Number: 82

Al-Omari, Lujain; Williams, Maegan; Jain, Sunil; and Franco Fuenmayor, Maria

Background:

Hiatal hernias (HH) are diaphragmatic hernias in which abdominal organs protrude through the esophageal hiatus of the diaphragm into the posterior mediastinum. HH in infants are sporadic and rare. Preterm monochorionic-monoamniotic twins with recurrent emesis had inconclusive radiographs with contrast study consistent with HH.



Methods:

Contrast swallow study was performed to diagnose hiatal hernias.

Results:

Hiatal hernia was diagnosed using contrast swallow study.

Conclusions:

Early diagnosis and treatment of hiatal hernias are essential to prevent severe complications. Complications include severe reflux, chronic gastritis, Barrett's esophagus, lower esophageal stenosis and volvulus. Radio contrast swallow study is the gold standard for diagnosis.

Incidence of Prematurity Comorbidities After Discontinuation of Prophylactic Indomethacin

Presenting Author: Lujain al Omari, MD; University of Texas Medical Branch

Poster Number: 83

Al-Omari, Lujain; Wheatley, Darrin; Franco Fuenmayor, Maria

Background:

Prophylactic Indomethacin (PI) was previously commonly used to treat patent ductus arteriosus (PDA) and intraventricular hemorrhage (IVH). It is not as effective in treating NEC and bronchopulmonary dysplasia (BPD). Adverse effects include oliguria, elevated creatinine (Cr) levels, necrotizing enterocolitis (NEC), and spontaneous intestinal perforation (SIP). Recent evidence regarding efficacy for IVH as well as the desire to implement alternative therapies for BPD and PDA led to discontinuation of PI use in our NICU.

Objective:

We compared the incidence of BPD, PDA and IVH for infants born at $\leq 1250g$ before and after PI discontinuation.

Methods:

We retrospectively reviewed 118 charts of infants born at $\leq 1250g$ who were admitted to our NICU from 1/2020 to 8/2022. Infants were divided into 2 epochs: PI (1/2020-7/2021) and post-PI discontinuation (8/2021-8/2022). Incidence of disease outcome and side effects was analyzed using SPSS.

Results:

118 infants were born during the 2 epochs- 68 received PI and 50 did not. Infants in epoch 1 had an average gestational age 25 ± 1.8 weeks vs 28.8 ± 2.1 ($p=0.305$) in epoch 2, and birthweight $772g \pm 191$ vs $1061.6g \pm 192$ ($p=0.130$). In epoch 1, the incidence of IVH was significantly higher at 41% vs 24% ($p=0.008$) despite PI discontinuation. Severity of IVH, incidence of PDA and BPD, PI adverse effects, and postnatal steroids, are denoted in Table 1. The incidence of PDA significantly increased from 31% to



52% post-PI discontinuation ($p=0.05$). More infants received medical treatment of PDA during epoch 2. However, of those treated, only 2 weren't diagnosed with BPD. Despite practice changes, the incidence of BPD was not significantly affected, including the use of postnatal steroids and home oxygen, similar to what previous studies have shown: PI reduces incidence of PDA and severe IVH but doesn't improve BPD outcomes significantly.

Conclusions:

PI is associated with lower rates of PDA, higher rates of overall IVH and no significant effect on BPD incidence, dexamethasone use for BPD and need for home oxygen support. Infants exposed to PI had higher Cr levels but similar rates of NEC and SIP. There were no adverse outcomes related to the practice change, though our sample size is small.

The Effect of Maternal von Willebrand's Disease on Neonates

Presenting Author: Lujain al Omari, MD; University of Texas Medical Branch

Poster Number: 84

Al-Omari, Lujain; Stranberg, Adam; and Jain, Sunil

Background:

Hyponatremia is commonly seen among neonates who are very ill or low birth weight. Neonatal hyponatremia is often asymptomatic, unless plasma sodium concentration decreases rapidly. We present a case of severe neonatal hyponatremia in an infant born to a mother with von Willebrand Disease (VWD) treated with 1-deamino-8-D-arginin-vasopressin (DDAVP).

Methods:

The infant's routine NICU labs at 10 hours of life showed severe hyponatremia (122 mmol/L). We explored possible causes of hyponatremia; urine osmolality, urine sodium and potassium levels were checked to evaluate mineralocorticoid deficiency and renal tubular dysfunction. All three values were normal. Serial urine labs remained normal, making the diagnosis of mineralocorticoid deficiency unlikely. Serial serum urea and creatinine levels were normal, decreasing the likelihood of renal failure. Inappropriate antidiuretic hormone secretion was considered, but urine output over the first 4 days of life remained normal.

Results:

After ruling out routine causes of hyponatremia, maternal serum sodium level was checked which showed severe hyponatremia (122 mmol/L), identical to the infant's serum sodium level. Given the normal urine sodium and normal serum BUN and creatinine, it is possible that there was a sodium shift from the fetus to the mother due to low maternal sodium secondary to DDAVP. The infant's fluid intake was restricted to 60 mL/kg/day and the infant's serial serum sodium levels were monitored. Gradually, serum sodium levels increased and normalized by day 4 of life.



Conclusion:

We presented a case of neonatal hyponatremia induced by maternal use of DDAVP during pregnancy. The effect of DDAVP on fetal sodium level is less likely crossing the placenta and acting on fetal DDAVP receptors. Rather, it is more likely caused by osmotic equilibration of sodium levels across the placenta. Our report emphasizes the importance of monitoring electrolytes in neonates born to mothers treated with DDAVP during pregnancy to correct electrolyte abnormalities quickly.

Risk Factors for Adverse Events Among the Norwood Patients: A Single Center Retrospective Study.

Presenting Author: Alaa Aljiffry, MD; Emory University school of medicine

Poster Number: 46

Alaa Aljiffry, MD1,2; Michelle E. Gleason, MPH1; Nikolay Braykov BS MS 1; Nicole Coolidge, MSN, RN, CPNP-AC, FNP-C1; Tawanda Zinyandu, MD MPH1; Sherry Smith, RN1; Nikhil Chanani, MD1,2; Subhadra Shashidharan, MD1,2

Introduction: Univentricular patients post Norwood palliation are at high risk for mortality and morbidity. Post-Norwood palliation mortality has been described as high as 10–15%. At the same time, post Norwood extracorporeal membrane oxygenation (ECMO) incidence has been described as high as 20–40%. This study aimed to evaluate clinical factors associated with postoperative adverse outcomes after the Norwood palliation.

Methods: We retrospectively studied newborns with single ventricle physiology who underwent Norwood palliation between June 2016 and September 2022. Clinical data were analyzed using summary statistics and bivariate and multivariate logistic regressions to assess the likelihood of adverse interstage outcomes following the Norwood palliation. Adverse outcomes were defined as any patient that had postoperative mortality, excessive length of stay (LOS) ≥ 55 days, heart transplant, and ECMO support. Variables that were significant in the bivariate comparison were assessed in the multivariate logistic regression, in addition to low birth weight and age at Norwood palliation, which was found to be significant in prior studies examining mortality.

Results: During the study period, 127 patients underwent Norwood palliation, of which 59 (46%) had an adverse outcome.

In a bivariate logistic regression analysis, black race (OR = 2.1; $p = 0.026$), postoperative respiratory complications (OR = 16.6; $p < 0.001$), and unplanned reinterventions (OR = 22.4; $p < 0.001$), postoperative neurological complications (OR=16.5, $p < 0.001$), sepsis (OR = 16.5, $p < 0.001$), renal failure ($p = 0.004$), cardiac arrest (OR=8.3; $p < 0.001$) and percentage of the length of stay on respiratory support (OR=1.05; $p < 0.001$) were significantly associated with an adverse outcome.

Risk factors with significant bivariable results in addition to low birth weight and age at Norwood palliation were included in the final model for multivariable regression; experiencing an adverse outcome was significantly associated with race (aOR = 5.1; $p = 0.049$), postoperative respiratory complications (aOR = 17.1; $p < 0.001$), and unplanned reinterventions (aOR = 9.5; $p < 0.001$).





Among Norwood patients with postoperative mortality, the median length of stay was substantially higher but not statistically significant ($P=0.085$).

Conclusions: Patients who are black, experience postoperative respiratory complications, and require unplanned reinterventions have higher odds of adverse outcomes post Norwood palliation.

Vpx and central polypurine tract synergistically enhance transduction efficiency, transduction kinetics, and protein expression of HIV-1 vector in human monocyte-derived macrophages

Presenting Author: Natalie Alvarez, Bachelor of Science; Emory University

Poster Number: 2

Alvarez, Natalie; and Kim, Baek

Background: Sterile alpha motif and histidine-aspartate domain containing protein 1 (SAMHD1) is a dNTPase known to limit dNTP pools in nondividing cells such as human monocyte-derived macrophages (MDMs). These low dNTP pools suppress HIV-1 reverse transcription kinetics in MDMs. However, Viral Protein X (Vpx), an accessory protein naturally found in Human Immunodeficiency Virus 2 (HIV-2) and some SIVs, degrades SAMHD1, thereby increasing dNTP pools, hence promoting permissive infection. Also, our previous study reported that the cPPT sequence facilitates the completion of HIV-1 reverse transcription especially when the reverse transcription step is kinetically delayed due to dNTP limitations in nondividing human lung fibroblasts. However, the role of cPPT during HIV-1 replication in macrophages, where SAMHD1 establishes low dNTP pools and kinetically restricts viral reverse transcription, remains unclear.

Methods: In order to test how SAMHD1 affects reverse transcriptase kinetics of an HIV-1 vector with an added cPPT, we conducted time-course analyses of 1) transduction efficiency and 2) protein expression/fluorescent intensity in MDMs transduced with HIV-GFP vector with and without cPPT in the presence and absence of the Vpx-VLP treatment.

Results and Conclusion: Our data demonstrate that while the addition of cPPT or Vpx alone increases in HIV-1 vector transduction efficiency in relatively small scales, both the cPPT and Vpx treatment together have a significant additive effect on transduction efficiency and fluorescence intensity (target protein expression levels) in the transduced MDMs. More importantly, the cPPT and Vpx treatment together significantly accelerated the kinetics of the HIV-1 vector transduction in MDMs. Our future direction involves quantitative real-time PCR assay to further elucidate how cPPT and Vpx together play a role in reverse transcription kinetics, and these results will be confirmed by employing a different type of HIV-1 vector system that already encodes its cPPT. Overall, our data demonstrate that the combination of cPPT and Vpx treatments synergistically enhances the HIV-1 vector transduction in nondividing MDMs, supporting a mechanistic interplay between cPPT and Vpx in MDMs.

Determining the Association of Hyperoxia while on Extracorporeal Life Support With Mortality in Neonates Following Norwood Operation





Presenting Author: Alan Amedi, BS; Emory University School of Medicine

Poster Number: 3

Alan Amedi, Ashley Harriott, Shayli Patel, Sean Evans, Amy Scheel, Yijin Xiang, Joel Davis, Amanda Harding, Subhadra Shashidharan, Alaa Aljiffry, David M. Kwiatkowski, Asaad G. Beshish

Background: Patients requiring extracorporeal life support (ECLS) due to cardiopulmonary failure are frequently exposed to supranormal blood oxygen tension (hyperoxia). There is limited data regarding the effects of hyperoxia in univentricular patients requiring ECLS following Norwood operation. We sought to evaluate the potential association of hyperoxia with inpatient mortality and other clinical outcomes among neonates requiring ECLS post-Norwood operation in a large volume center.

Method: Retrospective single-center study at an academic children's hospital. All neonates who required ECLS post-Norwood operation between January/2010 and December/2020 were included. Medical records were reviewed for patient characteristics, clinical variables, average partial arterial pressure of oxygen (PaO₂) during the first 48-hours of ECLS, and clinical outcomes. Analysis was performed using appropriate statistics with a significance level set at p=0.05.

Results: Sixty-five patients required ECLS post-Norwood. Using receiver operating characteristic (ROC) curve, mean PaO₂ of 182 mmHg in the first 48-hours on ECLS was determined to have the optimal discriminatory ability for mortality (sensitivity 68%, specificity 70%). Of the 65 patients, 52% had PaO₂>182 mmHg and were designated as hyperoxia-group. Patients in the hyperoxia-group had longer CPB-time (187 vs 165 minutes), shorter median duration from CICU arrival to ECLS-cannulation (13.28 vs 132.58 hours), higher serum lactate peri-ECLS-cannulation (14.55 vs 5.80), higher ECLS flows in the 1st 4-hours (152.68 vs 124.14), and higher mortality (77% vs 39%) (p<0.05). In the unadjusted analysis, using a derived cut-point, patients in the hyperoxia-group had 5.15-higher odds of mortality (p=0.003). However, this association was insignificant when adjusting for confounding variables (p=0.104). Using functional status scale, new morbidity (37.5% vs 21.1%) and unfavorable outcomes (12.5% vs 5.3%) was higher in the hyperoxia-group but did not reach statistical significance.

Conclusion: Neonates with hyperoxia (PaO₂>182 mmHg) during the first 48-hours of ECLS post-Norwood operation had 5-times higher odds of mortality in the unadjusted analysis, however, this was insignificant when adjusting for confounding variables. Patients in the hyperoxia-group had shorter duration from CICU arrival to ECLS-cannulation, higher serum lactate peri-ECLS-cannulation, and higher ECLS flows in the 1st 4-hours, (p<0.05). Multicenter evaluation of this modifiable risk-factor is imperative to improve the care of this high-risk cohort.

Executive Function Outcomes in School-Age Children with Congenital Heart Disease and Premature Birth

Presenting Author: Ishani Ammavajjala, Bachelor of Science (B.S.); Georgia State University

Poster Number: 97

Ammavajjala, Ishani; Winston, Molly; Lee, Susan McManus; and Ilardi, Dawn





Children diagnosed with congenital heart disease (CHD) are at-risk for neurodevelopmental differences, such as with executive functioning (EF; i.e., higher-order thinking, cognitive flexibility, planning). Separate studies have also consistently found that patients with premature birth demonstrate weak EF, which can impact behavior and school performance. Limited information is available about the combined risk of CHD and prematurity on EF. This study will explore EF in children with CHD alone and children with CHD born prematurely. It is hypothesized that children who are born prematurely with CHD will exhibit weaker EF skills than those with CHD alone.

A retrospective chart review included patients who completed a neuropsychological evaluation as part of the standard of care. Children between the ages of 4 and 18 (males = 17) were included if they had a diagnosis of CHD or CHD+prematurity (Pilot Sample: N=10 CHD, N=21 CHD+prematurity). A measure of child EF skills was included with a parent questionnaire: the Behavioral Rating Inventory of Executive Function, 2nd Edition (BRIEF-2). Preliminary analyses explored group differences in EF using independent samples t-tests. Additional analyses utilized Pearson correlations to explore the relationship between gestational age and EF. Final analyses will include more participants across both clinical groups.

Preliminary results indicate no significant differences in EF when comparing CHD to CHD+prematurity ($p > .121$). Qualitatively, the CHD+premature group shows weak EF, particularly in the Cognitive Regulation Index (CRI) of the BRIEF-2; however, analyses may be underpowered to detect significant differences in the pilot sample. There was a negative correlation between gestational age and the CRI ($p = .010$, $r = -.463$), such that lower gestational age is associated with poorer cognitive regulation.

Results from this pilot sample show lower gestational age confers additional risk for EF difficulties for children with a history of CHD. Significant differences between the CHD and CHD+prematurity populations are not observed in preliminary analyses. Final analyses will be updated with a larger sample. These findings help to elucidate neurodevelopmental outcomes for CHD+prematurity which can help to inform the clinical care of CHD patients.

PTGER4 - PGE2 Signaling Drives Expression of the Goblet Cell Marker Spink4 In Patient Derived Intestinal Organoids

Presenting Author: Murugadas Anbazhagan, PhD; Emory University

Poster Number: 72

Murugadas Anbazhagan, Jason Matthews, Subra Kugathasan

Background: PTGER4 has been genetically and functionally linked to Crohn's disease and intestinal repair, however the precise mechanisms are not fully understood. In the epithelium, PTGER4 is stimulated by prostaglandin E2 (PGE2) released by the mesenchymal stromal cells (MSC) to regulate differentiation of epithelial subtypes during repair. Here in, we modeled MSC-epithelial crosstalk using patient derived MSC, organoids, and with PGE2 stimulation to gain further insight into the molecular pathways involving PTGER4.



Methods: Rectal mucosal biopsies were obtained during colonoscopy from consented patients (non-IBD, CD and CD with perianal disease) at CHOA and immediately processed for organoid culturing. Rectal organoids were grown in Matrigel and Intesticult media. MSC were grown from rectal biopsies in alpha-MEM/PLA and the conditioned media used for PGE2 ELISA and organoid stimulation. Organoids were treated with 1 μ M PGE2 (and with various inhibitors) and subsequently harvested for RNA and protein extraction. Additionally, organoids were analyzed by immunofluorescence for marker gene expression.

Results: Analysis of MSC conditioned media from non-IBD and CD patients showed varying levels of PGE2 production, with most samples capable of inducing swelling when applied to patient organoids. These large cystic organoids could be phenocopied by the addition of PGE2, that showed a decrease in the levels of the stem cell marker Lgr5 but with an increase in levels of the goblet cell marker SPINK4. We observed consistent changes in the phosphorylation levels of HDAC4,5,7 and beta-catenin in patient derived organoids after PGE2 treatment and show that LMK-235 (HDAC4 inhibitor) and LB-100 (PP2A inhibitor) have patient specific effects on SPINK4 mRNA levels during PGE2 treatment. We observed notable differences in the levels of MUC-2 by immunofluorescence across patient organoids but did not observe an increase after PGE2 stimulation. Inhibition of gamma-secretase with DAPT during PGE2 treatment of organoids also increased SPINK4 mRNA levels.

Conclusion: We have uncovered additional evidence indicating PTGER4-PGE2 signals promote gene expression related to goblet cell differentiation. Our data shows a roll for PP2A, gamma-secretase and HDAC4 in regulating PTGER4-dependent SPINK4 expression, while also highlighting the molecular heterogeneity in patient response to PGE2 in PTGER4 signaling.

VALEROBETAINE IS A MICROBE-GENERATED METABOLITE THAT INFLUENCES THE GUT EPITHELIA

Presenting Author: Lauren Askew, BS; Emory University

Poster Number: 4

Lauren Askew, Anthony Gacasan, Andrew Neish, Rheinallt Jones

Background: A major impact of the microbiome on gut physiology is via the generation of bioactive metabolites and small molecules. In recent years, the realization that gut microbiota-generated metabolites can regulate signaling pathways in multiple organ systems has prompted interest in investigating the molecular mechanisms whereby these small molecules function. Employing advanced methodology to maintain axenic and gnotobiotic mice, and mass spectrometry-based metabolomics platforms for analysis of small molecules, our research group demonstrated remarkable differences in the metabolite composition of the mitochondria in germ-free and conventional mice. The most discriminatory metabolite generated by the microbiome was δ -valerobetaine (VB). Our previous studies showed that VB suppresses mitochondrial fatty acid oxidation in hepatic cells by decreasing cellular carnitine levels. We showed that VB is a central integrator whereby the microbiota influences host tissue energy metabolism. We hypothesize that VB can influence mitochondrial bioenergetics in cells within the intestinal epithelium, thereby impacting intestinal cell homeostasis and gut epithelia barrier integrity. **Methods:** Germ-free mice were treated intraperitoneally with VB or vehicle control and upon sacrifice, the colon and small intestine were removed. Swiss rolls were made from both colon and small





intestine and stained for proliferative and mitochondrial markers to assess the effect of VB on proliferation in the cell crypt and mitochondrial expansion. Furthermore, tissue samples were analyzed to assess whether VB alters the expression of markers of mitochondrial biogenesis markers and gut epithelial integrity. In addition, VB was administered to the media of Caco-2 cultured cells to determine the effect of VB on mitochondrial biogenesis. Results: Germ-free mice treated with 50uM of VB for 4 days had increased mitochondrial abundance (TOM20 staining) in the small intestine compared to vehicle treated control mice. Furthermore, VB treated germ-free mice had increased numbers of proliferating cells in the small intestinal crypts (quantifying Ki-67 positive cells). VB-treated mice also had a significantly higher expression of the regenerative stem cell markers Ly6A and Clu. Conclusions: Our results suggest that the novel microbiome-generated metabolite, VB, can induce mitochondrial biogenesis in the intestine, thereby implicating VB as an integrator of host cell and microbe interactions in intestinal epithelial homeostasis.

Factor VIII-specific T Follicular Helper (TFH) Cells Increase with Multiple Exposures to Factor VIII

Presenting Author: Deborah Baafi, Biology; Emory University

Poster Number: 98

Baafi, Deborah; McCoy W., James; Stowell R., Sean; Meeks L., Shannon; Patel R., Seema; Zerra E., Patricia

Hemophilia A is a bleeding disorder characterized by the absence or deficiency of the coagulation protein, factor VIII (FVIII). FVIII replacement products are the mainstay of treatment for bleeding episodes and the development of neutralizing anti-FVIII antibodies (inhibitors) represents a significant barrier to this therapy. Despite this, the immune factors that regulate anti-FVIII antibody formation remain incompletely understood.

We have previously shown that anti-FVIII antibody formation is a CD4+T cell-dependent process requiring multiple exposures to FVIII. This, combined with the knowledge that T follicular helper (TFH) cells facilitate long-lasting antibody formation, led us to hypothesize that FVIII-specific CD4+T cells proliferate upon multiple exposures to FVIII, with TFH cell expansion. An improved understanding of the overall timing of CD4+T cell activation in the immune response to FVIII is necessary for the development of strategies to prevent antibody formation.

To assess FVIII-specific CD4+T cell proliferation, we engineered FVIII-OVA, which contains the ovalbumin peptide recognized by OTII T cell receptor transgenic T cells. CFSE-labeled OTII splenocytes were transferred into mice with hemophilia A, followed by administration of FVIII-OVA. We observed that FVIII is unable to cause proliferation of CD4+T cells nor produce IgG antibodies following initial exposure, but instead significantly increases following the 3rd exposure to FVIII.

We next utilized a FVIII-specific MHC class II tetramer to further explore the kinetics of the CD4+T cell response and the other CD4+T cell subsets. B6 mice received 1-4 weekly doses of FVIII, followed by splenocyte evaluation by flow cytometry. B6 mice produce FVIII specific CD4+T cells that begin to proliferate and expand after 2 weekly injections of FVIII, with a significant increase following the 3rd



exposure. Additionally, FVIII-specific TFH cells expand after 2 doses of FVIII and increase with each subsequent exposure. Furthermore, anti-FVIII IgM formation peaks and anti-FVIII IgG formation begins after the 3rd FVIII exposure, at the time of CD4+T cell proliferation.

In summary, these findings suggest FVIII-specific CD4+T cell proliferation and antibody formation require 2-3 antigen exposures, and results in expansion of TFH cells. Our present findings and future work will help reveal important pathways to effectively target and prevent inhibitor production.

Intranasal gonorrhea vaccine elicits significant immune response in murine model

Presenting Author: Priyal Bagwe, B. Pharm; Vaccine Nanotechnology Laboratory, Center for Drug Delivery Research, Mercer University College of Pharmacy

Poster Number: 5

Bagwe P, Ferguson A, Zughaier S, D'Souza MJ

Background: Gonorrhea is a sexually transmitted disease (STD) caused by a bacteria named *Neisseria gonorrhoeae*. Gonorrhea is the second most prevalent STD in the United States, with it rapidly developing antibiotic resistance to many drugs that were used to treat it. There is currently no vaccine for gonorrhea. Testing in vivo immunogenicity of the whole cell inactivated gonococcal microparticulate vaccine for mucosal vaccination is the focus of this project. Methods: *Neisseria gonorrhoeae* was first grown and formalin inactivated. Then the formalin inactivated gonorrhea was encapsulated in a biodegradable pre-crosslinked albumin matrix. Then, using the Buchi mini spray dryer B-290, vaccine MP (Gc-MP) and adjuvant MP (Alum, AddaVax™ - analogue of MF59®) were created. Female mice were used to test this vaccine formulation's effectiveness in vivo. The mice received three intranasal vaccine doses: a primary dose followed by two booster doses which were given in two-week intervals. An indirect ELISA was used to measure the gonorrhea-specific total IgG, IgM, IgG1, and IgG2a levels in mice serum. After week 10 the mice were challenged intravaginally with live *Neisseria gonorrhoeae* following lower genital tract infection model. The rate of bacterial clearance and mucosal IgA levels were measured. Then at week 12, the mice were sacrificed, and their immune organs were isolated. By examining CD4+ and CD8+ markers from the spleen and lymph nodes, the T-cell immune response was evaluated. Results: When compared to the control group, ELISA found that the group receiving the adjuvanted gonorrhea vaccine had significantly greater total serum IgG, IgM, IgG1, and IgG2a levels. The immunized mice had a faster rate of clearance of the infection and significant mucosal IgA levels when compared to the control. The expression of CD4+ and CD8+ was also significantly greater in the lymph nodes and spleen of mice receiving the adjuvanted vaccine than in the control group. Conclusion: As a result, mucosal vaccination in mice promotes cellular and humoral immune reactions.

Investigation of MRD associated genes in pediatric T-ALL samples at diagnosis.

Presenting Author: Mojtaba Bakhtiari, MD; Emory University, School of Medicine

Poster Number: 73





Mojtaba Bakhtiari^{1,2}, Beena E. Thomas^{1,2}, Ryan J. Summers^{1,2}, Hope Mumme^{1,3}, William Pilcher⁴, Sunil S. Raikar^{1,2}, Sunita I. Park⁵, Sharon M. Castellino^{1,2}, Douglas K. Graham^{1,2}, Manoj K. Bhasin¹⁻⁴, Deborah DeRyckere^{1,2}, Swati S. Bhasin^{1,2}.

Background: T-Cell Acute Lymphoblastic Leukemia (T-ALL), characterized by the proliferation of immature T cells, accounts for ~15% of pediatric leukemias. Minimal residual disease (MRD) assessment after induction and consolidation phases is used to guide treatment decisions. Sustained MRD negativity (MRD-) has shown significant association with continuous remission while higher MRD burden (MRD+) is significantly associated with relapse and poor outcomes in T-ALL. Therefore, we have explored genes associated with MRD outcome in T-ALL bone marrows at diagnosis (Dx).

Methods: Single-cell RNA sequencing (scRNAseq) was performed on viably frozen bone marrow samples provided by the Aflac Leukemia and Lymphoma Biorepository at Children's Healthcare of Atlanta (CHOA) on ten pediatric T-ALL patients at Dx. The scRNAseq libraries were prepared using the 10X genomics Chromium single cell 3'v3 and 5'v1 reagent kits and sequencing was performed using massively parallel sequencing on the Novaseq S4 platform producing >20,000 reads per cell. The single cell count data was normalized using SC Transform function in Seurat v3.0 Bioconductor package.

Results: Out of the ten Dx samples, four were MRD+ and six MRD- after induction therapy. Differential gene expression analysis between the T-ALL blast cells at Dx, showed upregulation of genes such as LGALS1, ITGB1, HSH2D, and CLEC2B in patient samples that are MRD+ relative to those that are MRD-. Some of these genes are associated with chemoresistance, tumor survival, cell adhesion and immune response regulation. Signaling analysis between different cell types such as, NKs, DCs, B & T cells, Monocytes, Erythroid, and TALL blast cells, in the bone marrow microenvironment indicates greater interactions between the different cell types in the MRD- subset relative to MRD+ subset. These results suggest that the expression of select genes and signaling interactions in the T-ALL bone marrow at the time of diagnosis indicates association with MRD outcome.

Conclusion: Genes that are associated MRD can serve as prognostic/ therapeutic targets. By employing insights from systems biology analysis of pathways, networks, and cell-to-cell interactions between leukemia cells and other cells in the bone marrow microenvironment, a robust signature can be established at the time of diagnosis to predict future MRD.

Predictive Ability of Proband Autism Traits for Younger Sibling Traits and Diagnostic Outcomes in the First Two Years of Life

Presenting Author: Dorothy Balsler, BA; Emory University School of Medicine

Poster Number: 99

Kortanek, Eve; Balsler, Dorothy; White, Stormi; Klaiman, Cheryl; Jones, Warren; Klin, Ami; and Shultz, Sarah

Background: Younger siblings of autistic individuals are at elevated likelihood of receiving an autism diagnosis. Compared to the population prevalence of 2.8% (Maenner et al., 2023), ~20% of younger siblings receive an autism diagnosis (Ozonoff et al., 2011), suggesting a substantial genetic contribution





to autism. Girault et al. (2020) demonstrated that proband autism traits predict younger sibling diagnostic outcomes at 24 months but did not identify trait associations in sibling pairs. We aimed to replicate these findings and explore associations between sibling traits—both at and before 24 months—using additional autism assessments.

Methods: We assessed the predictive ability of proband Social Communication Questionnaire (SCQ) scores for younger sibling diagnostic outcomes, Autism Diagnostic Observation Schedule (ADOS) scores, and Mullen Scales of Early Learning (MSEL) scores at 24 months (N=87 sibling pairs). Additionally, we evaluated whether proband scores on the Social Responsiveness Scale (SRS) predicted younger sibling scores at 9, 12, and 18 months on the Early Screening for Autism and Communication Disorders (ESAC) (N=55 pairs), the Systematic Observation of Red Flags (SORF) (N=63 pairs), and the CSBS DP Infant-Toddler Checklist (ITC) (N=45 pairs). Logistic regression was used in the outcome analysis, and linear regression was used in all other analyses.

Results: Proband SCQ predicted younger sibling diagnostic outcomes (beta = .100, p = .007) as well as scores on the ADOS (beta = .249, p = .036) and MSEL (beta = -.261, p = .023) at 24 months. Further, proband SRS scores predicted younger sibling scores on the ESAC at 9 months (beta = .303, p = .027) but not 12 or 18 months (ps > .05).

Conclusions: We replicated Girault et al.'s (2020) finding that proband SCQ predicts younger sibling outcome at 24 months. Further, we found that proband SCQ predicts younger sibling ADOS and MSEL scores at 24 months. Proband RRB scores on the SRS also predicted early autism traits in younger siblings at 9 months but not 12 or 18 months. Our findings suggest that the genetic influence on autism traits may vary over developmental time and that proband profiles may inform optimal intervention approaches for younger siblings.

Cardiometabolic Risk in Children with Cerebral Palsy and its Relationship with Leptin

Presenting Author: Trevor Batson, MS; University of Georgia

Poster Number: 6

Batson, Trevor; Lee, Junsoo; Kindler, Joseph; and Modlesky, Christopher.

Background: Elevated cardiometabolic risk has been observed as early as childhood in those with cerebral palsy (CP). This risk includes increased rates of dyslipidemia and pre-diabetes and is related to elevated visceral adiposity. Adipose-tissue secreted hormones, such as leptin, are believed to be involved in the relationship between adiposity and cardiometabolic risk. However, this relationship has not been studied in children with CP.

Methods: Thirty ambulatory children with CP and 30 age-, sex-, and race-matched typically developing control children were tested for blood lipids, glucose, homeostatic model assessment of insulin resistance (HOMA-IR), and leptin. Total and visceral adiposity were assessed using dual-energy x-ray absorptiometry.



Results: There was no difference in BMI between groups ($p>0.05$), and children with CP had significantly higher fat-mass index (FMI) and visceral fat-mass index (VFMI) than controls (both $p<0.05$). Children with CP had higher leptin than controls ($p<0.05$). When leptin's relationship with adiposity and biochemical markers of cardiometabolic risk was examined, no group interactions were detected (all $p>0.05$); therefore, relationships were analyzed in both groups combined ($n = 60$). Leptin was positively related to BMI, FMI, and VFMI (r range = 0.611 to 0.914, all $p<0.001$). Leptin was also positively related to non-HDL-C, glucose, and HOMA-IR (r range = 0.335 to 0.704, all $p<0.05$). Moreover, leptin remained a significant predictor of glucose and HOMA-IR when BMI, FMI, or VFMI were included in the model (all $p<0.05$). Conversely, BMI and FMI were not significant predictors of any biochemical marker when leptin was included in the model (all $p>0.05$), and VFMI remained a significant predictor of HOMA-IR only ($p<0.05$).

Conclusions: Children with CP have higher circulating leptin than age-, sex- and race-matched typically developing control children which is related to their elevated total and visceral adiposity. Additionally, leptin is related to dyslipidemia and pre-diabetes in children with CP. Hyperleptinemia at least partly mediates the relationship between adiposity and cardiometabolic risk. Further investigation into the potentially adverse effect of leptin on other cardiometabolic risk factors and interventions to attenuate the effect in children with CP is warranted.

Caregiver Reflections on Participating in Early Autism Research

Presenting Author: Cynthia Belfleur, Psychology BA; Emory University

Poster Number: 100

Belfleur, Cynthia; Dunlevy, Megan; Shultz, Sarah; and Pickard, Katherine

Background:

Although early access to therapeutic services can support the quality of life of autistic individuals and their families, the average age of autism diagnosis is 52 months (Maenner et al., 2021). To expedite access to diagnosis and services, autism research has expanded to understand infant development using baby-sibling study designs. However, this research has yet to explore caregiver perspectives regarding participating in baby sibling research aimed at identifying early biomarkers of autism. Addressing this limitation will help align research with the goals of families and communities and considers the barriers to care. The current study retrospectively examines the motivation, challenges, and impact of developmental monitoring on caregivers' perception of their child's development.

Methods:

This study includes a sample drawn from 482 caregivers of children ages 0-3 years who participated in baby-sibling research that studies infant development. Participants will complete a survey to obtain demographic information, information on service utilization, and involvement in other research studies. After completing the survey, caregivers will participate in focus groups to explore how the previous study connects to their lived experiences, how participating aided in supporting their child's development, and what support systems they used when completing the studies. Rapid debriefing will





occur after each focus group, followed by thematic analysis to summarize primary themes related to study participation.

Results:

Data collection is ongoing, with an anticipated end by June 2023. We hypothesize that participants' perspectives will vary depending on their level of concern for their child's development, the amount of participation the caregivers had in the previous baby-sibling study, the burden of the study on their family, and whether an autism diagnosis was received.

Conclusion:

Caregivers' perspectives will allow early autism research protocols to address caregiver and family needs. Understanding what motivates families to participate in research will help to align research efforts with the priorities of families. Understanding the challenges experienced by families may help researchers reduce attrition. Knowing families' understanding of autism and how feedback is received will allow for more responsive methods to support families to achieve better outcomes for autistic individuals.

Sugar-sweetened beverage consumption and glycemic control in cystic fibrosis

Presenting Author: Lauren Bloom, MD; Emory University

Poster Number: 60

Bloom, Lauren; Wang, Yifei; Bai, Shasha; Du, Chenxi; Jones, Kymry; McNeany, Jocelyn; Ziegler, Thomas; Driggers, Chris; Daley, Tanicia; Freeman, A Jay; Stecenko, Arlene; and Alvarez, Jessica

Background: Cystic fibrosis-related diabetes (CFRD) is associated with an increase in morbidity and mortality with its genesis in early childhood. This study aimed to assess measures of glycemic control and determine their associations with SSB consumption and other carbohydrate intake variables in children with CF.

Methods: This is an ongoing, prospective study of CF patients, ages 6-18 years. Glucose tolerance status (normal (NGT) vs. abnormal glucose tolerance (AGT)), insulin secretion (Insulinogenic Index), whole body insulin sensitivity, and a corresponding disposition index were determined from oral glucose tolerance testing (OGTT). Dietary intake was assessed using a validated BEVQ-15 questionnaire and 24-hour recalls for assessment of dietary macronutrients and glycemic index. Glucose tolerance groups were compared using Kruskal-Wallis or Fisher's exact tests. Spearman correlations and multiple linear regression analyses were used to quantify the relationships between SSB intake, dietary variables, and glycemic outcomes.

Results: 44 children with CF were enrolled. Based on OGTT, 21 participants had normal glucose tolerance, 18 had impaired glucose tolerance, 2 had CFRD, and 3 were indeterminate. Demographic characteristics did not differ between the NGT and AGT groups. The insulinogenic index and oral disposition index were significantly lower in those with AGT compared to NGT ($p = 0.004$ and 0.015 ,



respectively). Other measures of glycemia did not significantly differ between NGT and AGT groups. Participants reported a mean daily intake of 18.26 oz of SSB, with no significant difference between those with NGT and AGT. SSB intake was not associated with any glucose tolerance outcomes when adjusted for age. Dietary recalls showed a positive association between glycemic index and 2-hour glucose levels ($r = 1.336$, $p = 0.002$) and HOMA-IR ($r = 0.022$, $p = 0.026$). Other dietary variables did not significantly correlate with glycemic outcomes.

Conclusions: We found a significant difference in dynamic insulin secretion between pediatric patients with CF with AGT compared to NGT. Among the dietary variables assessed, only higher dietary glycemic index was associated with higher 2-hour glucose and increased insulin resistance. Longitudinal studies of larger cohorts are required to better understand the association between dietary intake and glycemic control in children with CF.

Creation and Characterization of SARS-CoV-2 Variant Testing Panels Using Remnant Clinical Samples For Diagnostic Assay Testing.

Presenting Author: Heather Bowers, Bachelor of Science - Biochemistry; Emory University

Poster Number: 47

Heather. B. Bowers, Morgan Greenleaf, Courtney Sabino, Eric Lai, Grace Yu, Anne Piantadosi, Ethan Wang, William O'Sick, Kaleb McLendon, Julie A. Sullivan, Gregory L. Damhorst, Wilbur Lam, Leda Bassit, Anuradha Rao

Soon after the first appearance of SARS-CoV-2, the need for rapid, accurate, and widely available testing quickly became apparent. As a part of the NIH's Rapid Acceleration of Diagnostics program (RADx), the analytical team at Emory was tasked with verifying SARS-CoV-2 rapid detection tests for accuracy and sensitivity. This need deepened when the virus began mutating and it was unknown how well current tests performed against these rapidly arising new variants. To help evaluate current as well as developing SARS-CoV-2 detection kits, a uniform testing panel is created using the clinical samples that remain after initial testing. Here, after extensive quality control, remnant clinical samples (RCS) of known lineage are pooled together, serially diluted, blinded (to eliminate bias for visually read tests), and used for analytical testing. As a new variant gains dominance across the country, a new panel is created using RCS of that lineage and used for test verification. By creating these uniform panels, tests can be directly compared to one another allowing for determination of how well each test was performing against each other and if there was any detection difference between the previous and current variants. Using RCS enables us to prepare panels rapidly, such that tests can be evaluated concurrent with variant appearance. This data is crucial in ensuring that the SARS-CoV-2 rapid tests on the market, and those in development can detect the newest variant accurately. Three years into the pandemic, it has become clear how essential rapid detection tests are for preventing spread of pathogens, especially now that so many young children are back in school full-time. Knowledge gained from panel-making and testing techniques is also being implemented to evaluate rapid tests that detect other pathogens such as Influenza A, Influenza B, RSV, and Monkeypox.



Leveraging International Partnerships Among Stakeholders to Enhance Early Childhood Development

Presenting Author: Susan Brasher, PhD, MSN, BSN; Emory University Nell Hodgson Woodruff School of Nursing

Poster Number: 49

Brasher, Susan; Getachew Hailu, Selam; Cranmer, John; Gebremariam Gobezeayehu, Abebe; Becklenberg, Amy; Hall-Clifford, Rachel; Biza, Heran; Shiferaw, Meseret; Stapel-Wax, Jennifer; Darcy Mahoney, Ashley

Background

Ethiopia ranks among the top 10 nations globally for number of children under the age of five with a developmental disability (DD), including neurodevelopmental disability (NDD). Factors increasing the risk of DD and ND in Ethiopia include malnutrition, poverty, and limited primary prevention. Early language interactions between caregivers and young children are strongly associated with enhanced language and cognitive development. Affordable and accessible interventions aimed at supporting early language environments, particularly in Low-Income Countries (LICs), have the potential to improve developmental and health outcomes. Talk With Me Baby (TWMB) is a universal design, public-action strategy that increases early language interactions with demonstrated successful implementation in low- and middle-income U.S. regions. The purpose of this study was to leverage existing partnerships to gain insight on ways to linguistically and culturally tailor TWMB to be implemented in Ethiopia.

Methods

This project builds from established partnerships with the Ethiopian MOH that have spanned more than a decade in support of the government's maternal, neonatal, child health and nutrition intervention efforts. Using a community-based participatory research (CBPR) approach, our team of U.S and Ethiopian stakeholders built capacity among Ethiopian professionals in community, clinical and academic settings on ways to enhance neurodevelopment. Key informant interviews with stakeholders in Ethiopia were conducted (n= 3). A team of U.S. and Ethiopian clinicians and researchers (n=10) culturally and linguistically adapted TWMB and held virtual trainings in Ethiopia among pediatricians, psychologists, and nurses (n=14). Focus groups were then conducted to gain insight into future implementation (n=14).

Results

Semi-structured interviews and focus groups provided insight to the adoptability and acceptability of TWMB. Complementary materials to support implementation were co-created in Amharic, including (a) training manual, (b) training videos, (c) visual aids (posters, brochures), (d) facilitator guide, and (e) strategies to embed TWMB into routine care.

Conclusions

This study was a pivotal step in preparing TWMB to be implemented in Ethiopia in an effort to promote affordable and accessible ways to promote neurodevelopment in LICs. By culturally and linguistically adapting TWMB, our findings are readily poised for implementation as well as adaptation in similar global contexts.





Leveraging Interdisciplinary Partnerships within Hospital Systems to Improve the Language Environments of Infants in the Neonatal Intensive Care Unit

Presenting Author: Susan Brasher, PhD, MSN, BSN; Emory University Nell Hodgson Woodruff School of Nursing

Poster Number: 48

Brasher, Susan; Nelson, Jennifer; Becklenberg, Amy; Stapel-Wax, Jennifer

Background:

Early language exposure and rich social interactions play a significant role in brain development. The first 1,000 days of a child's life have been identified as a critical time of rapid brain growth and development. Considering how language is shaped by the surrounding environment, it is important to enhance the language environments of the most vulnerable infants, those in the Neonatal Intensive Care Unit (NICU) who face increased developmental risk. The purpose of this study was to engage Registered Nurses (RNs) and Allied Health Professionals (AHPs) on ways to implement an early language program, Talk With Me Baby (TWMB), in the NICU.

Methods:

This study was guided by the Practical Robust Implementation and Sustainability Model (PRISM) to examine the program (intervention), external environment, implementation and sustainability infrastructure, and recipients. This model examines how these variables interact to impact the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) of a program (intervention). Recipients received the TWMB training followed by breakout sessions to model skills. A qualitative descriptive design was utilized to identify contextual factors that enhanced TWMB implementation in the NICU. Four focus groups of RNs and AHPs (n=31) were conducted. Focus groups were audio recorded, transcribed, and thematic analysis was guided by the RE-AIM model.

Results:

Participants identified ways to enhance early language exposure through TWMB in the NICU, including tailoring approaches to behavioral and stress cues, education for parents, coupling language with routine care, professional characteristics, organizational characteristics, and the current state of local NICU readiness to implement TWMB. Results inform important next steps for future reach, effectiveness, adoption, implementation, and maintenance of TWMB.

Conclusions:

RNs and AHPs play a vital role in providing early language and social interaction to infants in the NICU. Such interdisciplinary collaboration has the potential to improve quality of care to NICU infants by building a collaborative and nurturing early language and social environment. By utilizing the concepts of TWMB, RNs and AHPs can educate and train families to provide rich language opportunities for their



infant, which has the potential to provide an equitable foundation of language exposure for the most vulnerable infants.

HIV-Exposed Uninfected Infants: Role of Extracellular Vesicles at the Maternal-Fetal Interface

Presenting Author: Dara Brena, M.S.; Morehouse School of Medicine

NIH/NICHD R01HD097843, NIH/NIMHD/RCMI 2U54MD007602-31A1, NIH/RCMI U54 Pilot grant

Poster Number: 7

Brena, Dara; Huang, Ming-Bo; Thompson, Nia; Bond, Vincent C.; Johnson, Erica L.

Background/Significance: HIV-Exposed Uninfected (HEU) infants have a 3.9-fold greater risk for infectious-based mortality as compared to unexposed infants. While the exact etiology for the clinical burden HEU infants face is unknown, abnormalities in their innate immune system coincide strongly with a clinical window of vulnerability to infectious pathogens. Extracellular vesicles (EV) are key mediators of maternal-fetal networking, known to propagate HIV pathogenic immune alterations, and contributory in various pregnancy complications and pregnancy-associated diseases. In this study, we aim to optimize a protocol for EV isolation at the maternal-fetal interface and characterize their cargo.

Methods: With written informed consent, maternal blood and placenta will be obtained from HIV-infected and uninfected pregnant women recruited from Grady Memorial and Emory University Midtown Hospital in Atlanta, GA. Clinical samples will be processed for plasma and primary trophoblast cells. Cells will be exposed to HIV and different regimens of antiretroviral drugs. We will develop and optimize a protocol to isolate EVs from maternal plasma and placental cells. Nanoparticle tracking analysis and western blots (CD63, TSG101, APOB, Albumin, and HIV p24) will be used to validate the EV fractions. EV pro-inflammatory cargo will be characterized through a multiplex ELISA.

Results: EVs derived from maternal plasma and placental cells will be isolated and purified through an optimized protocol of iodixanol density gradient ultracentrifugation. We intend to evaluate effective separation of EVs from HIV particles as well as minimize albumin and lipoprotein contamination. Comparisons of pro-inflammatory EV cargo could provide insights into the in utero HIV and ART mediated mechanisms that underly HEU fetal immune deficits.

Conclusions and Implications: This study seeks to address the knowledge gap for HEU infant morbidity and mortality. Within the landscape of precision-medicine, studying EV cargo could aid the identification of potential biomarkers and therapeutic targets to improve HEU infant clinical outcomes.

Surgical Excision versus Sclerotherapy for Pediatric Preauricular Cysts: A Scoping Review

Presenting Author: Ashley Catanzarite, BA; Medical College of Georgia AU/UGA Medical Partnership

Poster Number: 8

Catanzarite, Ashley; Arya, Priya; Matthews, Saria; Shah, Jay; and Govil, Nandini





Background

Preauricular cysts are common, benign congenital malformations that are often asymptomatic. More extensive treatment such as surgical excision is needed when cysts are complicated by discharge or infection. Preauricular cysts have a variable rate of recurrence, even after surgical excision, with studies reporting from 0% to 42% recurrence rates. There is a recent review analyzing recurrence and complication rates between two surgical techniques, however no studies have been conducted on sclerotherapy versus surgical excision in the pediatric population. This scoping review aims to analyze differences in long-term outcomes between the two procedures in pediatric patients with preauricular cysts.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Scoping Review (PRISMA-ScR) will be followed and selected databases will be searched. Publications that study pediatric preauricular cysts, surgical intervention, sclerotherapy treatment, and rates of recurrence and complications will be included. Two independent reviewers will screen the publications and analyze them. Discrepancies will be resolved by two additional reviewers.

Results

Data analysis is ongoing looking for differences in recurrence rates and complications between surgical intervention and sclerotherapy. Qualitative data including patient demographics, pathology-proven cyst type, and any pre-treatment performed will also be included in the analysis if available.

Conclusions

Pediatric preauricular cysts treated with surgical excision have a considerable recurrence rate. Newer treatments such as sclerotherapy may result in less recurrence and complications than surgical excision. This study will potentially elucidate the need for future research analyzing recurrence rates between the two interventions to further determine optimal treatment for pediatric preauricular cysts.

TikTok and Pediatric Cochlear Implants

Presenting Author: Ashley Catanzarite, BA; Medical College of Georgia AU/UGA Medical Partnership

Poster Number: 9

Catanzarite, Ashley; Matthews, Saria; Gowen, Erin; and Govil, Nandini

Background

TikTok is a significant source of entertainment for the public, and it has also become a major source of health information. Studies have analyzed TikTok videos about various diseases and treatments, however, pediatric cochlear implants have not been studied specifically. The term #cochlearimplants has 186.2 million views on TikTok, and the videos are produced from a wide variety of sources including patients, families, physicians, and companies. This study aims to examine the content, purpose,





engagement, quality, and reliability of pediatric cochlear implant TikTok videos to better understand the information that the public is consuming about pediatric cochlear implants.

Methods

The search on the TikTok application will be performed using the term #cochlearimplants. The search will be completed on a single day, and the top 100 videos portraying pediatric cochlear implants will be included. Non-English videos, advertisements, and repeated videos will be excluded. One reviewer will analyze and categorize the content of the videos including author, content, purpose, and engagement. Two reviewers with doctorate level degrees and expertise in their fields will independently analyze the videos using the Patient Education Materials Assessment Tool for Audiovisual Materials (PEMA-A/V) criteria for understandability and actionability and the DISCERN criteria for reliability.

Results

Data analysis will look for differences in engagement with videos across authorship and content groups. Additionally, further data analysis will compare quality and accuracy of the videos rated using PEMA-A/V and DISCERN criteria across authorship and content groups.

Conclusions

The content, quality, and reliability of information about cochlear implants on TikTok is likely to show variability. This study will potentially highlight the need for providers of cochlear implants to engage with platforms such as TikTok to provide evidence-based and helpful content, as well as talk to their patients about what they have heard about cochlear implants on social media.

Characterization of the Placental Proteome during Congenital CMV Infection

Presenting Author: Rana Chakraborty, MD, DPhil; Mayo Clinic

Poster Number: 102

SK Farnan, Sintim-Aboagye E, Lal S, Mejia-Plazas MC, Verma N, Littlefield D, Johnson EL, Rametse CL, Gray CM, Schleiss M, Norgan A, Robinson J, Enninga EAL, Chakraborty R

Background

The worldwide prevalence of cytomegalovirus (CMV) infection is estimated to be 83-100%.^{1,2} In pregnancy, transmission to the fetus can occur through the placenta with 0.4-2.3% of all newborns affected.³ The phenotype of congenital CMV (cCMV) has a spectrum of severity, with 10-20% of exposed neonates exhibiting severe clinical manifestations.⁴ HCMV has a wide range of tropism and can infect epithelial, myeloid, and endothelial cells. However, the cellular mechanisms of fetal CMV infection across the placenta are not yet fully delineated,⁵ and how these influence disease severity in exposed fetuses during gestation. Here, we used the NanoString™ Digital Spatial Profiler (DSP) to characterize the cell-specific proteomic profile in placental tissue from infants with cCMV.

Methods





Placental tissue from 5 CMV-affected and 4 CMV-unaffected pregnancies were retrieved from the Mayo Clinic tissue repository. Immune cells were identified by CD45 positivity and cytotrophoblasts (CTBs) identified by CK7. The cell-specific proteome of these tissues was identified using the NanoString™ immune cell and cell death panels. Data was analyzed by NanoString™ GeoMx technology.

Results

Unsupervised clustering illustrated a distinct proteome in the immune cell compartment of CMV-positive compared to CMV-negative placental tissue (Figure 1). Linear Mixed Model (LMM) analysis revealed that immune cell related proteins were significantly overexpressed in CMV-positive tissue as were four proteins associated with cell death: BIM, BCLXL, PARP, neurofibromin (Figure 2).

Clustering did not demonstrate a distinct proteome in the CTB compartment (Figure 3), but LMM analysis illustrated that two immune markers (CD44 and HLA-DR) and one cell death protein (BCL6) were overexpressed by CTBs in CMV positive tissue (Figure 4).

Conclusions

The proteome of immune cells, and to a lesser extent in CTBs in placentae from CMV-affected pregnancies differs from CMV-unaffected pregnancies with overexpression of proteins associated with immune activation and cell death. With new screening initiatives set to improve identification of cCMV, our results provide a starting point to identify specific biomarkers and immune pathways associated with disease severity. These biomarkers and pathways may also serve as novel antiviral targets in the treatment and management of cCMV.

Single cell transcriptomic mapping reveals altered neuroendocrine cell populations and defective chemosensory functions in the ileal mucosa from Crohn's tissue

Presenting Author: Bindu Chandrasekharan, PhD; Emory University

Poster Number: 103

Chandrasekharan, Bindu; Hwang, Yeonjoo; Maddipatla, Sushma C; Murthy, Shanta; Dodd, Anne; Kolachala, Vasantha; Gibson, Greg; Cutler, David J; Qiu, Peng; Matthews, Jason D; and Kugathasan, Subra.

Background: The neuroendocrine system (NES), composed of specialized epithelial cells (enteroendocrine cells, EEC) plays a central role as the chemo sensor of gut luminal contents by virtue of their 'neuropod' connections with intrinsic primary afferent innervation of the gut. In addition to antibacterial peptides and mucins, the EECs secrete a variety of gastrointestinal (GI) peptide hormones that regulate satiety, water and nutrient absorption, and GI motility for proper growth and development. Here we investigated the comparative effects of inflammation on NES by single cell transcriptomic mapping of the inflamed ileum from CD patients. Methods: Ileal mucosal biopsies were collected from 14 consented CD patients (8 inflamed, 6 non-inflamed) during endoscopy at Children's



Healthcare of Atlanta. Samples were digested into single cells with cold protease before encapsulation with a 10x Chromium controller. After library preparation, sequencing was performed with the Illumina NovaSeq at 50k reads per cell. Reads were aligned to the human reference genome with Cell-Ranger and count matrices were analyzed with Seurat (v4.3.0) after filtering out low-quality cells. Clusters were manually annotated and PCA was performed on the non-inflamed and inflamed cells contributing to each cluster. Differential gene expression was performed using the Seurat findMarkers function. Results: Single cell analysis on 33,317 inflamed cells and 27,432 non-inflamed cells resulted in 30 cellular subtypes. Differential gene expression in the inflamed EEC (annotated based on markers viz Chromogranins A & B, Peptide YY, neurotensin, NeuroD1 and carboxypeptidase E) revealed enrichment of innate immune pathways including Interferon-inducible genes (IFI6, IFI27) and defensin A6 (DefA6). In addition, we observed downregulation of neurotensin, the peptide hormone that inhibits ileal motility to enhance digestion and nutrient reabsorption time. Conclusions: Single cell analysis of inflamed ileum in CD reveals inflammatory signatures that negatively impact nutrient absorptive functions, possibly due to enhanced ileal motility (or a diarrheal phenotype). This could partly explain the nutrient malabsorption and growth failure, which is a common feature in CD patients.

Assessing Provider-Reported Use of Evidence-Based Early Intervention Practices Within Georgia's State Funded Early Intervention System

Presenting Author: Emma Chatson, B.A.; Emory University School of Medicine

Poster Number: 104

Emma Chatson, Hannah Davies, Brooke Demetri, Millena Yohannes, Nicole Hendrix, Katherine Pickard

Background: Naturalistic developmental behavioral interventions (NDBIs) are considered a validated intervention approach for young autistic children and children who have an increased likelihood of being autistic (Tiede & Walton, 2019). The use of NDBIs has been popularized through family-centered care models in Early Intervention (EI) systems as NDBIs can be embedded within family routines and actively involve key family members (Aranbarri et al., 2021). Research is needed to understand the provider- and system-level factors that influence practices in community-based EI systems and to develop solutions for better implementation methods (Stahmer & Aarons, 2009; Stahmer et al., 2020).

Methods: One hundred EI providers (Mage=47.2 years, SD=12.55) participated in a survey examining: 1) demographic information including years of experience working within EI systems and with autistic children; 2) attitudes towards evidence-based practices; 3) perceived system-level organizational resources and supports; 4) provision of family-centered care practices; 5) delivery of NDBI strategies in their most recent session; and 6) level of experience with manualized NDBI programs. Descriptive statistics were used to examine provider-reported NDBI program competencies and strategy use; linear regression models were used to examine factors predicting NDBI use.

Results: On average, providers reported using developmental and behavioral NDBI strategies across 57.5% and 57.8% of their last session, respectively. Use of developmental and behavioral NDBI strategies in providers' most recent session were strongly correlated ($r = 0.84$; $p < 0.001$). Considering attitudes toward evidence-based practices, only provider openness to novel interventions was positively





associated with the use of developmental and behavioral NDBI strategies ($p < .001$). Provision of family-centered care practices was positively associated with NDBI strategy use ($p < .05$). Further, select provider demographics, openness to new interventions, and family-centered care practices accounted for 40.4% of the variance in developmental NDBI use.

Conclusion: Although NDBI strategy use was not predicted by provider experiences or perceived organizational support, provider openness to new interventions and reported delivery of family-centered practices predicted the reported use of NDBI strategies. Future directions include mixed methods data collection across and within EI systems to better understand NDBI use and ultimately facilitate NDBI implementation in community-based health systems.

The Role of SIX1 in the Pathogenesis of Pediatric Acute Leukemias

Presenting Author: Dongdong Chen, MS; Emory University

Poster Number: 105

Chen, Dongdong; Aumann, Waitman; Lavau, Catherine; Reese, Travis; Ford, Heide; and Wechsler, Daniel

Background: SIX1, a transcription factor of the Sine oculis homeobox family, is highly expressed during development, and its expression is silenced post-embryogenesis. SIX1 and its cofactor EYA2 are overexpressed in various solid tumors, and increased SIX1 expression predicts poor clinical outcomes. However, a role for SIX1 in leukemias has not been studied. Our previous studies identified SIX1 as a novel target gene in leukemias that harbor CALM-AF10 translocations, which are seen in 5-10% of T-ALL (T-cell acute lymphoblastic leukemia) and 1-2% of AML (acute myeloid leukemia) and which are characterized by increased HOXA gene expression. We performed next generation sequencing on CALM-AF10 transduced hematopoietic stem cells (HSCs) and murine CALM-AF10 leukemia cells treated with the CRM1 inhibitor Leptomycin B, which impairs CALM-AF10 binding to HOXA genes. We identified SIX1 as one of eleven differentially expressed genes, with the remaining 10 being HOXA genes. This study aims to evaluate the role of SIX1 in CALM-AF10 and other acute leukemias.

Methods: SIX1 gene and protein expression were assessed in CALM-AF10, Jurkat T-ALL and NOMO1 AML leukemia cell lines. SIX1 was overexpressed by retrovirally transducing SIX1 vectors into fetal liver HSCs (FL-HSCs) and immortalization was assessed using colony assays. SIX1 was knocked-down by lentivirally transducing shRNAs targeting SIX1 into CALM-AF10 leukemia cell lines. The effects of SIX1 knockdown and of an inhibitor of the SIX1/EYA2 interaction (compound 8430) on cell proliferation were assessed using Cell-Titer-Glo assays. The synergy between CRM1 Nuclear Export Inhibitor KPT-330 and 8430 was assessed using SynergyFinder2 <https://synergyfinder.fimm.fi/>.

Results: SIX1 gene and protein expression were increased in CALM-AF10 and Jurkat, but not NOMO1 or normal bone marrow cells. SIX1 overexpression in FL-HSCs was sufficient for immortalization. SIX1 knockdown in CALM-AF10 leukemia cells decreased cell proliferation. Additionally, compound 8430 decreased proliferation of CALM-AF10 and Jurkat cells, with limited effect on NOMO1 cells. The addition of KPT-330 to 8430 was synergistic in CALM-AF10 cells and, to a lesser degree, in Jurkat cells.



Conclusions: SIX1 plays a role in the pathogenesis of pediatric acute leukemias. Combination treatment with 8430 and KPT-330 may be a potential novel therapeutic approach for CALM-AF10 and other leukemias.

“I Get the Flavors and it Makes Me Love Vaping More:” How and Why Youth Users Modify Electronic Nicotine Delivery Systems

Presenting Author: Victoria Churchill, PhD, MPH; Morehouse School of Medicine

Poster Number: 74

Churchill, Victoria; Fairman, Robert; Brown, Devon; Massey, Zachary; Ashley, David; and Popova, Lucy

Background: Youth in the United States (US) are using electronic nicotine delivery systems (ENDS) at a high rate. Modifications to ENDS by youth can introduce additional health hazards which have not been previously considered. To better understand these risks, we need more information on what these modifications are, the motivations behind them, and the sources of information on modifications.

Methods: Utilizing a trained moderator, in 2020-2021, we conducted one-on-one interviews with 19 youth ENDS users aged 16-17 years old living in the US and analyzed their responses using a qualitative description approach.

Results: The most prominent modification was to the e-liquid; youth indicated that they mixed e-juices to create new flavors and added substances not intended for vaping, as well as illicit drugs such as cannabis and cocaine. Few youths from our sample were interested in achieving a specific nicotine level to vape, and modifications to the battery and coil/wick were less frequently mentioned. Some of these modifications were motivated by a desire to achieve specific experiences with their device. At other times, modifications were made due to necessity because of limited access to ENDS devices and supplies. YouTube and peers were the main sources of information about modifying.

Conclusions: Youth are making modifications that are both intended and unintended by the manufacturer. Adding illicit drugs and other substances not made for vaping is of particular concern. Understanding how youth modify ENDS and how that changes their use is important to guide regulatory policy intended to reduce harm to youth from ENDS use

Social and Educational Outcomes Among Adults with Congenital Heart Disease by Severity: A Report from the Congenital Heart Disease Project to Understand Lifelong Survivor Experience (CHD PULSE)

Presenting Author: J'Neka Claxton, MPH; Emory University

Poster Number: 106

Claxton, J'Neka S.; Velani, Romie N.; Ilardi, Dawn; Jacobs, Jeffrey; Knight, Jessica; McHugh, Kimberly E.; Dailey-Schwartz, Andrew; Anderson, Susan; Kuo, Krisy; Aldoss, Osamah; Canter, Charles; Gaitonde, Mansi; John, Anitha; Malikarjun, Gurumurthy H.; Mar





Background:

We aimed to compare social and educational outcomes among patients with history of intervention for congenital heart disease (CHD) vs. their siblings, and to determine whether these outcomes varied by CHD severity.

Methods:

Between 2021-2022, we performed a cross-sectional survey of adults with history of intervention for CHD at 8 centers of the Pediatric Cardiac Care Consortium, a large US-based registry of pediatric cardiac procedures. Survey questions assessed developmental concerns, highest educational level, income, financial stability, and marital status. Outcomes were compared between respondents with CHD (combined and by disease severity) and siblings, accounting for correlation. Individuals with chromosomal anomalies were excluded.

Results:

Respondents included 2190 with CHD and 221 siblings, with no differences between the groups by sex (female: 58% v 63%) or age (median: 31 v 31 years). Compared to siblings, individuals with CHD were less likely to report freedom from developmental concerns (75% v 86%, $p < 0.01$), less likely to complete college (60% vs 69%), $p=0.009$ and have income \geq \$75000 (36% v 46%, $p = 0.006$), but there were no significant differences in financial stability or marital status. By CHD severity, single ventricle patients had worse outcomes on all domains.

Conclusion:

Compared to their siblings, adults with CHD have a lower freedom from developmental concerns, and a lower academic and income attainment. This emphasizes that screening for social and educational barriers could potentially improve medical care delivery to patients with CHD.

Elexacaftor-tezacaftor-ivacaftor did not curtail sputum myeloperoxidase in a cohort of adults with cystic fibrosis

Presenting Author: Genoah Collins, MS in Chemistry; Emory University

Poster Number: 107

Collins, Genoah L.; Moncada-Giraldo, Diego; Cammarata-Mouchtouris, Alexandre; Tirouvanziam, Rabindra; and Chandler, Joshua D.

Introduction: Cystic fibrosis (CF) is a genetic disorder occurring from defects in the cystic fibrosis transmembrane conductance regulator (CFTR). People with cystic fibrosis (PwCF) develop chronic inflammation in the lungs associated with high luminal concentrations of myeloperoxidase (MPO), an enzyme highly abundant in neutrophils that produces the oxidant hypochlorous acid and has been correlated with lung structural damage in PwCF. Elexacaftor-tezacaftor-ivacaftor (ETI) improves lung function and longevity in PwCF but its impact on inflammation, including MPO abundance and activity, is not well understood. We investigated whether MPO activity and/or protein concentration were





differentially abundant in sputum from a cross-sectional cohort of adult PwCF taking ETI compared to PwCF who were not taking any modulator therapies.

Methods: Sputum donated from clinically stable PwCF between the ages of 21-66 (30.3 ± 8.6 ; $n=32$ specimens from 31 unique donors) was obtained from the Emory CF Biospecimen Registry. The frequency of F508del CFTR homozygosity in the clinically stable subjects was 50.0% and the male-to-female ratio was 19:13. Additional samples from $n=11$ donors between the ages of 22-42 (30.5 ± 6.3 ; F508del homozygosity 27.3%; male-to-female ratio 6:5) experiencing acute pulmonary exacerbations (APEs) were also collected. Activity and abundance of MPO were quantified by Amplex Red oxidation and ELISA, respectively, in a serial assay. Statistical analysis was carried out using the Mann-Whitney signed rank test.

Results: Among clinically stable subjects, ETI therapy did not affect sputum MPO activity (ETI: 5460 ± 7201 ng/ml, and non-ETI: 4978 ± 4918 ng/ml; $p=0.7053$) or protein concentration (ETI: 4475 ± 5695 ng/ml non-ETI: 4033 ± 3940 ng/ml; $p=0.8798$). We also analyzed a subset of samples from PwCF experiencing APE. In this case, ETI therapy also did not affect sputum MPO activity (ETI: 3208 ± 2186 ng/ml, non-ETI: 6317 ± 5160 ng/ml; $p=0.3290$) or protein concentration (ETI: 2966 ± 2215 ng/ml, non-ETI: 6235 ± 3497 ng/ml; $p=0.1775$).

Conclusion: We found that sputum MPO activity and abundance are not significantly decreased in PwCF on ETI therapy, suggesting ETI may not control this aspect of the inflammatory burden of lung disease. Further research is needed to ascertain whether adjunct therapy may also be necessary in addition to ETI to control inflammation.

Deep Mutational Scanning of SMARCB1 Reveals a Role of DP2 in SMARCB1-deficient Cancers

Presenting Author: Garrett Cooper, BS, Genetics; Emory University

Poster Number: 10

Cooper, Garrett; Lee, Benjamin; Chen, Victor; Hong, Andrew

Background: Malignant rhabdoid tumors are one of the most aggressive and lethal cancers in pediatric oncology with overall survival rates of 20-25% despite intensive multi-modal therapies. Loss of SMARCB1 is the primary recurrent genetic alteration found in over 90% of cases. SMARCB1 is a critical component of the BAF chromatin remodeling complex, a complex which controls gene transcription by positioning nucleosomes at gene regulatory regions. Recent advances have implicated SMARCB1 loss in several other cancers broadly referred to as SMARCB1-deficient cancers. More generally, alterations in SMARCB1 have been identified in 1% of all cancers. Due to the limited number of patients presenting with SMARCB1-deficient cancers, our understanding of mutational spectrum of SMARCB1 remains limited.

Methods: We have previously performed deep mutational scanning to elucidate the functional consequences of all possible single amino acid substitutions in SMARCB1. These library of mutants was re-expressed in a pool of SMARCB1-deficient cells to assess their functional consequences.



Results: We have since identified a cluster of four residues within the RPT2 domain of SMARCB1 that are particularly intolerant to mutation. Structural rendering of the assembled BAF complex reveals that this cluster of residues directly interacts with a neighboring histone reader subunit, DPF2. Mutating one of these four residues in the RPT2 domain seems to confer a loss-of-function phenotype when re-expressed in SMARCB1-deficient cells. Further, we have observed a decrease in DPF2 association with the BAF complex upon introduction of this same mutation.

Conclusion: These data suggest that SMARCB1 exerts its tumor suppressor function at least partially through its interaction with DPF2, and that patients presenting with missense mutations in these residues may have similarly aggressive cancers as SMARCB1-deficient cancers.

Prophylactic Postoperative Peritoneal Dialysis in Pediatric Cardiac Critical Care: A matched cohort study

Presenting Author: Olivia Cote, BS; Emory University School of Medicine

Poster Number: 11

Olivia Cote; Ashley Harriott; Ambika Menon; Rohali Keesari; Subhadra Shashidharan; Michael P. Fundora; Asaad G. Beshish; Richard U. Garcia

Background: Outcomes of postoperative prophylactic peritoneal dialysis (PPD) after pediatric cardiac surgery has been reported with mixed results. We aimed to compare outcomes between patients who did and did not receive PPD following cardiac surgery in our institution.

Methods: Single center, retrospective matched cohort study of patients 0 – 31 days-old who underwent cardiac surgery between 01/2010 and 03/2022. Patients who received PPD were matched 1:1 with those who did not by age, gender, and surgical complexity (STAT score). Primary outcome was to reveal a difference in the time to negative fluid balance between groups. Secondary outcomes were to compare overall fluid balance, post operative morbidity, and mortality between the groups. Data reported as median (interquartile range). McNemar's test and Wilcoxon signed rank test were used for comparison. Significance considered at $p < 0.05$.

Results: The study included 448 patients, comprising 224 patients who underwent PPD (exposed) and 224 who did not (unexposed). median age and weight at surgery were 6 days (IQR 4, 10) and 3.2 kg (IQR 2.8, 3.6), respectively. Compared to the unexposed group, patients in the PPD group had shorter time to negative fluid balance (1.0 vs. 2.0 hours, $p < 0.01$), less positive fluid balance on postoperative day 1 and 2 (68 vs. 119 mL and 78.5 vs. 171 mL, respectively, $p < 0.01$), lower rates of stage 2 & 3 acute kidney injury (13.4% vs. 30.4%, $p < 0.01$), longer cardiopulmonary bypass time (165 vs. 132 min, $p < 0.01$), lower rate of requiring extracorporeal life support (4.9% vs 10.3%, $p = 0.03$), lower vasoactive inotropic scores at hours 0-24 and 24-48, and lower mortality rate (3.3% vs. 13.6%, $p < 0.05$).

Conclusion: Our study findings suggest that patients who underwent PPD had an improved fluid balance during the first 48-hours after cardiac surgery, had lower rate of AKI, and lower rates of morbidity and



mortality compared to those who did not receive PPD. These findings suggest that PPD may be associated with improved clinical outcomes in this patient population. However, future prospective multicenter studies and randomized studies are required to further investigate these findings.

Care Coordination, Family-Centered Care, and Shared Decision-Making Among Families with Cerebral Palsy

Presenting Author: Sarah Creveling, M.S. Kinesiology; Georgia Southern University

Poster Number: 108

Creveling, Sarah; Keko, Mario; Rochani, Haresh; McIntyre, Allison; Maitre, Nathalie Linda; Vova, Joshua; Modlesky, Christopher; and Colquitt, Gavin

Background and Objective(s):

Cerebral Palsy (CP) is one of many developmental disorders originating in infancy, all requiring care coordination for medical complexities, family-centered teams, and shared decision-making to achieve best outcomes. However, CP is the most common physical disability across the lifespan and may require a more customized approach to healthcare systems organization. We aimed to compare children with CP and those with other special health care needs (CSHCN) across important aspects of medical home management.

Methods:

Participants included parent respondents to the 2016-2020 (5 years combined) National Survey of Children's Health (NSCH). Among 174,551 respondents, 565 children had documented CP and another 39,835 had CSHCN. The 2016-2020 NSCH was conducted by the US Census Bureau online and by mail. Participants were selected with a validated, household pre-survey screener and asked to answer a child-level questionnaire for a randomly selected child in their household. CSHSN were oversampled. Variables collected included care coordination, family-centered care, and shared decision-making. Binary logistic regression analyses were performed, adjusting for age, income, sex, and race after multiple imputations to address missing data.

Results:

Notably, 35.2% of children with CP vs. 30.9% of CSHCN lived in households qualifying for government assisted healthcare due to low income, and disproportionately lived in non-white families. Fewer children with CP compared to CSHCN were reported as receiving effective care coordination (defined by the Maternal and Child Health Bureau; 40.3% vs 46.79%; $p = 0.002$). After controlling for confounders, children with CP were 22% less likely to receive effective care coordination ($p = 0.005$). There were also significant differences inequities in receipt of care coordination in the poorest families ($p = 0.0001$). There were no significant differences between groups in receipt of family-centered care (79.03% vs 80.78%) or shared decision making (88% vs 90.41%).

Conclusions/Significance





The World Health Organization's International Classification System on Functioning, Disability, and Health provides a framework for care coordination and should be implemented for children with CP in the US as best practice. Despite this, the majority of families of children with CP lack effective care coordination.

Limited Throw Distance was Associated with Limited Upper Extremity Power in Children with Cerebral Palsy

Presenting Author: Cory Cribb, M.S. Kinesiology, B.S. Exercise Science; University of Georgia

Poster Number: 13

Cory F. Cribb, Sarah Creveling, Katelyn Jackson, Christopher M. Modlesky, Noelle Moreau, Li Li, Gavin Colquitt

Background and Objectives: Early participation in ballistic skills such as kicking, throwing, and striking during physical activity are essential for children to develop and maintain muscle power. However, children with cerebral palsy (CP) participate less in physical activity than typically developing children (TDC). This study aimed to examine differences in upper extremity muscle power and motor skill performance in children with CP compared to TDC.

Methods: We recruited 20 children between the ages of 12 and 21; 10 children with CP within Gross Motor Function Classification system levels I-III (Mage=17.6 y/o; SD = 3.1) and 10 TDC (Mage=17.4 y/o; SD=3.7). Participants completed tests of maximal upper extremity muscle power, maximal throwing distance and accuracy, and throwing accuracy as measured in absolute error (ABSerr). All tests included five trials and were conducted while seated in a wheelchair and using the less affected arm for children with CP and the dominant arm for children in the TDC group. Participants completed maximal power attempts using a Concept2™ SkiErg (Morrisville, Vermont, USA) and peak power was recorded in Watts (W). For tests of maximal distance, participants were seated with 90° angles at the hip, knee, and ankle. They threw a softball covered in chalk as far as possible. The furthest distance of five attempts was recorded. For throwing accuracy, participants threw a softball covered in chalk to a custom-made, eight-by-eight foot target overlaid with 2-inch gridlines and 3 concentric circles at 2/3 of the maximal throwing distance. Using the coordinates of the throws, the radius from the center of the target was calculated and the average of all five radii was used to determine ABSerr.

Results: Children with CP produced 47% less maximal upper extremity muscle power (M=17.8 W; SD=12.0 W) than TDC (M=33.1 W; SD=11.8 W) ($p=0.01$). Children with CP threw at a distance 52% less (M=775.0cm; SD=599.99) than TDC (M=1,611.7cm; SD=513.1) ($p<.05$). There were no significant differences in accuracy.

Conclusions: Children with CP had less upper extremity muscle power and threw shorter distances than their typically developing peers. The reduced throwing distance was proportional to the reduced muscle power.



The Development of a Novel Throwing Task for Children with Cerebral Palsy

Presenting Author: Cory Cribb, M.S. Kinesiology, B.S. Exercise Science; University of Georgia

Poster Number: 12

Cory F. Cribb, Sarah Creveling, Katelyn Jackson, Christopher M. Modlesky, Noelle Moreau, Li Li, Gavin Colquitt

Background: Individuals with cerebral palsy (CP) who experience general motor delays and other activity limitations may lack key fundamental motor skills. The overhand throw is a skill that requires muscle recruitment patterns to generate muscle power. This study aimed to develop a valid and reliable overhand throw test to assess motor skill performance and muscle power.

Methods: Fifteen adolescents with spastic CP (M=17.3 y/o; SD=2.9) participated in two separate testing sessions within 7-14 days. Participants were required to have diagnosis of CP, be within levels I-III of the Gross Motor Function Classification Scale (GMFCS), be cleared for physical activity by a medical professional, and be able to independently perform an overhand throw with the less-affected arm. Participants were seated in a standard wheelchair and instructed to throw a standard softball covered in chalk as far as possible (Maxdist). The greatest distance from 5 attempts was recorded in centimeters (cm). Participants were placed 2/3 of Maxdist and threw to the center of an eight-by-eight-foot target overlaid with gridlines. Five throws were performed and the average radii of all throws were used to determine absolute error (ABSerr). To cross-validate the maximal throwing to muscle power, maximal attempts on a Concept2TM SkiErg (Morrisville, Vermont, USA) were performed with their less-affected arm five times. The peak power of all attempts was recorded in Watts (W).

Results: Intertrial variability fell into the excellent range for maximal distance in cm (ICC=.98, p<.01) and within the good range for maximal muscle power (ICC=.85, p<.01). ABSerr fell within a moderate range (ICC=.53, p<.05). Standard errors of measurement showed that maximal distance, maximal muscle power, and Abserr were all within acceptable ranges. There was a strong positive relationship between the maximal distance of the overhand throw and maximal power (r=.90, p<.01).

Conclusions: The new throwing assessment provides a reliable measure of upper extremity motor skill performance and a valid estimate of upper extremity muscle power in adolescents with spastic CP. It may also be used to test the effectiveness of interventions aimed at improving upper extremity motor skill performance and muscle power.

Prevalence of atopy in a cystic fibrosis pediatric population

Presenting Author: Priscila Cunha, MD; Emory University

Poster Number: 85

Cunha, Priscila; Lee, Tricia

Background: Scientific data has shown that the CFTR protein is responsible for more than ion transport. Studies suggest that a mutation in CFTR can lead to Th2 cell activation and an increase in pro-





inflammatory cytokines. Gastrointestinal symptoms of food-induced anaphylaxis are also related to CFTR dependent chloride transport. Additionally, as CFTR regulates skin barrier secretions, dysfunction could lead to increased rates of atopic dermatitis.

Methods: We hypothesize that patients with cystic fibrosis (CF) are more likely to develop atopic dermatitis, allergic rhinitis, food allergies and asthma. Filtering by ICD-10 code in the Slicer Dicer tool in epic, we identified all cystic fibrosis patients within all locations of the Children’s Healthcare of Atlanta. Among all CF patients we ran two separate reports: one to identify patients with either allergic rhinitis or food allergies or eczema using ICD-10 codes; another to identify reports of food allergy within the allergy tab.

Results: We identified a total of 755 CF patients. On the report based on ICD-10 codes there were: 1 patient allergic to eggs, 1 allergic to peanuts, 3 with unspecified food allergies, 11 with seasonal allergies and 20 with unspecified allergies. Surprisingly we identified no patients with eczema. Using the allergies reported on the allergy tab there were: 11 patients allergic to peanuts, 8 allergic to eggs, 5 allergic to tree nuts, 7 allergic to shellfish, 4 allergic to fish, 2 allergic to soy, 0 allergic to shrimp, 2 allergic to wheat and 7 allergic to milk.

Conclusions: There was inconsistency between the prevalence of atopy based on ICD-10 codes versus based on data on allergy tab. Since the latter is self-reported it may capture reactions that are not truly allergic in nature but also could include patients that have a true allergy but were never seen for this diagnosis in our system. If we base our prevalence of atopy on ICD-10 codes, it appears that our CF population has a lower prevalence of atopy than the general pediatric population. Further manual chart review is needed to determine which patients have true allergies and to characterize CF patients with allergies versus those without.

Targeted screens of Interferon Stimulated Genes (ISGs) for pro-viral and anti-viral activity against Hepatitis B virus in primary hepatocyte systems

Presenting Author: Georgios Dangas, B.S.; Emory University

Poster Number: 109

Dangas, Georgios; Athanasiadis, Antonios; Park, Paul; Shue, Taylor; Jones, Christopher Edward; Levenson, Kenneth Charles; de Jong, Ype; and Michailidis, Lefteris

Hepatitis B virus (HBV) chronically infects approximately 296 million worldwide and ~820,000 die each year due to HBV-related complications. Widely used nucleoside analogs efficiently suppress the virus yet do not result in a cure. Understanding how interferon-stimulated genes (ISG) contribute to curing HBV has the potential for more targeted and better-tolerated antiviral strategies.

HBV studies are usually performed in hepatoma cell lines like HepG2 upon overexpression of the HBV receptor NTCP. These HepG2-NTCP cells support HBV replication and provide a good platform for virus-host interaction studies. However, due to the transformed nature of cancer cell lines, the most physiologically relevant cells for HBV studies are primary human hepatocytes (PHH). We routinely use a cell culture system we developed which is based on the isolation and culturing of primary hepatocytes





that have been expanded in liver chimeric humanized mice and we termed mouse-passaged (mp)PHH. Our studies here focus on specific ISGs and their effect on HBV replication and innate immune responses.

Previously, we conducted a targeted screen to interrogate the effect of 400 genes in the context of HBV infection. These genes are members of the ISGs and have been previously shown to be induced by interferon. Here, we further validated known and novel ISG hits including TREX1, MAFF, and Tetherin for their activity in HBV infection in both HepG2-NTCP and mpPHH. The initial approach was to overexpress (OE) individual genes, establish stable cell lines and interrogate the effect on HBV replication markers. We also targeted these genes with knockout and knockdown experiments using CRISPR/Cas9 techniques.

Taken together, these studies will give insights into the role of specific ISGs in the context of HBV infection in cell culture systems and will advance our understanding of virus-host interactions toward the development of novel antiviral strategies against chronic HBV.

Recurrence Rates of Autism Spectrum Disorder within Elevated Likelihood Younger Siblings by 36-months

Presenting Author: Hannah Davies, Bachelor of Science in Neuroscience; Emory University

Poster Number: 101

Ainsley Buck, Hannah Davies, Ami Klin, Warren Jones, Sarah Shultz, Stormi White, and Cheryl Klaiman

Background: Etiology of autism spectrum disorder (ASD) is unknown but genetically-linked. So, younger siblings in families with 1+ child with autism are at an elevated likelihood (EL) to be diagnosed with ASD compared to the general population. Previous literature estimates sibling recurrence rates (RRs) at ~20% (Ozonoff et al., 2011, Jones & Klin, 2013). Recent work suggests only half of EL siblings develop typically (McDonald et al., 2020).

Objectives: Determine RRs for ASD in a more recent sample of EL younger siblings (evaluated 2015-2023) and identify assessment measures that differentiate ASD from non-ASD outcomes.

Methods: EL younger siblings (n=137, n_{male}=88, n_{female}=49) were enrolled at birth and received diagnostic assessments at 24 (n=45; Mage(SD)=24.27(1.97) months) or 36 (n=92; Mage(SD)=35.74(3.36) months). The Autism Diagnostic Observation Schedule-2 (ADOS-2) and Mullen Scales of Early Learning (MSEL) were administered and used for clinician best estimate (CBE) diagnoses, which were determined by two blinded clinicians who conducted assessments. Some participants (n=76) underwent a subsequent diagnostic review where two additional blinded clinicians reviewed assessment information to confirm diagnoses. RRs were calculated using CBEs and again with diagnostic review diagnoses. To determine which assessment measures differentiated ASD from non-ASD outcomes, binary regressions and ROC analyses using ADOS-2 (social affect, restricted and repetitive behaviors) and MSEL scores (visual reception, fine motor, receptive language, expressive language) were performed.



Results: Using CBEs, the ASD RR was 37.96%. 27.73% of the sample was classified as broader autism phenotype, 3.65% non-ASD developmental delays, and 30.66% unaffected. With diagnostic review data, RR increased to 48.68% (driving factors to be investigated). All models significantly differentiated between ASD and non-ASD outcomes (all $p < .001$). ADOS total scores and MSEL composites best classified outcomes (AUCADOS=.976; AUCMSEL=.840).

Conclusions: From 2012 to 2022, CDC estimates of ASD prevalence increased from 1/69 (Christensen et al., 2012) to 1/44 (Maenner et al., 2021). As knowledge of early childhood autism has improved, we hypothesized that RRs would increase to encompass atypical development not previously classified as ASD. Our RR of 37.96% parallels this trend. Our findings underscore the criticality of developmental monitoring and surveillance of EL younger siblings.

Influence of Clinician Certainty on Diagnostic Stability for Younger Siblings at Elevated Likelihood of Autism Spectrum Disorder

Presenting Author: Hannah Davies, MS; Marcus Autism Center

Poster Number: 110

Davies, Hannah; Buck, Ainsley; Klin, Ami; White, Stormi; and Klaiman, Cheryl

Background: Autism spectrum disorder (ASD) can be diagnosed in toddlerhood and is more prevalent in families who have another child with ASD. Developmental screening is imperative but can be more challenging for siblings at elevated likelihood (EL) of ASD. To better understand the unfolding of diagnostic trajectories, some children may benefit from additional evaluations due to clinician uncertainty (Klaiman et al., 2022). In this longitudinal study, we investigated whether clinician certainty of diagnosis at 24 months influences diagnostic stability upon 36-month re-evaluation.

Methods: EL younger siblings ($n=58$) received clinician best estimates (CBE) of diagnosis during 24-month ($Mage(SD)=24.51(\pm 0.92)$ months) and 36-month ($Mage(SD)=37.36(\pm 2.08)$ months) evaluations, generating four independent groups: (1) ASD CBEs (ASD, $n=17$); (2) broader autism phenotype CBEs (BAP, $n=10$); (3) unaffected CBEs (UN, $n=14$); and (4) variable CBEs (variable, $n=17$). Clinician certainty of CBE was measured using a 5-point, 20% increment scale, ranging from 0-100% certainty. Influence of clinician certainty on CBE assignment at 24 and 36 months was determined by between group ANOVAs and paired samples t-tests.

Results: At 24 and 36-month evaluations, clinicians reported the highest level of certainty when assigning CBEs for 42.4% and 52.5% of cases respectively. Although clinician certainty of CBE broadly increased with child age, there were no significant differences in clinician certainty between 24- and 36-month evaluations within any groups ($ps > 0.05$). Clinician certainty at 24 months had a main effect on CBE assignment ($ps < 0.001$). Clinician certainty was significantly higher for ASD and unaffected CBEs than for BAP ($p_{ASD}=0.002$; $p_{UN}=0.007$) and variable ($ps < 0.001$) CBEs. There was no significant difference in clinician certainty at 24 months for those with BAP and variable CBEs ($ps > 0.05$).

Conclusions: Although clinicians felt slightly more confident in assigning CBEs later in development, diagnostic certainty within each group was relatively consistent across both evaluation periods. Similar





to McDonnell and colleagues (2019), clinicians felt less certain diagnosing children with moderate levels of observable ASD symptoms (e.g., BAP and variable diagnoses) and this uncertainty continued despite child aging. Consistent uncertainty surrounding BAP diagnoses at 36 months could suggest diagnostic instability and the need for further evaluation later in life to ensure service accessibility.

Factors Contributing to a Change in Diagnosis from 24 to 36 Months in Younger Siblings at Elevated Likelihood of Autism Spectrum Disorder

Presenting Author: Hannah Davies, MS; Marcus Autism Center

Poster Number: 111

Davies, Hannah; Buck, Ainsley; Jones, Warren; Shultz, Sarah; Klin, Ami; White, Stormi; and Klaiman, Cheryl

Background: The etiology of autism spectrum disorder (ASD) is largely genetic, with affected families being at elevated likelihood (EL) of ASD. Earlier screening benefits EL siblings because 86.3% of ASD diagnoses made before 36 months maintain stability (Rondeau et al., 2011); however, false negative rates can reach over 40% which poses a problem for service accessibility (Ozonoff et al., 2015). Assessing phenotypic trends influencing diagnostic outcome at 24- and 36-months can help minimize future misdiagnoses associated with borderline phenotypes.

Methods: EL younger siblings (n=63) completed 24-month and 36-month assessments, generating four clinician best estimate (CBE) groups: (1) true positive, ASD CBEs (TP, n=18); (2) true negative, non-ASD CBEs (TN, n=33); (3) false negative CBEs (FN, n=7); and (4) false positive CBEs (FP, n=5). CBE of diagnosis was made using the Autism Diagnostic Observation Schedule-2 (ADOS-2), Mullen Scales of Early Learning (MSEL) and overall diagnostic impressions (Lord et al., 2012, Mullen, 1995). Influence of ADOS-2 sub-scores [social affect (SA) and restricted and repetitive behavior (RRB)] and MSEL sub-scale scores [receptive language (RL) and expressive language (EL)] on CBE change were determined by between group ANOVAs.

Results: There was a significant effect of 24- and 36-month ADOS-2 sub-scores and MSEL sub-scale scores on CBE change ($p < 0.036$). FN participants had significantly lower ADOS sub-scores than TP participants at 24 months ($p < 0.010$) and significantly higher ADOS sub-scores and significantly lower EL scores than TN participants at 36 months ($p < 0.033$). FP participants had significantly higher ADOS sub-scores than TN participants ($p < 0.032$) at 24 months and significantly lower SA scores than TP participants at both evaluations ($p < 0.042$). At 24 months, RL scores were significantly lower for FN than TN participants and significantly higher for FP than TP participants ($p < 0.049$).

Conclusions: ASD presentation can drastically change over one year. FN and FP participants' 24-month RL scores were indicative of their 36-month CBE, suggesting that RL could be an early predictor of CBE for siblings with borderline phenotypes. ADOS-2 sub-scores suggest that FN participants may experience developmental regression and/or difficulty meeting increased social demands after 24 months while FP participants may gain age-appropriate social-communication skills after 24 months.



Prior SARS-CoV-2 Infection and Risk of Subsequent COVID-19-Related Hospitalization: A Test Negative Design

Presenting Author: Khalel De Castro, B.S.; Emory University

Poster Number: 112

De Castro, Khalel; Tippett, Ashley; Hussaini, Laila; Salazar, Luis; Reese, Olivia; Taylor, Meg; Ciric, Caroline; Choi Chris; Taylor, Grace; Puzniak, Laura; Hubler, Robin; Valluri, S; Lopman, B; Kamidani, S; Rostad, CA; McLaughlin, J; and Anderson EJ

Background: Previous evidence suggests that prior SARS-CoV-2 infection provides some protection against reinfection. The extent of protection against severe outcomes, such as hospitalizations, afforded by prior infection is not certain. We used a test-negative design to evaluate the effectiveness of prior COVID-19 against acute respiratory infection-related (ARI) hospitalizations.

Methods: From May 2021 – Feb 2022, we enrolled subjects who are ≥ 18 years of age and hospitalized with Acute Respiratory Infection (ARI) symptoms at 2 hospital sites associated with Emory University. Enrolled patients participated in an interview regarding medical, social and vaccination history. Enrolled patients provided an NP swab or standard of care sample for COVID-19 testing. Medical records, past medical history, and vaccine documentation were also reviewed and abstracted. Analysis performed using SAS v.9.4. Characteristics compared with bivariate analysis (two-tailed p-value < 0.05) and generated a stepwise logistic regression model with inclusion in the model set at 0.05.

Results: Of the 1343 patients enrolled in our study, 684 (50.9%) were SARS-CoV-2 positive and 66 (4.9%) had a prior infection. Reinfections represented 15/684 (2.2%) of COVID-19 related hospitalizations. Crude odds ratio (OR) 0.27 (95% CI 0.15, 0.48). Adjusted OR 0.26 (95% CI 0.14, 0.49).

Conclusions: Reinfections represented a small proportion (2.2%) of COVID-19-related hospitalizations. Prior SARS-CoV-2 infection provided short-term 74% (95% CI 51, 86) protection against COVID-19-related ARI hospitalizations. More data is needed about the duration of prior infection protection, variant-specific estimates, and the impact of vaccination by number of doses.

Predictors of Participation in Autism Evidence-Based Practice Training Within an Early Intervention System

Presenting Author: Brooke Demetri, Neuroscience (BS); Marcus Autism Center, Emory University School of Medicine

Poster Number: 114

Demetri, Brooke; Chatson, Emma; Davies, Hannah; Yohannes, Millena; Buck, Ainsley; Balser, Dorothy; Hendrix, Nicole; and Pickard, Katherine

Background: To help foster early access to autism intervention, there is a growing interest in delivering Naturalistic Developmental Behavioral Interventions (NDBIs) in Early Intervention (EI) systems for children aged 0-3 years with developmental delays. Although EI providers who participate in NDBI





training can increase their fidelity to these models, not all providers complete implementation initiatives; further, limited research has examined provider- and system-level factors that predict the extent to which providers participate in NDBI training. The objectives of this study are to examine: (1) factors that predict uptake of NDBIs within Georgia's EI system; (2) factors that predict EI providers' perceptions of feasibility and acceptability of NDBIs; and (3) how providers deliver NDBI after training.

Methods: Fifty-seven providers participated in one of two NDBI training opportunities: (1) Project ImPACT; or (2) the Autism Navigator. Prior to training, providers completed measures of demographic information, attitudes, and perceived support to attend training. Following training, providers participated in group consultation and completed measures of feasibility, acceptability, and intervention delivery. Linear and logistic regression models were used to examine predictors of EI provider participation in NDBI training. Descriptive statistics were used to examine delivery of intervention following training.

Results: 91.1% of providers reported they learned new skills by attending training. Results from a binary logistic regression model predicting NDBI training demonstrated that the specific training opportunity (i.e., Project ImPACT or the Autism Navigator) predicted training completion above and beyond provider attitudes, level of training support, and years of experience. Of the EI providers who completed training (n=40) and consultation (n=37), 54.8% indicated delivering either Autism Navigator or Project ImPACT to additional families on their caseload.

Conclusion: Preliminary findings suggest specific NDBI training content and structure may impact provider engagement within EI systems. Although data collection is ongoing, these findings provide insight into training processes by which NDBIs can be translated into EI systems and the factors that influence their use by EI providers. This may allow for developing implementation strategies and training methods in partnership with EI providers that support provider use of NDBI models, allowing for family access to evidence- based treatment.

Caregiver Perspectives on Participating in Pediatric MRI Research

Presenting Author: Brooke Demetri, Neuroscience (BS); Marcus Autism Center, Emory University School of Medicine

Poster Number: 113

Demetri, Brooke; Reineri, Carly; Sholar, Brittany; and Shultz, Sarah

Background: Longitudinal studies of brain development have the potential to provide insight into neural mechanisms underlying various neurodevelopmental disabilities. In contrast to studies of adults and school-aged children, neuroimaging studies of infants face additional challenges acquiring high-quality usable data, which often requires infants to be scanned during natural sleep. Although MRI is a non-invasive imaging technique, the prospect of caregivers enrolling their infants in clinically unnecessary MRI can be overwhelming. Additionally, since the commitment to participate in longitudinal MRI research can be demanding, participant attrition often poses additional challenges to longitudinal work. Given the challenging nature of pediatric neuroimaging research, efforts aimed at minimizing participant





attrition while maximizing useful MRI data collection are crucial. The objective of this study is to elicit caregiver feedback through the use of focus group interviews about their experiences participating in MRI research, suggestions for infant MRI protocol improvement, and why they chose to participate in the research. Our goal is to better understand how we can revise our current protocols for infant neuroimaging studies to improve enrollment, data acquisition and lower participant attrition rates.

Methods: 13 caregivers were recruited from a group of caregivers who completed a longitudinal infant MRI study at the Marcus Autism Center. The infants enrolled in the MRI study were either at low or elevated likelihood for autism. Three focus groups were conducted (3-5 caregivers per group) where a semi-structured interview was used to elicit caregiver feedback. Emerging themes from the focus group responses were identified.

Results: Overall, caregivers recalled a positive experience in participating in our longitudinal infant MRI study and, if given the opportunity, would participate again. Caregivers also provided feedback for improving recruitment strategy, study materials, and study protocols. Caregivers reported experiencing anxiety around whether or not their infant would successfully complete the entire MRI protocol and provide usable data. Contributing to science was the most common motivator participating in research.

Conclusions: Our findings provide critical insight into the experience of participating in infant MRI research from the caregiver point of view, which will allow researchers to improve participant experience in the field of infant neuroimaging.

Ibutilide for Chemical Cardioversion of Atrial flutter and Fibrillation in Pediatrics

Presenting Author: Brooke Evans, MD; Emory

Poster Number: 86

Evans, Brooke; Whitehill, Robert

Background: Atrial Flutter (AFL) and atrial fibrillation (AF) are arrhythmias that can present in children and young adults with congenital heart disease or structurally normal hearts. Traditional methods of restoring sinus rhythm include electrical cardioversion and pharmacologic cardioversion. Ibutilide has been used in the adult population due to its quick onset and efficacy but data is lacking in pediatrics. The objective of this study is to evaluate single center safety and efficacy of chemical cardioversion with ibutilide.

Methods: Retrospective cohort study at Children's Healthcare of Atlanta (CHOA) including all patients who underwent chemical cardioversion with ibutilide from January 2011- July 2022. Patients were identified by pulling all doses of ibutilide during the time period. Patients were excluded if available records were insufficient. The primary outcome was conversion to sinus rhythm. Major adverse events included arrhythmia or cardiac arrest.

Results: 37 patients received Ibutilide, median age 16 years (IQR 15,17). 12 for AFL and 24 for AF. 1 patient's rhythm was not further defined. 16 patients had structural heart disease; 6 with single ventricle physiology. 12 patients had new or worsened ventricular dysfunction. Ibutilide was successful





25 of 37 patients (469). 11 patients required electrical cardioversion after ibutilide failed. Major complications included 2 patients with torsade de pointes. One patient went into PEA arrest following torsade de pointes and required intubation. There were no deaths directly linked to administration. Seven individual patients had complications following Ibutilide administration; 3 had arrhythmia, 3 had hypotension, and 4 had EKG changes (elongated QTc).

Conclusion: Ibutilide can be used for chemical cardioversion in pediatrics with 69% efficacy in this cohort. Major safety concerns included torsades de pointes in 2 patients. Ibutilide is relatively effective and safe in this population. Other complications included hypotension and QTc prolongation, suggesting ICU level care for administration. Future study to be done to risk stratify patients for ibutilide and investigate for cost benefits from avoiding sedation and cardioversion.

Early ART plus immune interventions to limit SIV reservoir establishment in infant rhesus macaques

Presenting Author: Omotayo Farinre, Ph.D; Emory University

Poster Number: 75

Omotayo Farinre, Tzoalli Anaya, Lexy King, Stephanie Ehnert, Sherrie Jean, Greg Laird, Rosemarie Mason, Mario Roederer, Jeffrey Safrit, Maud Mavigner, Ann Chahroudi

Background

Antiretroviral therapy (ART) successfully controls viremia in HIV-1 infection. However, persistent reservoirs of latently infected CD4+ T-cells remain the major obstacle to cure. In this infant nonhuman primate (NHP) model, we tested the hypothesis that a combination of interventions given at the time of ART initiation may restrict reservoir size by accelerating the loss of infected CD4+ T-cells. The interventions used included N-803, an IL-15 super-agonist known to enhance immune responses through activation and proliferation of T and NK cells, a cocktail of anti-SIV Env-specific rhesus IgG1 monoclonal antibodies (RhmAbs) to promote infected cell clearance through antibody-dependent cellular cytotoxicity.

Methods

Twenty-two infant rhesus macaques were orally infected with SIVmac251 at 4 weeks of life and started on ART +/- additional interventions 1-2 weeks post-infection, divided into 3 groups: i) ART only, ii) ART+SIV RhmAbs, and iii) ART+SIV RhmAbs+N-803. Animals were longitudinally monitored for plasma viral loads and CD4+ T-cells were isolated from blood and lymph nodes to measure the impact of interventions on the viral reservoir using qPCR to quantify total SIV DNA/RNA and intact proviral DNA.

Results

ART suppressed viral loads below the limit of detection and no significant differences was detected in the decay of viremia across groups. Levels of CD4+ T-cell-associated DNA and RNA declined on ART in all groups with the greatest fold change between weeks 0-26 of ART found in the group that received SIV RhmAbs without N-803 ($p=0.018$ vs controls). However, intact proviral SIV-DNA did not differ between



groups at week 26 in CD4+ T-cells from blood or LN. The group that received SIV RhmAbs + N-803 showed an unexpected increase in SIV-RNA at week 16 of ART in CD4+ T-cells from blood and LN, possibly as a delayed consequence of N-803-mediated immune stimulation.

Conclusions

Early intervention with ART in the infant rhesus macaques was effective in suppressing viremia. The addition of SIV RhmAbs to ART improved the elimination of infected cells but did not impact the level of persistent, intact SIV once viral loads were suppressed. Disproving our initial hypothesis, N-803 did not limit reservoir establishment.

Keywords: SIV, cure, nonhuman primates

Promoting Equity in Language Input Through Talk With Me Baby: An Interdisciplinary Perspective

Presenting Author: Lama Farran, Ph.D., CCC-SLP; University of West Georgia

Poster Number: 157

Lama K. Farran, PhD, CCC-SLP, Susan N. Brasher, PhD, RN, CPNP, FAAN, & Jennifer L. Stapel-Wax, PsyD

Background

Early language exposure impacts children's overall developmental trajectories. Georgia data shows 66% of 3rd graders are not reading proficiently, suggesting insufficient early language exposure, especially in families who come from culturally and linguistically diverse backgrounds and rural areas. Programs that promote rich language input are needed to support the wellbeing of young children. This study examines the impact of Talk With Me Baby (TWMB) training on the preparation of preservice professionals working with families and young children, thereby maximizing access to equitable language input and addressing service disparities of underserved populations.

Methods

Using the Practical Robust Implementation Science Model (PRISM), this study: (1) expands previous TWMB implementation to other disciplines, (2) examines variables that impact feasibility, acceptability, adoption, and sustainability of TWMB training in rural communities, and (3) identifies barriers and facilitators to TWMB integration.

An exploratory sequential mixed methods approach was used. Participants included 43 preservice students (74.29% White; 21.43% Black) in speech-language pathology, special education, and early childhood education at the University of West Georgia (UWG). A pre- and post-survey (Likert scale; open-ended questions) elicited input on modifications to enhance TWMB implementation. Student focus groups and interviews with leadership explored perceived acceptability, adoption, and sustainability as well as system-level constraints of TWMB training and implementation.

Results





Post-survey results revealed support of TWMB training, with high perceived acceptability, adoption, and sustainability (mean scores range 6.13-6.66 on a 7-point Likert; SD range 1.34-1.62). Open-ended survey analysis revealed 95% of participants indicated high satisfaction and likelihood of adopting TWMB in future careers. Students expressed the need for hands-on training and exposure to real-life scenarios before working with parents. Leadership interviews revealed support for preservice TWMB training and concerns regarding potential faculty burden and TWMB integration into existing curricula.

Conclusions

Building caregiver capacity through TWMB training across disciplines is the first step in inducing change by building a strong language foundation during the early years of life. TWMB is accessible and free to students and families. Longitudinal investigations that track students from preservice to inservice can inform our understanding of TWMB implementation with underserved populations from diverse cultural, linguistic, and economic backgrounds.

Caregiver greeting to infants under 6 months already reflects emerging differences in those later diagnosed with autism

Presenting Author: Aiden Ford, B.S.; Emory University

Poster Number: 14

Aiden Ford, Hasse Walum, Beyonce Brice, Hely Patel, Sanjana Kunnikuru, Warren Jones, Gordon J. Berman, Sarah Shultz

Background: As infants develop, caregivers intuitively adjust their behavior to match and then scaffold their infant's emerging skills, such that changes in caregiver behavior are expected to reflect changes in infants' developing social abilities (Shultz, Klin, Jones, 2018). One such example is caregiver greeting, the exaggerated, excited expression that caregivers present within the first seconds of seeing their infant to initiate reciprocal social interaction. We test the hypotheses that changes in caregiver greeting reflect infants' social abilities, and that differences in caregiver greeting may reflect emerging social disability in infants later diagnosed with autism.

Methods: We tested these hypotheses in the 0-6-month period using densely sampled, prospective, longitudinal data from 90 dyads with a neurotypical infant (NT), 43 dyads with an infant later diagnosed with autism (AUT), and 45 dyads with an infant not diagnosed with autism but with increased familial genetic likelihood for autism (el-nAUT).

Results: In NT dyads, the greatest increase in greeting occurred in the 2nd month, coinciding with the typical emergence of infants' active and intentional social interactions. In dyads with AUT infants, caregivers used greeting at later ages in development and did so less often. This difference was not observed in el-nAUT dyads. This decrease in greeting is not interpreted as any suboptimal behavior on the part of the caregiver, on the contrary, it reflects caregivers' remarkable ability to attune to the interactive needs of their infant. Finally, socioeconomic status (SES) was also associated with decreased caregiver greeting and partially mediated the difference between AUT and NT dyads.



Conclusions: Autism and SES impact how caregivers use greeting, and by extension, the mutually-adapted dynamics of dyadic interaction, one of infants' earliest and most foundational learning experiences. This finding marks the earliest demonstration of altered infant-caregiver interaction in autism, providing evidence of emerging social disability many months before overt features are present and years before a formal autism diagnosis is possible. Centering the infant-caregiver dyad in future studies can provide new evidence of how the accrual of small-scale differences, happening here within seconds of the start of an interaction, can indicate divergent developmental processes and emerging disability.

A Role For The Immune Checkpoint Siglec-15 In Promoting Immune Dysregulation in Lymphomas

Presenting Author: Dailia Francis, MD, PhD; Emory University School of Medicine

Poster Number: 115

Francis, Dailia B; Dougan, Jodi; Pillsbury, Claire; Park, Sunita; Liu, Linda; and Porter, Christopher

Background: Non-Hodgkin's Lymphomas (NHL) are a heterogeneous group of hematologic malignancies occurring in children and adolescents. Intensive multi-agent chemotherapy regimens has dramatically altered the treatment landscape, improving the 5-year event free survival for these patients. However, despite salvage therapies, survival remains unacceptably low at <30% in relapsed/refractory disease. This highlights an urgent, unmet need. Siglec-15 (Sig-15), is a critical immune suppressor that is highly expressed in various human cancers and intra-tumoral myeloid cells. Importantly, inhibiting Sig-15, either through genetic knockout or knockdown, has a restorative effect on local anti-tumor immune responses and abrogated tumor progression. While reported in solid malignancies, a role for Sig-15 in promoting disease progression in hematologic malignancies has not yet been described.

Methods: Sig-15 expression was evaluated in primary human lymphoma patient samples as well as various lymphoma cell lines using western blot, quantitative PCR as well immunohistochemistry and immunofluorescence methods. The impact of NF-kB signaling on Sig-15 expression was interrogated in human lymphoma cell lines using various pharmacologic agents including phorbol myristate acetate (PMA), Ionomycin, CD40-Ligand and BOT-46 which either induce or inhibit NF-kB activity. Sig-15 expression was then assessed by western blot and PCR analysis. Sig-15 expression was inhibited through genetic downregulation in the well-established murine lymphoma cell line A20 and injected into immune competent and immune deficient mice to determine the effect on tumor progression and survival.

Results and Conclusions: Western blot shows higher Sig-15 expression in lymphoma cell lines compared to healthy donor peripheral mononuclear cells. Immunohistochemistry of a tumor microarray and validation samples from children shows high Sig-15 expression in NHL (Diffuse Large B Cell and Burkitt's Lymphomas) samples with distinct staining patterns based on subtype. Stimulation of NF-kB signaling induces increased expression of Sig-15 in lymphoma cells and appears to stabilize Sig-15 in the presence of concurrent inhibition. Lastly, knockdown of Sig-15 in A20 cells abrogates disease progression in immune competent but not immunodeficient recipients, consistent with a role for Sig-15 in immune



evasion in lymphoma. Together, these data implicate Sig-15 as an immune checkpoint that may be inhibited therapeutically to promote an immune response to lymphoma cells.

Lactococcus lactis subspecies cremoris is a highly efficacious probiotic driving metabolic changes in the prevention of metabolic disease.

Presenting Author: Camilo Anthony Gacasan, BS Biomedical Science; Emory University

Poster Number: 15

Gacasan, C. Anthony; Naudin, Crystal; Askew, Lauren; Neish, Andrew and Jones, Rheinalt

Background: With over two-thirds of US adults either overweight and obese and one-fifth of US children aged 2-19 years, the prevalence and comorbidity associated with metabolic syndrome are of significant consequence to the US population. Dietary supplementation with beneficial microbes may be an integral tool to add to our therapeutic toolbox to mitigate the comorbidity associated with increased weight. Our research group has previously identified the microbe *Lactococcus lactis subspecies cremoris* (LLC) as a highly efficacious probiotic in the attenuation of western style diet induced metabolic syndrome phenotypes and through the utilization of ultra-high pressure liquid chromatography coupled to high resolution mass spectrometry (UHPLC-HRMS) we show that this may be in part due to changes in gut-derived small molecules.

Methods: C57BL/6 mice were fed a western style high fat, high carbohydrate diet and were supplemented with 1x10⁹ colony-forming units of LLC (ATCC 19257), *Lactococcus lactis Rhamnosus GG* (LGG) as a control bacteria (ATCC 53103), or an HBSS vehicle control 3 times per week for 16 weeks to assess for effects on long term metabolic outcomes. Small molecule metabolomic analysis was conducted on the serum of mice treated with western style diet supplemented with the same probiotic experimental groups for 4 weeks, metabolites measured via UHPLC-HRMS and analyzed with publicly available computational tools and functional pathway enrichment algorithms.

Results: Mice fed a western style diet supplemented with LLC gained less weight, developed less hepatic inflammation and steatosis, and lower overall cholesterol levels than mice fed control bacteria. LLC fed mice showed a discrete population of serum metabolites when compared to either vehicle or control bacteria and demonstrated functional enrichment in pathways related to fatty acid metabolism and activation and cholesterol metabolism.

Conclusions: LLC is a highly efficacious probiotic that when supplemented in the context of a high fat and high carbohydrate diet in mice results in a distinct population of gut derived changes in serum metabolites that may be driving the decreased weight gain, decreased liver adiposity and inflammation, and reductions in serum cholesterol we observed.

A Multidisciplinary Intervention for Encopresis in Children with ASD

Presenting Author: Mayank Gandhi, M.S.; Mercer University





Poster Number: 116

Gandhi, Mayank; Argueta, Tracy; Call, Nathan; Muething, Colin; Scheithauer, Mindy; Scahill, Lawrence; Rock, Chelsea; Coleman, Laura; Gillespie, Scott; Lomas Mevers, Joanna

Background: Encopresis [i.e., incontinent bowel movements (BM)] is a common problem in children with autism spectrum disorder (ASD) (Lancioni et al., 2001). It presents a challenge for parents and there is a lack of empirically supported treatments for achieving long-term bowel continence for children with ASD.

Method: This was a single site randomized clinical trial designed to evaluate Multidisciplinary Intervention for Encopresis (MIE) with autistic children between the ages of 5 and 12. One hundred seventeen (117) children were randomly assigned to MIE or Treatment as Usual (TAU) for 8 weeks. Treatment as Usual (TAU) or a 10-day MIE. TAU offered a 1-2-hour caregiver training in clinic or by telehealth from a licensed psychologist, which consisted of developing a sit schedule, delivering reinforcers for continent bowel movements (BMs), and how to respond to incontinent BMs. The 10-day clinic-based MIE included structured thirty-min sits each day. If a continent BM did not occur during the planned sits, a behavior therapist administered a liquid glycerin suppository. Continent BMs resulted in praise, highly preferred reinforcers based on parent report, and completion of the intervention for the day. Suppository dosing was conditionally reduced to achieve independent continence.

Results & Conclusion: Children randomized to the MIE demonstrated a statistically significant improvement in encopresis providing evidence that this treatment is efficacious for treating encopresis in children with ASD.

Case Study: Instrumented Gait Analysis in a Child with Chromosome 19p Deletion Syndrome

Presenting Author: Mark Geil, PhD; Kennesaw State University

Poster Number: 158

Geil, Mark; Schrader, Tim

Background: Chromosome 19p Deletion Syndrome is a rare condition that occurs when a copy of genetic material on the short arm of chromosome 19 is missing. Among the many sequelae associated with the syndrome are reduced muscle tone, delays in gross motor skill development, and ataxia, all of which can affect walking gait.

The National Library of Medicine states that only about 10 affected individuals have been described in the literature. While scant research describes age of onset of walking in children with this condition, we are not aware of any published clinical gait analyses.

Methods: 3D instrumented gait analysis was conducted on a 12-year-old female with Chromosome 19 Deletion Syndrome, ADD, and mild developmental delays. The patient presented with right foot varus gait with a large, painful callus laterally, 5/5 motor strength in all lower limb muscle groups, and normal





sensation. Overground walking at a self-selected speed was assessed using a Vicon motion analysis system. The subject walked with shoes and an AFO and SMO.

Results: Compared to normative data for 11-13 year olds, the subject walked slower (1.14 vs. 1.34 m/s) with a lower cadence (109 vs. 122 steps/min) and with an increased percent of the cycle in stance phase. Kinematics showed bilateral asymmetry in foot progression, ankle angles in multiple planes, and pelvis angles. Right foot progression deviations were associated with excessive plantarflexion in late stance that did not translate into increased push-off force for propulsion. Excessive swing phase knee flexion bilaterally was likely a consequence of ankle plantarflexion and muscle involvement.

Conclusions: To our knowledge, these are the first published clinical gait data for an individual with Chromosome 19 Deletion. The condition may present with complicated gait deviations requiring careful consideration of surgical or other therapeutic options, which might include tendon lengthening or split or full transfers. Clinical gait analysis may assist in such planning and in understanding these complex presentations.

A Quality Improvement Initiative to Improve Surgical Site Infections In Pediatric Patients After Cardiothoracic Surgery

Presenting Author: Cassidy Golden, B.A.; Emory School of Medicine

Poster Number: 16

Cassidy Golden, Kathy Murphy RN, Joshua M Rosenblum MD PhD, Charlotta Eriksson, Parker Dunaway, Christina Calamaro PhD, Mohua Basu, Nikhil Chanani MD, S Shashidharan MD, Michael P Fundora MD

Background:

Since 2013, the Heart Center at Children’s Healthcare of Atlanta (CHOA) followed the standard best practice bundle recommended by Children’s Hospital’s Solutions for Patient Safety Network to prevent surgical site infections (SSIs). Despite following the bundle there was a noted increase in SSIs compared to the PC4 benchmark rate. The aim of this project was to reduce SSIs and standardize a bundle among pediatric patients post-cardiothoracic surgery.

Methods:

A multidisciplinary workgroup was established in 2015 to explore cases of SSIs. Initial Plan-Do-Study-Act (PDSA) cycles included supplying families with extra preoperative chlorohexidine gluconate wipes to use if surgery was rescheduled, improvements to the environment of care, replacing bath basins with Comfort Cloths, and scripted discharge phone calls focused on the surgical site. We also contacted PC4 centers with low SSI rates for additional bundle elements via the PC4 website. From October 2019 to December 2020, five additional PDSA cycles were undertaken. These cycles included standardized wound dressing preferences, weekly wound rounds, RedCap tracked wound healing, oral hygiene, daily linen changes, and dedicated patient specific stethoscopes. When discharged, photos of surgical wounds (provided by caregivers with permission) flagged as “in need of close follow up” were uploaded to the EMR with text message follow up to families on bathing.





Results:

In 2015, the SSI rate was 2.12 per 100 cases. By 2020, SSI rates decreased to 0.95 per 100 cases. SSI rates continued to decline to 0.61 per 100 cases by 2022.

Conclusion:

Since 2015 and with the implementation of several PDSA cycles, SSI rates have significantly decreased and remained low in pediatric patients after cardiothoracic surgery. Implementing hygiene bundles, standardized wound dressings, and post-discharge procedures contributed to maintaining low rates. Ongoing efforts continue to monitor SSI rates and the need for additional PDSA cycles.

Hepatic Response to Initiation of Veno-Arterial ECMO in Pediatric Patients

Presenting Author: Matthew Goldstein, DO; Children's Healthcare of Atlanta (CHOA)

Poster Number: 62

Goldstein, Matthew; Zinyandu, Tawanda; Davis, Joel; Fundora, Michael; Viamonte, Heather; and Maher, Kevin

Background

Extracorporeal membrane oxygenation (ECMO) is utilized as a rescue therapy for children with cardiorespiratory failure. These patients are at risk for end organ dysfunction due to hypoxia, ischemia, and reperfusion injury. Little is known about hepatic response to initiation of Veno-Arterial (V-A) ECMO in the pediatric population. The aim of this study is to evaluate the impact of initiating V-A ECMO on hepatic function in pediatric patients.

Methods

A retrospective review of patients placed on V-A ECMO at Children's Healthcare of Atlanta between July 2013 to May 2022 was performed following IRB approval. Data was obtained from the EMR and our institutional ECMO database which included NICU, PICU and Cardiac ICU patients. Data reviewed included: demographics, liver function tests, coagulation studies, survival, hepatic ultrasound, and ECMO run characteristics. Patients were further stratified into 6 groups based on their diagnosis at time of cannulation: cardiac (structural pathology), Pulmonary embolism, sepsis, pulmonary hypertension, respiratory, and others. "Others" included HLH, toxic ingestion, foreign body leading to asphyxiation, arrhythmia and pericarditis. Data was collected from the day prior to ECMO initiation to ECMO day 14. ECPR patients were excluded.

Results

There were 224 patients identified with ages ranging from 1 day to 22 years. Median ALT prior to ECMO cannulation was 24 U/L (IQR: 16-53) and median AST was 58 U/L (IQR: 32-116). The median AST demonstrated a transient rise, peaking at day 2 with a gradual return to baseline throughout the ECMO course. The median ALT did not show a similar trend. At baseline, median AST levels were similar



between survivors and non survivors (50U/L vs. 57U/L $p=0.55$) however, the mean response to ECMO initiation between survivors and non survivors was significantly different ($p=0.003$). This difference persisted throughout the 14 days of observation with survivors having lower median AST values than non-survivors throughout the ECMO course.

Conclusions

Initiation of V-A ECMO does not compromise hepatic function based on evaluation of transaminases. Patients with elevated transaminases on initiation of ECMO have a reduction to normal levels during their VA ECMO course, and non-survivors have higher transaminases compared to survivors.

Utilization of Early Extubation in Pediatric Liver Transplantation is Associated with Improved Postoperative Outcomes

Presenting Author: Matthew Goldstein, DO; Children's Healthcare of Atlanta (CHOA)

Poster Number: 61

Goldstein, Matthew; Liu, Katie; and Gilbertson, Laura

Background: Early extubation is becoming more common in pediatric liver transplant centers. However, there is minimal data on how this technique may affect postoperative recovery.

Methods: Data was collected retrospectively from pediatric patients who underwent liver transplantation from January 2015 to June 2021. Wilcoxon rank-sum test was utilized to compare extubation status and postoperative outcomes for non-normal data and t-test for normal continuous data. Postoperative complications of hepatic artery thrombosis, portal vein thrombosis, surgical re-exploration, and re-transplantation within 1 week were grouped together to account for the relative infrequency of these events.

Results: 173 patients who underwent liver transplantation were analyzed, with 121 patients (69.9%) successfully extubated immediately postoperatively in the operating room. Patients immediately extubated had older age (6.4 vs 5.2 years), lower PELD/MELD score (category 1A 5.8% vs 28.8%), and were more likely to present from home (77.7% vs 34.6%). Intraoperative factors associated with successful immediate extubation were decreased transfusion burden (mean 16.0 mL/kg [SD 21.3] vs 77.0 mL/kg [SD 88.6]), shorter surgical time (mean 332 minutes [SD 66.5] vs 392 [SD 112]), and full abdominal closure (81% vs 21%). 3 patients (2.5%) in the immediate extubation group required re-intubation while having overall decreased high flow nasal cannula requirements (mean 0.21 days [SD 0.71] vs 0.71 [SD 1.58]). They also had a decreased incidence of postoperative infections (9.9% vs 26.9%). The postoperative complication rate was lower in the immediate extubation group (24.8% vs 36.5%), but the difference was not statistically significant. The overall incidence of death (0 vs 5.8%), PICU length of stay (4.7 vs 11.4 days), and hospital length of stay (13.1 vs 22.8) was decreased in the immediate extubation group.

Conclusion: Approximately 70% of our pediatric liver transplant patients were successfully immediately extubated postoperatively in the operating room. Those patients were found to require less high flow



nasal cannula, had lower infection rates, shorter ICU and hospital lengths of stay, and decreased incidence of death. Overall, our results show that with proper patient selection and the utilization of an appropriate postoperative pain regimen in the ICU, immediate extubation allows for improved recovery after pediatric liver transplantation.

Incidence, Risk Factors and Outcomes of Acute Kidney Injury After Pediatric Cardiac Surgery

Presenting Author: Klevi Gollosi, B.S.; Emory University School of Medicine

Poster Number: 17

Klevi Gollosi, BS; Shayli Patel, BA; Maximilian Brady, BS; Yijin Xiang, MPH; Stella Shin, MD; Scott Sutherland, MD; Mohan John, MD; Richard U. Garcia, MD; David Kwiatkowski, MD; Asaad G. Beshish, MD

Introduction: The onset of acute kidney injury (AKI) following pediatric cardiac surgery has been reported previously. However, peri-operative risk factors and short-term outcomes have varied significantly between reports. We aimed to describe the behavior of postoperative AKI at our institution.

Methods: Single center, retrospective cohort study of patients who underwent STAT 3, 4, and 5 cardiac surgeries between 01/2016 and 12/2021. The primary outcome was to reveal the incidence of AKI, defined using the KDIGO scoring system, at our institution. We then divided the cohort into patients with stage 2/3 AKI and those with stage 1 or no AKI. Secondary outcomes were to compare overall fluid balance, postoperative morbidity, and mortality between the two groups. Analysis was performed using appropriate statistics with a significance level of $p = 0.05$.

Results: Our study included 1199 patients. The median age and weight at the time of surgery were 75 days (IQR 7, 1005) and 3.4 kg (IQR 2.8, 4.32), respectively. There were 25.1% (302) patients who developed stage 2/3 AKI. When comparing patients who developed stage 2/3 AKI with those with stage 1 or no AKI, patients in the stage 2/3 AKI group had longer cardiopulmonary bypass time (142 vs 132 min., $p < 0.001$), longer cross clamp time (81.5 vs 78 min., $p = 0.049$), lower preoperative serum creatinine (0.3 vs 0.4, $p < 0.001$), longer duration of mechanical ventilation (MV) (66.2 vs 33.63 hours, $p < 0.001$), higher rates of cardiac arrest (14.2 vs 5.8%, $p < 0.001$), required more postoperative extracorporeal life support (ECLS) (12.9 vs 4.6%, $p < 0.001$), had longer overall length of stay (19 vs 14 days, $p < 0.001$), and higher rate of operative mortality (14.6 vs 4.2%, $p < 0.001$). There was no difference between the groups in total urine output and volume status on postoperative days 1 and 2.

Conclusion: We delineate those patients who developed postoperative stage 2/3 AKI had longer CPB and cross-clamp times, longer duration of MV, higher rates of cardiac arrest, required more postoperative ECLS, had longer length of stay, and higher operative mortality. Future prospective, multi-center studies and randomized studies are required to further investigate these findings.

Early Life Pain Alters The Response To An Immune Challenge In Adult Male And Female Rats





Presenting Author: Morgan Gomez, M.Sc.; Georgia State University

Poster Number: 18

Gomez, Morgan; Macik, Melani; Harder, Hannah; Pandit, Malika; and Murphy, Anne

Background: Premature infants are more likely to be admitted to the Neonatal Intensive Care Unit (NICU) where they experience upwards of 10-18 painful procedures each day, often without anesthesia or analgesia. Preclinical and clinical studies have shown that neonatal pain disrupts normal CNS development in multiple ways that persist into adulthood. We have previously reported that early life pain results in an exaggerated febrile response following an immune challenge (administration of lipopolysaccharide; LPS) in adulthood. Administration of LPS induces the release of inflammatory cytokines in the periphery to stimulate prostaglandin E2 (PGE2) production. Centrally, PGE2 binding to the EP3 receptor (EP3R) within the hypothalamic median preoptic area (MnPO) induces a pyrogenic (fever) response. Here, we investigate if early life pain (ELP) alters PGE2 signaling within the MnPO. Methods: Male and female rats were exposed to a short-term inflammatory insult induced by intraplantar administration of 1% carrageenan on the day of birth (P0). In adulthood (P60-P90), Thermicron iButtons were implanted to monitor core body temperature; 14 days later, LPS was injected to elicit an immune response. Rats were sacrificed at one of 3 time points post-LPS: 24 hours, group peak fever, or 2 hours. Brain tissue was analyzed via immunohistochemistry for VGAT, VGLUT, Fos and prostaglandin receptor 3 within the MnPO and Cox-2 within the organum vasculosum of the lamina terminalis (OVLT). A whole brain survey of Fos activation patterns was also conducted for analysis of the global brain response to LPS. Results and Conclusions: LPS administration resulted in an elevated febrile response in ELP males and females compared to controls and increased sickness behaviors in ELP females. Immunohistological analysis revealed sex and treatment differences in cellular activation in several brain regions and increased receptor and transporter expression in the MnPO in ELP rats. Cox-2 expression is also increased at peak fever in ELP rats. Together, these studies are consistent with clinical studies reporting children experiencing unresolved pain during the perinatal period show an increased severity of sickness behavior and altered immune signaling following exposure to a pathogen and will provide a foundation for future studies examining the biological underpinnings.

MicKey Button Vesicostomy in Pediatric Kidney Transplant Recipients –Single Center Experience

Presenting Author: Brittney Grabowski, MSN; Children's Healthcare of Atlanta

Poster Number: 117

Grabowski, Brittney; Combs, Meredith; Londeree, Jackson; Arceo-Olaiz, Ricardo; Smith, Edwin; Garro, Rouba

Background: Obstructive uropathy is a common cause of end-stage renal disease in pediatric kidney transplant (KT) recipients. Management of ongoing bladder dysfunction post-transplant can be a challenge with potential effects on long-term graft outcomes. We evaluate the course and outcomes of MicKey button vesicostomy at a high-volume pediatric transplant hospital as a temporary measure for bladder drainage post-transplant (Bartsch et al., 2002)





Methods: We performed a retrospective chart review of 200 active pediatric (≤ 21 years of age) KT recipients at our center. We identified nine patients with a Mickey button vesicostomy. Four out of nine (44%) had an existing Mickey button vesicostomy at time of transplant. Five out of nine (56 %) patients underwent Mickey button vesicostomy placement posttransplant. The median time to Mickey placement post KT was 30 months.

Results: Recurrent urinary tract infection (UTI) was common among all patients who underwent Mickey button vesicostomy placement. Of the nine patients, eight were converted to other means of urinary diversion with media time of placement to conversion or removal of 1,011 days. The majority of patients were transitioned to Mitrofanoff for ongoing bladder management (50%), with the remaining opting for closure (25%) or cutaneous vesicostomy (25%). The most common cause of Mickey removal or conversion was recurrent UTI and rising creatinine. The most common bacteria causing symptomatic UTI was *Pseudomonas aeruginosa*. Bacterial colonization was common, occurring in seven out of nine patients (78%). The most common bacteria causing colonization was *E. Coli*. The mean eGFR at the time of Mickey placement was 57.3 (29.2) mL/min/1.73 m² compared to 47.4 (24.3) mL/min/1.73 m² at time of removal.

Conclusions: Mickey button placement posttransplant is used as a means for temporary urinary diversion in pediatric KT patients but may impose high risk of UTI development and worsening graft function. Future state of this project will involve evaluating the effect of Mickey button vesicostomy on graft function over time and compare outcomes to a convenience sample of pediatric KT patients who underwent alternative means of urinary diversion.

Measurement of PM2.5 and Particulate Black Carbon in Indoor and Outdoor Air at Childcare Centers and Residential Environments in the Atlanta Metropolitan Area

Presenting Author: Roby Greenwald, PhD; Georgia State University

Poster Number: 93

Yu Jung Lin, Roby Greenwald

Background: Particulate matter less than 2.5 μm (PM2.5) and specifically particulate black carbon (BC) are well-known to have adverse human health effects. Children are a recognized at-risk population for these pollutants; however, both exposure and health outcome assessment is logistically and ethically difficult in this age range. The ongoing Air Pollution Exposure in Childcare Settings (APECCS) study measures indoor and outdoor air pollution exposure in children 3-4 years old who attend childcare centers in the Atlanta metropolitan area. APECCS performs health outcome assessment through the non-invasive collection of saliva samples for metabolome-wide association analysis. This presentation pertains to PM2.5 and BC measurements conducted in winter 2023.

Methods: We conducted 4-week sampling campaigns in winter 2023 at two childcare centers: a “distant” site not near a major highway (0.75 miles from highway I-20) and a “near-road” site adjacent to a 14-lane segment of highway I-75/85 as well as a freight rail corridor, MARTA station, and several parking garages. We used multiple microsensor devices to measure PM2.5 and a microaethalometer to





measure BC. Each week, two participants also performed residential and transportation environment measurements.

Results: Indoor and outdoor PM_{2.5} and BC concentrations are higher at the near-road site than the distant site. Near-road PM_{2.5} was 11.43 $\mu\text{g}\cdot\text{m}^{-3}$ compared to 8.19 $\mu\text{g}\cdot\text{m}^{-3}$ the distant site. Near-road BC was 1.16 $\mu\text{g}\cdot\text{m}^{-3}$ and distant BC was 0.84 $\mu\text{g}\cdot\text{m}^{-3}$. At both sites, PM_{2.5} did not exhibit pronounced diurnality. In contrast, near-road BC levels did exhibit a diurnal pattern consistent with changes in traffic volume with periodic increases associated with nearby locomotives. At participants' homes, high concentrations of PM_{2.5} and BC concentration were observed during meal preparation.

Conclusion: BC concentrations at both the near-road and distant site are influenced by motor vehicle emissions. Other additional combustion sources such as heavy-rail locomotives were observed to have significant impact. Indoor BC levels are highly-correlated with outdoor BC, indicating infiltration of ambient air pollution to indoor spaces. PM_{2.5} levels are consistent with region-wide changes in air quality influenced by meteorology. Indoor PM_{2.5} is also correlated with ambient levels with a significant contribution from indoors sources such as cooking activities.

Exposure Assessment for Gas-Phase Air Pollution at Childcare Centers: Oxides of Nitrogen and Ozone Results from the Air Pollution Exposure in Childcare Settings Study

Presenting Author: Roby Greenwald, PhD; Georgia State University

Poster Number: 92

Jack Alperstein, Yu Jung Lin, Roby Greenwald

Background: The ongoing Air Pollution Exposure in Childcare Settings (APECCS) study measures indoor and outdoor air pollution exposure in children 3-4 years old who attend childcare centers in the Atlanta metropolitan area. Sampling campaigns last four consecutive weeks at each site and also include air quality measurements in residential and transportation microenvironments. APECCS collects weekly saliva samples for metabolome-wide association analysis. This presentation pertains to oxides of nitrogen (NO_x) and ozone (O₃) measurements conducted in winter 2023.

Methods: We used light-absorption instruments to measure both NO_x and O₃. Both instruments monitored ambient air quality exclusively. NO_x is the sum of NO and NO₂, and NO₂ is measured directly by absorption at 405 nm and NO indirectly by chemically oxidizing to NO₂. O₃ is measured by absorption at 254 nm. We collected data with 1-minute time resolution and aggregated to 1-hour averages.

Results: At the two daycare centers monitored, we found different diurnal patterns in NO_x and O₃ concentration. The first center is 0.75 miles from a major interstate highway (I-20) but otherwise not near a major air pollution source. The mean NO_x concentration was 22.1 ppb, and diurnal variability paralleled highway traffic volume. O₃ levels were modest at this location (mean = 21.8 ppb, max = 43 ppb) and demonstrated a diurnal pattern corresponding to available sunlight. The second center is located adjacent to a freight rail corridor, MARTA station, parking garage, and a major 14-lane interstate highway (I-75/85). NO_x levels at this location were higher (mean = 27.2 ppb) and exhibited a diurnal pattern consistent with traffic volume with additional increases in NO_x observed to correspond to the





presence of freight locomotives. This sampling campaign occurred later in the season with longer day lengths and more intense sunlight, and O₃ levels were higher (mean=27.8 ppb, max= 50.4 ppb).

Conclusions: NO_x concentrations at childcare centers are associated with proximity to combustion sources. This is related to motor vehicle traffic with the additional contribution of nearby sources including locomotives. O₃ levels in the winter season were modest due to reduced solar intensity (and the dependence of O₃ concentration on solar intensity).

Low arginine bioavailability and clinical outcomes in children with sickle cell disease (SCD) hospitalized with vaso-occlusive pain episodes (VOE).

Presenting Author: Dunia Hatabah, MD; Emory University

Poster Number: 76

Hatabah, Dunia; Bakshi Nitya; Brown, Lou Ann; Harris Frank; Leake Deb; Korman, Rawan; Rees, Chris A, Griffiths, Mark; Dampier, Carlton; Morris Claudia R

Background: Global arginine bioavailability ratio (GABR) (Arginine/[Citrulline+Ornithine]) is associated with clinical outcomes including pain, pulmonary hypertension risk and mortality in SCD. We have previously shown that patients with SCD-VOE have an altered arginine metabolome. Arginine is a conditionally essential amino acid synthesized from citrulline in the kidneys. During VOE, hemolysis leads to the release of erythrocyte-arginase (arginine-metabolizing enzyme) that converts arginine into ornithine. Arginine-to-ornithine ratio (arg/orn) is a biomarker of arginase activity, while GABR incorporates the impact of kidney function on global arginine bioavailability. The association between arginine bioavailability and clinical outcomes has not been sufficiently explored in children with SCD-VOE.

Objective: To evaluate associations between arginine bioavailability and clinical outcomes in children with SCD-VOE receiving intravenous (IV) arginine replacement therapy (ART).

Methods: Double-blinded randomized-controlled trial of ART (n=72) vs. placebo (n=36) in hospitalized children with SCD-VOE requiring IV opioids (protocol in Reyes et al 2022, AmJHematol). Time-to-crisis-resolution (time-of-study-drug-delivery to last IV opioid in hours), total IV opioid use (morphine equivalents, mg/kg) and targeted amino acids were obtained at hospital presentation before study drug delivery and at discharge. Mean±SD and Pearson correlation analyses between groups were performed where appropriate.

Results: Plasma arginine levels were low at VOE presentation (mean 50±28 μM), with hypoarginemia (<60 μM) found in 74% of patients. Arg/orn correlates to arginase concentration (r= -0.38, p<0.0001). Time-to-crisis-resolution strongly correlates with total opioid use (r=0.72, p<0.0001). Arginine bioavailability at presentation inversely correlates to time-to-crisis-resolution for both arg/orn and GABR (r= -0.39 p=0.01) in the placebo arm only, which was lost after arginine therapy (arg/org: r= -0.06, p=0.7; GARB: r= -0.04, p=0.7). Similar trends are observed for total opioid use.



Conclusion: Low arginine bioavailability predicts worse clinical outcomes in patients with SCD-VOE, including a longer time-to-crisis resolution and a greater use of IV opioids. Arginine bioavailability may represent a novel biomarker of SCD-pain severity. This data further confirms arg/orn as a surrogate for arginase activity reflective of hemolytic rate as previously described. ART ameliorates the influence of arginine deficiency on clinical outcomes related to pain in SCD. An NHLBI/PECARN supported phase-3 trial of ART is ongoing.

LiverQuant: An improved method for precise quantitative whole slide histologic analysis of liver digital pathology

Presenting Author: Dominick Hellen, BA; Emory University

Poster Number: 19

Dominick J. Hellen, Saul J. Karpen

Background: Current means to quantify cells, gene expression, and fibrosis of liver histological slides are not standardized in the research community and typically rely upon data acquired from a limited selection of random regions identified in each slide. As such, analyses are subject to potential selection bias as well as a limiting number of analyzable data elements throughout the slide, leading to significant increases in intra- and inter-experimental variables. We present an automated whole-slide approach to quantify cells and fibrosis in standard liver slide histology, termed “LiverQuant”.

Methods: Fibrosis (Sirius Red), cholangiocyte (keratin 19), and macrophage (F4/80) counts were analyzed from the same mouse liver slides using 3 methodologies: manual count, FIJI, and LiverQuant. Whole-slide scans of digitized histologic images were used to render a more comprehensive analysis of presented data elements. Histologic images were prepared and analyzed using a sequence of customizable GROOVY-based scripts within Qupath. The scripts are tailored toward generating an average staining intensity, followed by automated batch quantification of the anticipated cellular matrices. We utilized standard metrics, such as accuracy, rate of detection, and slide areas covered by maximum region of interest (ROI), to assess and establish the validity of LiverQuant.

Results: The package of scripts in LiverQuant, when compared to two conventional methodologies of histological quantification (Manual and FIJI) demonstrated comparable accuracy of detection and quantification of fibrosis and cell counts. Importantly, LiverQuant had 2 significant advantages over conventional quantitative methodologies: increased speed, and a 50-fold greater tissue area coverage. We utilized LiverQuant to accurately measure various hepatic cell types and degree of fibrosis in our laboratory's newly established genetic mouse model of biliary atresia, the liver conditional knockout of Pkd1l1 (PMID 36645229).

Conclusion: LiverQuant, using publicly available open-source code (GitHub), improves the reliability and reproducibility of experimental results while reducing the time scientists require to perform bulk analysis of liver histology. This analytical process is readily adaptable by most laboratories, requires minimal optimization, and its principles and code can be optimized for use in other organs.



Investigating the Impact of Intervention Time on Development in African American Children with Autism Spectrum Disorder

Presenting Author: Mackenzie Hines-Wilson, B.A.; Emory University School of Medicine

Poster Number: 118

Mackenzie Hines-Wilson, Stormi White, Anna Abbacchi, Jennifer Lowe, John Constantino, Ami Klin, Warren Jones, Daniel Geschwind, Cheryl Klaiman

Background: Compared to non-Hispanic White children, African American (AA) children experience a persistent delay in receiving an autism spectrum disorder (ASD) diagnosis (Constantino et al., 2020). AA children with ASD have double the likelihood of having co-occurring intellectual disability (ID) (Meanner et al., 2021). Prior studies have yet to investigate average amount of intervention time AA children receive per week post-ASD diagnosis and the impact on development.

Methods: AA toddlers with ASD ($n=46$, $\text{Mage}(\text{SD})=27.26(4.65)$ months) enrolled in a longitudinal genetics study. Developmental skills at time 1 (T1) and at a follow-up visit (T2) 18 months later were assessed with the Mullen Scales of Early Learning (MSEL) (which is standardized for developmental age) and the Autism Diagnostic Observation Schedule (ADOS-2). T1 and T2 intervention hours were assessed with the ACE 3 Intervention History survey.

Results: Paired-samples t-tests were used to compare the toddlers at T1 and T2. Intervention ranged from 0-1.75 hours (T1) and 0-20.00 hours (T2). At T2, the toddlers received significantly more ($t(45)=-4.91, p<.001$) intervention time ($M(\text{hours})(\text{SD})=4.13(4.96)$) compared to T1 ($M(\text{hours})(\text{SD})=0.45(0.60)$). MSEL domain age equivalent scores were significantly higher at T2. Visual reception increased from 17.62($\text{SD}=5.82$) months to 30.59($\text{SD}=11.41$) months ($t(36)=-7.09, p<.001$). Fine motor increased from 18.93($\text{SD}=5.17$) months to 31.48($\text{SD}=11.38$) months ($t(41)=-9.60, p<.001$). Receptive language (RL) increased from 12.05($\text{SD}=6.97$) months to 24.95($\text{SD}=13.98$) months ($t(41)=-6.35$). Expressive language (EL) increased from 13.08($\text{SD}=6.99$) months to 25.94($\text{SD}=14.04$) months ($t(38)=-6.99, p<.001$). ADOS-2 total and social affect scores were significantly ($t(25)=2.72, p=.012$; $t(25)=3.48, p=.002$, respectively) lower at T2 ($M(\text{points})(\text{SD})=19.08(5.58)$; $M(\text{points})(\text{SD})=14.04(4.52)$, respectively) than T1 ($M(\text{points})(\text{SD})=21.62(5.10)$; $M(\text{points})(\text{SD})=16.81(3.80)$, respectively). Within-group correlations showed ST/OT hours were positively associated with increased RL ($r=.393, p=.029$; $r=.736, p=.001$, respectively) and EL ($r=.384, p=.033$; $r=.719, p=.002$, respectively) t-scores at T2.

Conclusions: Given the benefits from a modest increase in intervention post-diagnosis, it is probable that an increase in intervention time would result in even greater gains and reduce the burden of ID. Given that the average amount of intervention received was less than 5 hours/wk and the average recommended (Hyman et al., 2020) is 20-25 hours/wk, more effort is needed to ensure children are receiving adequate intervention to help them reach their potential.

Improving Early Detection of Abnormal GMA in the NICU – Challenges and Potential Solutions

Presenting Author: Ryan Huang, MPH; Emory University





Poster Number: 120

Huang, Ryan; Kjeldsen, Caitlin; Moran, Megan; Scarbrough, Paige; Jung, Joon; Boswell, Lynn; Ostrander, Betsy; Ayala, Lauren; Mazur, Margaux; Duncan, Andrea; Jedraszko, Aneta; deRegnier, Raye-Ann; and Maitre, Nathalie L.

Background: Extremely preterm infants are 20 times more likely to develop cerebral palsy and 9-10 times more likely to develop other neuro-motor delays than term infants. Improved early detection has decreased time to diagnosis; however, current methods used in the NICU, such as the General Movements Assessment (GMA), are resource-intensive and prone to interpretation bias and reliability concerns. To study these implementation challenges, the US EDI for CP Network has begun a new initiative leveraging both advanced GMA examiner reads and a previously developed automated detection method with a pressure-sensor mat (GMat). Here, we report preliminary findings surrounding the implementation of inter-examiner reliability.

Methods: The current implementation study included 93 infants (36 0/7 and 44 6/7 PMA) across four sites. Simultaneous video and GMat recordings of the infant's movements were conducted at the bedside and independently scored by two randomized advanced GMA examiners. Monthly examiner meetings resolved discrepancies between normal and abnormal (Cramped synchronized, CS) scores using global review and General Movement Optimality Scoring (GMOS) in more challenging cases. We conducted descriptive analyses and Cohen's kappa to review inter-examiner reliability.

Results: Of 93 recordings (mean PMA = 37.9 weeks, SD = 2.1), 11 videos (11.8%) were coded as CS. Overall, 78 videos received a unanimous score (normal or abnormal), and 15 videos (16.1%) had discrepant results that required resolution via the monthly examiner meetings. Of the 15, one was finalized as CS, while all others were coded as poor repertoire (PR). 4 of 15 required GMOS scoring to differentiate patterns. After the first meeting and GMOS, the kappa statistic improved from 0.36 to 0.43. Of note, the unrefined GMat sensor algorithm detected 100% of CS for the final read but misclassified 10% as false positives – examiners classified them as PR.

Conclusion: Our preliminary findings highlight moderate agreement between randomized trained GMA examiners, which improved with monthly reviews. This finding warrants further investigation into inter-examiner reliability and optimized implementation of GMAs across NICU settings. We anticipate the study to guide the eventual implementation of this early detection method for all NICU infants using a refined GMat algorithm.

Higher Parental Regulation/Structure is Associated with Greater Infant Sensitivity & Attraction to Parent in Infants with Disabilities

Presenting Author: Junwen Huang, Associate of Arts; Emory University

Poster Number: 119

Huang, Junwen; Maitre, Nathalie; Ryals, Paige Scarbrough; Dudley, Tytiona; and Neel, Mary Lauren

Background





Parenting characteristics, including warmth, sensitivity, and structure, are associated with improved developmental outcomes in infants with disabilities. Emotional connection (EC) is a validated psychological construct that is foundational to the parent-infant relationship. EC may mechanistically link parenting input and child development. To investigate this link, we examined parenting characteristics associated with parent-infant EC.

Methods

Our prospective observational cohort study included infants 4-14 months corrected age (CA) with or at high-risk for cerebral palsy (CP). Participants completed two research lab visits 6 weeks apart, with a Parenting Styles and Dimensions Questionnaire (PSDQ) and a 5-minute parent-child video-recorded free play session. We coded the play session using the Welch Emotional Connection Screen (WECS) for sensitivity/reciprocity, attraction, vocal communication, and facial expressiveness in parent and child. We focused on PSDQ warmth and regulation subscales, scoring acceptance/encouragement versus reasons/explanations, respectively. We performed linear regressions adjusting for repeated measures between parenting style components on PSDQ and parent-infant EC on WECS.

Results

In total, 63 measurements were obtained from 35 dyads, 65% black, 20% Hispanic (29 dyads completed both visits). Mean gestational age of infants was 33 weeks (SD) and mean CA was 9 months (SD). Parents with higher PSDQ regulation scores displayed higher WECS sensitivity (coeff=0.335, p=0.010). More importantly, children of parents with higher PSDQ regulation scores also displayed higher WECS sensitivity scores (coeff=0.267, p=0.041), as well as higher WECS attraction to parent scores (coeff=0.316, p=0.015). Parental warmth on the PSDQ was not significantly correlated with any WECS scores.

Conclusion

This is the first study to examine associations between a validated parenting questionnaire and WECS coding. It adds to an emerging body of evidence suggesting the particular importance of parental regulation, akin to parental structure, for infants at high-risk of disabilities. Opportunities abound for interventions to support parental structure in infants with and at high-risk for CP.

Comparative Single Cell Analysis of Inflamed vs Non-Inflamed Crohn's Disease Ileal Mucosa Reveals Both Shared and Unique Inflammatory Signatures

Presenting Author: Yeonjoo Hwang, MS; Emory University

Poster Number: 123

Hwang, Yeonjoo; Maddipatla, Sushma C; Murthy, Shanta; Dodd, Anne; Kolachala, Vasantha; Gibson, Greg; Cutler, David J; Qiu, Peng; Matthews, Jason D; and Kugathasan, Subra

Background





Crohn's disease (CD) is an inflammatory bowel disease characterized by relapsing and remitting mucosal injury along the gastrointestinal (GI) tract, most often affecting the ileum. The inflammatory response induces cellular and transcriptional changes that are not yet fully understood. Thus, we used scRNA-seq to examine cell-type differences in inflamed versus non-inflamed ileal tissues from CD patients to better define the cellular and transcriptional changes that occur during inflammation.

Methods

Ileal mucosal biopsies were collected from 14 consented CD patients (8 inflamed, 6 non-inflamed) during endoscopy at Children's Healthcare of Atlanta. Samples were digested into single cells with cold protease before encapsulation with a 10x Chromium controller. After library preparation, sequencing was performed with the Illumina NovaSeq at a depth of 50k reads per cell. Reads were aligned to the human reference genome with Cell-Ranger and the count matrices were analyzed with Seurat (v4.3.0) after filtering out low-quality cells. Clusters were annotated manually, and downstream Principal Component Analysis (PCA) and differential gene expression analysis were performed to examine differences between inflamed and non-inflamed samples.

Results

33,317 inflamed and 27,432 non-inflamed cells were clustered into 30 cellular subtypes. Interestingly, the cell proportion of inflammatory macrophages was increased in the non-inflamed samples relative to the inflamed, while those of several B cell clusters were increased in the inflamed. PCA indicated significant separation by phenotype in many clusters including inflammatory macrophages, B cells, and stromal cells, whereas there was no significant separation in goblet cells. Macrophages exhibited decreased expression of S100 genes and increased expression of CFD, PPIF, CRIP1 and HLA-DRB5 in inflamed samples. Additionally, the B cells of inflamed samples expressed less immunoglobulin genes and more GUCA2A, which is an activator of intestinal guanylate cyclase.

Conclusions

Our analysis of CD ileal mucosa revealed differing cell proportions between inflamed and non-inflamed regions, significant separation of inflamed and non-inflamed cells in many clusters, and several changes in the expression of genes involved in immune and intestinal processes. Further analyses, such as GSEA, are being performed to examine the implicated pathways and characterize the active inflammation state in the ileum of CD patients.

Chronic ethanol exposure induces mitochondrial dysfunction and alters gene expression and metabolism in human cardiac spheroids

Presenting Author: Hyun Hwang, B.S.; Emory University School of Medicine

Poster Number: 121

Hwang, Hyun; Liu, Rui; Eldridge, Ronald; Hu, Xin; Forghani, Parvin; Jones, Dean; and Xu, Chunhui

Background





Chronic alcohol consumption in adults can induce various cardiac toxicities such as arrhythmias, cardiomyopathy, and heart failure. Prenatal alcohol exposure can increase the risk of developing congenital heart defects among offspring. Understanding the molecular mechanisms underlying long-term alcohol exposure-induced cardiotoxicity can help guide the development of therapeutic strategies.

Methods

Cardiomyocytes derived from human-induced pluripotent stem cells (hiPSC-CMs) were engineered into cardiac spheroids and treated with clinically relevant concentrations of ethanol (17 and 50 mM) for 5 weeks. The cells were then analyzed for changes in mitochondrial features, transcriptomic and metabolomic profiles, and integrated omics outcomes.

Results

Following chronic ethanol treatment of hiPSC-CMs, a decrease in mitochondrial membrane potential and respiration and changes in expression of mitochondrial function-related genes were observed. RNA-sequencing analysis revealed changes in various metabolic processes, heart development, response to hypoxia, and extracellular matrix-related activities. Metabolomic analysis revealed dysregulation of energy metabolism and increased metabolites associated with the upregulation of inflammation. Integrated omics analysis further identified functional subclusters and revealed potentially affected pathways associated with cardiac toxicities.

Conclusion

Chronic ethanol treatment of hiPSC-CMs resulted in overall decreased mitochondrial function, increased glycolysis, disrupted fatty acid oxidation, and impaired cardiac structural development.

Space microgravity increases expression of genes associated with proliferation and differentiation in human cardiac spheres

Presenting Author: Hyun Hwang, B.S.; Emory University School of Medicine

Poster Number: 122

Hyun Hwang, Antonio Rampoldi, Parvin Forghani, Dong Li, Jordan Fite, Gene Boland, Kevin Maher, and Chunhui Xu

Background: Space microgravity can significantly change cell activities and function. Previously, we reported upregulation of genes associated with cardiac proliferation in cardiac progenitors derived from human induced pluripotent stem cells (hiPSCs) that were exposed to space microgravity for 3 days.

Methods: Here we investigated the effect of long-term exposure of hiPSC-cardiac progenitors to space microgravity on global gene expression. Cryopreserved 3D hiPSC-cardiac progenitors were sent to the International Space Station (ISS) and cultured for 3 weeks under ISS microgravity and 1G conditions.

Results: RNA-sequencing analysis revealed upregulation of genes associated with cardiac differentiation, proliferation, and cardiac structure/function and downregulation of genes associated with extracellular



matrix regulation in the ISS microgravity culture compared with the ISS 1G culture. Gene ontology analysis and Kyoto Encyclopedia of Genes and Genomes analysis identified upregulation of biological processes, molecular function, cellular components, and pathways associated with cell cycle, cardiac differentiation and function.

Conclusion: Taking together, these results suggest that space microgravity has beneficial effect on differentiation and growth of cardiac progenitors.

Examining Early Intervention providers' perception of implementing parent-mediated intervention model

Presenting Author: Nailah Islam, Bachelor of Science; Emory

Poster Number: 124

Islam, Nailah; Chatson, Emma; Demetri, Brooke; Yohannes, Millena; Pickard, Katherine; Hendrix, Nicole

Background: State funded Early Intervention (EI) programs provide families with the necessary tools to navigate autism spectrum disorder and developmental delays by teaching caregivers to implement evidence-based intervention strategies. Parent mediated interventions (PMIs) are an effective approach in intervention (Nevill et al., 2018) that have been the focus of implementation efforts within EI systems (Stahmer et al., 2020). While the effectiveness of PMIs has begun to be established within EI systems, less is known about the EI provider's experience implementing PMIs. This study's objectives were to: 1) Examine EI providers' perspectives on the feasibility of delivering Project ImPACT (Ingersoll & Dvortcsak, 2019); 2) Understand the reach to children enrolled in EI services; and 3) Examine providers' intent to sustain the program following training efforts.

Methods: Sixteen providers within Georgia's EI system participated in an exit interview after training in Project ImPACT and attending group consultation. The exit interview was semi-structured focusing on 1) overall impressions of the intervention; 2) how providers decided who to deliver the intervention to and why; 3) whether the intervention was delivered to families on the provider's caseload as well as in the context of the research study; 4) the feasibility of learning and implementing Project ImPACT; 5) any adaptations made to the intervention; and 6) providers' intent to sustain the intervention with future EI families. Thematic analysis was used to summarize primary qualitative themes.

Results: Qualitative analysis is ongoing. Primary themes present in the interviews included providers' overall satisfaction with Project ImPACT, adaptations made based on family needs and priorities, the number of families who received the interventions and plans for future implementation.

Conclusion: Preliminary results from this study suggests that providers perceive Project ImPACT feasible to implement although may be adapted in response to family circumstances. Importantly, while providers reported delivering Project ImPACT to many families on their caseload, they described specific decisions around who they delivered the programs to. Limitations include not having exit interviews from providers that prematurely ended training or did not enroll in training. Continued investigation into the experience of EI providers when implementing PMIs is needed



Association of Age with Acuity and Severity of Illness at Initial Presentation in Children, Adolescents, and Young Adults with Leukemia and Lymphoma

Presenting Author: Tarun Jain, MD; Emory University/Children's Healthcare of Atlanta

Georgia CTSA TL1 TR002382 and UL1 TR002378, 2022-2024

Poster Number: 63

Jain, Tarun; Ji, Xu; Himes, Alexandra; DeGroot, Nicholas; Coxhead, Cortland; Mertens, Ann; and Castellino, Sharon M.

Background:

Adolescent and Young Adult (AYA) patients diagnosed with cancer at ages 15-39 years often have increased morbidity and mortality compared with younger patients, partly due to differences in cancer biology and access to healthcare resources. Acuity and severity of illness at presentation is an outcome measure understudied in this vulnerable population.

Objective:

To characterize the acuity and severity of illness at initial presentation of a hematologic cancer by patient age.

Design/Methods:

We performed a retrospective analysis of a cohort of patients diagnosed with leukemia or lymphoma in 2010-2018 at Children's Healthcare of Atlanta. We abstracted data on intensive care unit (ICU) resource use in the first 72 hours of care, stage at diagnosis in lymphomas, and white blood cell (WBC) count and central nervous system disease in leukemias from medical records. Bivariate comparisons were performed on the data abstracted to date.

Results:

For leukemia, a higher proportion of patients less than 15 years of age presented with a WBC count of over 50,000 cells/microliter than patients 15-21 years of age (19% vs. 5%, $P=0.35$). No statistically significant difference in ICU resource use was observed across age groups. For lymphoma, no statistically significant difference was seen in stage or ICU resource use across age groups.

Discussion/Conclusions:

These preliminary results set the stage for continued data abstraction for the entire cohort, as well as for multivariable analysis that will test the association of acuity and severity of illness with age, adjusting for health insurance status, race, ethnicity, and local-area social vulnerability. Our findings will help inform strategies toward narrowing age disparities in outcomes of AYA hematologic cancers.



Hip joint kinematics and performance on a progressive lateral step-up test in children with cerebral palsy

Presenting Author: Shelley Jakiel, MBA, BS, LAT/ATC/OTC; University of Georgia

Poster Number: 20

Jakiel, Shelley; Whitten, Sydney; Batson, Trevor; Colquitt, Gavin; Li, Li; Vova, Joshua; Shen, Ye; and Modlesky, Christopher M.

Background: Cerebral palsy (CP) is associated with muscle weakness and limited mobility. The lateral step-up test (LSUT) is used to assess functional muscle strength. This study aimed to determine how hip joint kinematics of the more affected limb (MAL) during a LSUT are different in children with CP compared to typically developing controls and if the differences are related to LSUT performance. We hypothesized that 1) children with CP would have less hip flexion, hip abduction, and hip extension velocity during the concentric phase (i.e., push-off) of the LSUT, and 2) the expected lower LSUT performance in children with CP would be related to less hip flexion and extension velocity.

Methods: Twenty-three ambulatory children with spastic CP (5-11 y) and 23 typically developing controls were matched by age, sex, and race. Participants wore 53 reflective markers on bony prominences. The LSUT consisted of 20 s trials that progressively increased in step height (0, 10, 15, and 20 cm). Participants stood with the MAL stationary and the less affected limb alternating between platforms. Participants completed maximum repetitions during trials. Kinematic data were collected through motion capture and processed through Visual 3D.

Results: There were no group differences in hip flexion at any step height (all $p < 0.001$). Compared to controls, children with CP demonstrated less hip abduction at 10, 15, and 20 cm and less hip adduction velocity at 10 and 20 cm (all $p < 0.05$). In children with CP, hip flexion angle was negatively related to LSUT performance at 10 and 20 cm ($r_s = -0.422$ to -0.444 , $p < 0.05$), whereas hip flexion angle was positively related to LSUT performance at 0 and 10 cm in controls ($r_s = 0.454$ to 0.653 , $p < 0.05$). Hip extension velocity was positively related to LSUT performance at 10 cm, but only in children with CP ($r_s = 0.480$, $p = 0.021$).

Conclusion: The hip joint kinematics during lateral stepping are complex in children with CP and may require simultaneous evaluation of the knee and ankle to better understand their role while performing an LSUT.

Melatonin Regulates the Immune System of the Placenta Through its Circadian-Regulated Properties

Presenting Author: Tyana Joseph, N/A; Morehouse School of Medicine

Poster Number: 21

Joseph, Tyana T.; Thompson, Nia; Ogbuehi, Ulochukwu Bethel; Johnson, Erica L.

Background: Placental cells contain melatonin's synthesizing enzymes, serotonin N-acetyltransferase (AANAT) and N-acetylserotonin methyltransferase (ASMT), and melatonin's receptors, MT1 and MT2,





which are all expressed circadianly and regulated by endogenous melatonin. Thus, these cells rhythmically produce higher melatonin concentrations than the pineal gland during pregnancy. This allows melatonin to serve as a direct free-radical scavenger with potent immunomodulatory properties that enhance phagocytosis and lymphocyte proliferation and stimulate cytokine production during viral infection (HCMV) throughout gestation. Furthermore, substantial evidence links the circadian clock and melatonin with the synchronous programming of the immune system during pregnancy. Therefore, melatonin synthesis and activity in immune cells at the maternal-fetal interface are essential to maintain and placental homeostasis by increasing antioxidant activity, promoting an immunoregulatory environment, regulating circadian clock gene expression.

Methods: With written informed consent, placenta from healthy women (>18 years) will be collected from Emory University Midtown Hospital in Atlanta, GA. We will isolate decidual mononuclear cells, macrophages, and trophoblast cells from the term placenta. We will also culture trophoblast cell lines (JEG-3). Cells will be treated as follows: HCMV, LPS, 1mM Melatonin, LPS + 1mM Melatonin, and HCMV + 1mM Melatonin. We will determine the expression of melatonin-synthesizing enzymes (AANAT and ASMT), melatonin's receptors (MT1 and MT2), clock genes (BMAL1, CLOCK, PER, AND CRY1), and innate immune system activity (TLR4) through RT-qPCR.

Results: Data will be collected to determine the role of circadian-regulated melatonin during HCMV infection at the maternal-fetal interface. We will also elucidate if melatonin impacts the innate immune system by inducing a change in TLR activity after HCMV infection.

Conclusion: This data will suggest that melatonin is an essential molecule in maintaining the immune system of the placenta through its circadian-regulated properties. Furthermore, it may also suggest melatonin as either a therapeutic or biomarker for placental development abnormalities leading to preterm birth, preeclampsia, and intrauterine growth restriction (IUGR). Understanding melatonin's role at the maternal-fetal interface is crucial to develop therapeutic strategies to reduce adverse pregnancy outcomes.

Long non-coding RNA MALAT1 Regulates HMOX1 in Sickle Cell Disease-associated Pulmonary Hypertension

Presenting Author: Bum-Yong Kang, PhD; Emory University

Poster Number: 94

Viranuj Sueblinvong, Sarah S. Chang, Jing Ma, David R. Archer, Benjamin Kopp, Roy L. Sutliff, Changwon Park, Michael Hart, and Bum-Yong Kang

Rationale: Pulmonary hypertension (PH) causes morbidity and mortality in sickle cell disease (SCD). The release of heme during hemolysis triggers endothelial dysfunction and contributes to PH. Long non-coding RNAs (lncRNAs) may play a pivotal role in endothelial dysfunction and PH pathogenesis. This study determines lncRNAs that are affected by SCD and identifies MALAT1 as an important regulator of heme oxygenase-1 (HMOX1).





Methods and Results: Total RNAs were isolated from 15-17 weeks old sickle cell (SS) mice and littermate control (AA) lungs and subjected to lncRNA expression profiling using the Arrystar™ lncRNA array. Raw signal intensities were normalized in quantile method by GeneSpring GX software. Volcano plot filtering was used to screen for differentially expressed lncRNAs with statistical significance (fold change >1.5, $p < 0.05$). A total of 2,302 lncRNAs were upregulated and a total of 2,546 lncRNAs were downregulated in lungs of SS mice compared to AA mice. To validate differentially expressed lncRNAs in human and mouse, 6 lncRNAs were selected for quantitative PCR. We found that the levels of metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) were increased in SS mouse lungs. Human pulmonary artery endothelial cells (HPAECs) were treated with hemin and analyzed for MALAT1 or HMOX1 levels, which were increased in hemin-treated HPAECs. Lastly, loss of MALAT1 function reduced HMOX1 levels and increased ET-1 and VCAM1 levels.

Conclusion: These results suggest that SCD modulates MALAT1-HMOX1 axis and further characterization of MALAT1 function may provide new insights into SCD-associated endothelial dysfunction, PH pathogenesis, and identify novel therapeutic targets.

Young Women Accept a Developmentally Appropriate Cardiovascular Risk Assessment Tool That Changes Their Perceived Risk of Heart Disease

Presenting Author: Brianna Karim, BS; Emory University School of Medicine

This study was funded by NHLBI R03 HL155253 (PI: Gooding) and supported by the Georgia Clinical and Translational Science Alliance through the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1

Poster Number: 125

Karim, Brianna; Jergel, Andrew; Bai, Shasha; Bradley, Kolbi; Alvarez, Santiago J. A.; Gilmore, Amanda K.; Greenleaf, Morgan; Kottke, Melissa J.; Parsell, Maren; Patterson, Sierra; Sotos-Prieto, Mercedes; Zeichner, Elizabeth; and Gooding, Holly C.

Background: Cardiovascular disease (CVD) remains the leading cause of death for women in the US, yet many young women are unaware of their lifetime risk of CVD. We employed user-centered design principles to adapt a validated CVD risk prediction tool for young women.

Hypothesis: We hypothesized that young women would rate the tool (HerHeart) as user-friendly, be likely to recommend it to their friends, experience a change in their perceived risk of CVD, and report intent to change their health habits after engaging with it.

Methods: We recruited 60 young women ages 13-20 from two clinical practices in Atlanta, GA to engage with the HerHeart CVD risk prediction tool. Participants rated the tool's usability via the Website Analysis and Measurement Inventory (WAMMI), which is scored from 0 to 95. Participants rated their perceived 10-year and lifetime risk of CVD on a visual analog scale from 0 (Never going to happen) to 10 (Definitely will happen) before and after completing the tool. Participants reported their likelihood of recommending the tool to their friends and changing their health habits from 0 (Not likely at all) to 10 (Extremely likely).





Results: Participants rated the tool's usability highly on the WAMMI, with a median of 80 (74, 85). Participants' perceived 10-year risk of a heart attack increased from a median of 1 (0, 3) to 2 (1, 4), and perceived lifetime risk increased from a median of 2 (0, 4) to 3 (2, 6), on the 10-point scale after engaging with the tool. Participants were more than likely to recommend HerHeart to their friends, with a median of 8 (7, 10) and to report intent to change their health habits, with a median of 8 (7, 10) after completing the tool. Participant data captured in the HerHeart tool are shown in the Table.

Conclusions: The HerHeart tool is acceptable to young women and demonstrates potential for changing their risk perception and improving their health habits to reduce their risk of CVD. Future input from clinicians will include the feasibility of incorporating the tool in clinical practice.

Development of a pain-free nebulization technique a radical cure for pediatric patients against COVID-19

Presenting Author: Rama Kashikar, Masters in Pharmaceutical Sciences; Mercer University

Poster Number: 22

Rama Kashikar, Arun K. Kotha, Mahavir Chougule

Since the beginning of the COVID-19 pandemic, it has been well-documented that older adults and those with underlying health conditions are at a higher risk for severe illness and death from the virus. However, it is essential to consider the impact of COVID-19 on children. While children are less likely to experience severe illness from COVID-19 compared to adults, they are not completely immune to the virus. Children with underlying medical conditions are at a higher risk for severe illness from COVID-19. While the severity of COVID-19 in children may be lower overall, protecting children from the virus is still crucial.

In this investigation, we have utilized the factorial design-based strategy to develop the NLs with a set target profile. The objective of the present study was to develop and optimize Camo-loaded pegylated Nanoliposomes (Camo-peg-NLs) using Box Behnken Design (BBD) method.

We used the ethanol injection method to prepare Camo-peg-NLs formulations using the BBD approach. We selected the concentration of DPPC, concentration of Cholesterol, and concentration of DOPE-PEG 2000 as independent variables and particle size, polydispersity index, zeta potential, entrapment efficiency, and drug load as dependent variables. The target profile of NLs was particle size ranging within 150-200nm, polydispersity index of 0.1-0.3, and zeta-potential close to neutral. We set the entrapment of the optimized formulation to be greater than 60% and the drug load to be greater than 30% w/w.

We prepared 15 Camo-peg-NL formulation batches by dissolving 50mg drug in 0.9% Sodium Chloride in 20mL of aqueous medium containing the drug and 1.3mL ethanol to dissolve the lipids. Optimized formulation was selected based on polynomial equations. The % EE and % DL were found to be in the range of 26-70% and 18-54% respectively.



Camo-peg-NL formulation of size of 188.68 ± 2.02 nm with 44.57 ± 1.60 % w/w drug load was prepared and optimized with quality by design approach. Further studies will include the testing of nebulization, a pain-free route of administration for pediatric use using the NGI to determine the reach of formulation to target site and release studies to determine the dosing frequency.

Could Problem-Solving Style Predict Burnout in Pediatric Emergency Physicians?

Presenting Author: Naghma Khan, MD; Emory University School of Medicine

2021 Annual Grant for Emergency Medicine (GEM\$) and The Wilbur and Hilda Glenn Family Foundation

Poster Number: 159

Khan, Naghma; Puccio, Gerard; Jergel, Andrew

Background

Pediatric Emergency Physician (PEM) work entails adaptability, flexibility, decisiveness, and action and the work is complex and multidimensional. One needs to be adept at creative problem-solving (CPS). Emergency physicians have one of the highest rates of burnout (BO) and attrition. The field of applied creativity focuses on the characteristics of the creative person, process, environment and finally the product. It delineates a variety of processes and tools needed for effective CPS with the goal to enhance teamwork and creative outcomes. The risk of BO related to creative mindset is unknown.

Design/Methods

This is a prospective, non-experimental, cross-sectional empirical study involving PEMs in a large hospital system. Maslach Burnout Index (MBI) is a 3-dimensional measure of BO: Emotional Exhaustion (EE), Depersonalization (DP) and Personal Accomplishment (PA). FourSight is a 4-dimensional psychological tool that identifies individuals' cognitive preferences (not competency) within the CPS process: problem clarification (Clarifier); idea generation (Ideator); solution development (Developer); and solution implementation (Implementer). Data was analyzed using descriptive statistics, linear and multivariate regression analysis (IBM SPSS Version 28.0.0.0 and RStudio 4.2.1). Significance was set at $p < 0.05$ for each test.

Results

Of the 88 PEM's invited, 75 (85.2%) completed the study. Median age: 43; Female: 59%; White: 47%. The Clarifier mindset (slope: 0.84, 95% CI [0.33, 1.34], $p = 0.002$) and the Developer mindset (slope: 0.59, 95% CI [0.16, 1.02], $p = 0.009$) correlated with risk of EE. No relationship was found between mindset and DP. An Ideator mindset showed a statistically significant correlation (slope: 0.33, 95%CI [0.07, 0.59], $p = 0.014$) with a positive sense of PA. All results held on multi-regression analysis with mindset as the dependent variable and years of practice, total hours worked/week, gender, and educational debt as predictors.

Conclusion(s)





Results of this study show that CPS style is a powerful predictor of BO, showing even stronger predictive value than hours worked/week and years in practice. The field of creativity has well-established and empirically proven training methods, hence the predictive relationship found between CPS preferences and BO begs the question as to whether training in applied creative-thinking methods might be useful in mitigating BO among PEM's.

Obstructive Sleep Apnea and Short Term Post-Surgical Outcomes in Pediatric Cardiac Critical Care

Presenting Author: Adil Khan, M.D.; Emory University

Poster Number: 87

Adil Y. Khan, MD; Brian A. Curry, MD; Rohali Keesari, MPH; Richard U. Garcia, MD

Background

Obstructive sleep apnea (OSA) has been associated with negative cardiovascular effects and negative outcomes following cardiovascular surgery in the adult population. The study's main objective was to evaluate if there is a similar association in children aged 1-18 years old.

Methods

In a single center retrospective matched cohort study, data was collected on 1-18 years old patients exposed to OSA. These patients were matched 1:1 by age, sex, and severity with patients not exposed to OSA, but who were admitted to the cardiac intensive care unit (CICU) following cardiac surgery between Jan 2012 and Dec 2021. Primary outcome was a composite variable: "bad outcome," consisting of prolonged CICU stay, prolonged duration of mechanical ventilation, need for extracorporeal membrane oxygenation, presence of arrhythmia, and death. McNemar's test and Wilcoxon signed rank tests were used for comparison between the two groups with a significance threshold set at $p \leq 0.05$.

Results

The study comprised of 80 patients exposed to OSA and 80 unexposed patients before cardiac surgery. The median age and weight at surgery were 5.3 years (IQR: 2.6-11.2) and 18.1 kg (IQR: 12.4-39.2), respectively. There were 92 (57.5%) males and 29 (18.6%) had single ventricle physiology. In the OSA group, the apnea-hypopnea index (AHI) was 4.3 (2.8-7.1), the REM AHI was 8.6 (IQR:3.2-13.3), 6.8% used CPAP at home, and their lowest saturation was 80% (IQR:80-90%). Chromosomal anomalies were significantly higher in the OSA group compared to non-OSA group (26.3% vs. 62.5%, $p < 0.01$). However, there was no significant difference in "bad outcomes" between the two groups (41.3% vs. 42.5%; $p = 0.873$). Additionally, no other significant differences were found in the multiple perioperative variables collected between the two groups.

Conclusion

We report no significant difference in short-term post-surgical outcomes between children with and without OSA who underwent cardiac surgery. This is in contrast to what has been reported in the adult population previously. The study further stresses the significant differences between children and





adults, not just restricted to size and weight. Future prospective studies should continue to describe the relationship between OSA and outcomes after cardiac surgery in children.

Differential Voice Modulation of Mothers of Preterm Infants

Presenting Author: Caitlin Kjeldsen, PhD Candidate in Speech and Hearing Science; Emory University

Poster Number: 23

Kjeldsen, Caitlin; Neel, Mary Lauren; and Maitre, Nathalie L.

Background

Hospitalized preterm infants have limited exposure to infant-directed speech and singing (IDSpeech, IDSinging), critical building blocks for neurodevelopment. Characteristic acoustic modulations of these registers facilitate learning and development including language and emotional connection. In preterm infants, however, interruption to typical gestation and developmental disruptions of the NICU impede the language, emotional, and social learning facilitated by mother's voice in utero and after birth.

Objective

This prospective pilot study sought to characterize the acoustic properties of the IDSpeech and IDSinging of mothers of preterm infants (N=44) and correlate these measures with degree of maternal bondedness, attunement, and depression.

Methods

Mothers were recorded during adult-directed speech (ADSpeech), IDSpeech, and IDSinging and completed questionnaires (Mother-to-Infant Bonding Scale, Baby Care Questionnaire, and Edinburgh Postnatal Depression Scale) to measure bondedness, attunement (reliance on baby cues), and depression.

Acoustic measures commonly assessed with term infants were assessed with this preterm cohort: fundamental frequency (f0) metrics, vowel duration and space, production rate, and relative intensity. Acoustic parameters were compared using related-samples Friedman's test followed by pairwise comparisons with Bonferroni correction. Acoustic measures significantly different between recording conditions were then correlated with mother's self-reported questionnaire scores using linear or logistic regression.

Results

Mothers of preterm infants differentially modulate their voices when speaking or singing to their infant compared to an adult. Significant differences between ADSpeech and IDSpeech were found in f0 variability ($p < .0001$), f0 range ($p < .0001$), vowel duration ($p < .021$), and production rate ($p < .009$). Significant differences between IDSpeech and IDSinging were found in all f0 measures ($p < .01$), production rate ($p < .0001$), and relative intensity ($p < .0001$). Lower perceived bondedness or attunement or increased risk for depression did not decrease mothers' ability to modulate their IDLang (all $p > .05$).



Conclusions

Mothers of preterm infants differentially modulate their voices during adult versus infant-directed speech, and between two types of infant-directed registers: IDSpeech and IDSinging. These registers of IDLang could be a valuable tool in the NICU to quantify and promote IDLang to facilitate learning, interaction, and parent-infant bonding for preterm infants and their parents.

Deletion of the biliary atresia candidate gene, *Pkd1l1*, impairs biliary epithelial cell organoid structural integrity

Presenting Author: Caroline Klindt, MD; Emory University Department of Pediatrics, Hepatology, and Nutrition

Poster Number: 64

Klindt, Caroline; Hellen, Dominick J.; Lee, David H.; Bennett, Ashley L.; Dawson, Paul A. and Karpen, Saul J.

Background: Biliary atresia (BA) is the main indication to liver transplantation in infants and has eluded major discoveries of etiopathophysiology for decades. A nationwide genomic study identified mutations in Polycystin 1 like 1 (PKD1L1) as candidate etiologic contributors. We have recently demonstrated that liver-specific deletion of *Pkd1l1* in mice results in liver pathobiology seen in human BA livers. The aim of this study was to elucidate the underlying mechanism of *Pkd1l1* dependent cell homeostasis within biliary epithelial cells (BECs).

Methods: BECs were isolated from 6–8-week-old male *Pkd1l1*^{Fl/Fl} (control) and *Pkd1l1*-deficient (KO) mice by fluorescence-activated cell sorting. BECs were assayed for their ability to proliferate, polarize, and form confluent monolayers on Transwell cell culture inserts. BECs were used to generate biliary organoids, that were incubated with DMSO, CDCA (100mM), UDCA (100mM) and Lipopolysaccharides (100U/ml LPS) for 24 hours. BECs and organoids were characterized by RT-qPCR and immunofluorescence.

Results: Two-dimensional cultures of KO BECs, compared to control, displayed perturbations in tight junction formation, cell matrices, and ability to proliferate. Biliary organoids derived from KO mice were significantly more abundant but smaller in size as compared to control (60204 mM² vs 2912 mM², 20-fold decrease; $p < 0.0001$). Organoids that were challenged with bile acids and LPS to induce a reactive biliary phenotype demonstrated aberrant expression of several inflammatory genes in KO versus control. Cytokines associated with the chemotaxis of leucocytes, like *Ccl5* (2.34 vs 13.89, 6-fold increase $p < 0.05$) were significantly higher in organoids comprised of KO cells than control cells. However, other cytokines like TNF- α and cell adhesion molecules like *Icam-1* did not increase in response to LPS in KO as observed in control (TNF- α : 6.53 vs 1.26, 5-fold decrease and *Icam-1*: 2.26 vs. 1.00, 2-fold decrease).

Conclusions: These studies demonstrate that the BA-candidate gene, *Pkd1l1*, is essential for the maintenance of normal BEC physiology and immunoregulatory function *in vitro* and provide further support that this mouse model of BA recapitulates features of impaired BEC structure and increased



immune activation as seen in human BA livers. As such, these isolated cells may be able to provide much-needed mechanistic understanding of this important disease.

Relationship between ARFID Symptomatology and Picky Eating Duration and Timing of Onset

Presenting Author: Megan Knedgen, M.A.; Childrens Healthcare of Atlanta

Poster Number: 126

Knedgen, Megan; Breiner, Courtney, Proctor, Kaitlin and Zickgraf, Hana

Background. Picky eating is common in childhood, peaking between ages 2 and 6 years then declining with age (Dovey et al., 2008). For some children, picky eating may persist beyond this normative period and pose threats to health and psychosocial functioning. Avoidant/restrictive food intake disorder (ARFID) is defined as a pattern of selective eating leading to significant medical and/or psychosocial impairment (American Psychiatric Association, 2013). The current study examines whether children who are persistent picky eaters endorse ARFID criteria differently from non-picky and normative picky eaters. **Method.** Participants (N=437) included parents of children ages 5-17 recruited from a nationally representative panel service to complete a study on their child's eating behavior. Parents completed the Nine-item ARFID Screen (NIAS) and reported the ages at which they perceived their children as picky eaters (e.g., between 1-2 years). Children were then categorized into groups: non-picky eaters (n=223), normative picky eaters (picky eating before age 6; n=102), persistent picky eaters (before and after age 6; n=71), and late-onset picky eaters (after age 6; n=41). One-way ANOVAs were conducted to examine differences on NIAS subscales and total scores between groups. Post-hoc analyses (Tukey HSD) were conducted to examine group differences for significant ANOVAs. **Results.** The groups differed (all $p < .05$) in mean NIAS subscales (picky eating, NIAS-PE; appetite, NIAS-A; fear, NIAS-F) and total scores (NIAS-T). A Tukey post hoc test found that NIAS-PE, NIAS-A, and NIAS-T were significantly lower in the never picky eaters than in the persistent and late-onset picky eaters (all $p < .05$). Additionally, NIAS-PE, NIAS-A, and NIAS-T were significantly lower in normative picky eaters than in persistent picky eaters, and NIAS-F scores were lower in non-picky eaters than in persistent picky eaters (all $p < .05$). There was no statistically significant difference in NIAS-PE, NIAS-A, NIAS-F, or NIAS-T between non-picky eaters and normative picky eaters. **Conclusion.** Findings from this study suggest that picky eating that persists beyond or is identified after the normative period is associated with elevated ARFID symptoms compared to normative and non-picky eaters. Given the health and psychosocial risks associated with ARFID, early identification and intervention for this group is warranted.

Outcomes Among Patients In and Out of Cardiac Care: The Congenital Heart Disease Project to Understand Lifelong Survivor Experience (CHD PULSE)

Presenting Author: Lazaros Kochilas, MD; Emory University

Poster Number: 161





Matthew E. Oster, J'Neka S. Claxton, Romie N. Velani, Krisy Kuo, Dawn Ilardi, Osamah Aldoss, Charles Canter, Mansi Gaitonde, Anitha John, Gurumurthy H. Malikarjun, Kimberly E. McHugh, David Overman, Geetha Raghuv eer, Jeff Jacobs, Brad Marino, Logan Specto

Background: Over the past 50 years, survival for those with congenital heart disease (CHD) has improved dramatically. With this improvement has come a need to understand outcomes beyond just mortality. The objective of the Congenital Heart Disease Project to Understand Lifelong Survivor Experience (CHD PULSE) is to assess the long-term outcomes among adult CHD patients both in and out of cardiology care.

Methods: Between 2021 and 2023, we performed a cross-sectional survey of individuals with history of intervention for CHD at 8 centers of the Pediatric Cardiac Care Consortium, a US-based registry of interventions for pediatric heart diseases. After linkage with the National Death Index through 2019, contact information for eligible individuals was obtained via Lexis Nexis.

Results: Among the 8,980 surveys sent, 1,759 surveys were received by July 2022 (19.6%). Respondents were more likely than non-respondents to be older (median age 32 years vs. 29 years, $p < 0.0001$) and female (54.8% vs. 45.2%, $p < 0.0001$), but there were no differences in severity of CHD between the groups ($p = 0.64$). Among respondents, 6.5% were considered to have single-ventricle CHD, 14.3% severe 2-ventricle CHD, 40.4% moderate CHD, 28.1% mild CHD, and 10.7% other types of CHD. Overall, 61% of respondents had seen a cardiologist in the last 2 years, but 26% had not seen one in the last 5 years. Those with single-ventricle CHD were most likely to have seen a cardiologist in the last 2 years (97%), and those with mild disease were most likely not to have seen a cardiologist in the last 5 years (54%).

Conclusions: While the likelihood of remaining in cardiac care increases with severity of CHD, a sizable percentage of patients with CHD have not seen a cardiologist in at least 5 years. CHD PULSE will provide unique insights into the outcomes of patients both in and out of CHD care.

Sex Effects on the Frequency of Social Smiling in Infants with and without Autism Spectrum Disorder

Presenting Author: Alp Koks al, A.B.; Marcus Autism Center

Poster Number: 127

Köksal, Alp; Pileggi, Moira; Jones, Warren; Shultz, Sarah

Background: Social smiles emerge at around 1-2 months and are a fundamental milestone for social communication (Anisfeld, 1982; Messinger and Fogel, 2007). Smiling expression diverges in atypically-developing infants: at 6 months, frequency of smiling is comparable between children on the Autism Spectrum and their typically-developing (TD) peers; it declines significantly until 12 months (Ozonoff et al., 2010). Additionally, females with ASD have stronger non-verbal communication skills than males in childhood (Park et al., 2012). We hypothesize that infants with ASD smile less than TD, and females with ASD smile more frequently than males.

Methods: Infants with ASD ($n = 43$, MAge at Evaluation (SD) = 9.95(2.07) months) and TD infants ($n = 108$, MAge at Evaluation (SD) = 9.37(0.83) months) were selected from a prospective longitudinal study of





infants at low- and elevated-likelihood for ASD. Smiling frequency was indexed by clinician observation during the Communication and Symbolic Behavior Scale (CSBS) administered at 9-24 months of age. Scores ranged from 0-6, indicating the number of smiles over six presses for attention.

Results: At 9 months of age, mean smiling frequency is significantly different between TD and ASD infants ($p=0.047$). There are significant differences between TD and ASD males ($n=60/31$, $p=0.011$) but not TD and ASD females ($p=0.749$). ASD females smile more frequently than males at 9 months ($n=12/31$, $p=0.0124$), but not at 12 months ($p=0.441$). From 9-24 months, smiling frequencies of all other groups increase (TD male: $p<0.001$, $r=0.263$; TD female: $p=0.001$, $r=0.251$; ASD male: $p=0.002$, $r=0.104$), while ASD females' smiling decreases ($p=0.114$, $r=-0.239$). A mixed linear model on trajectory of smiling frequency shows a nearly significant main effect of sex ($t=-1.737$, $p=0.08$) and a diagnosis-age interaction effect ($t=3.333$, $p=0.0009$).

Conclusions: The data shows an interaction effect of sex-diagnosis on smiling frequency within the first year of life, which over time is replaced by an age-diagnosis effect. This may have implications on social compensation mechanisms in females on the spectrum, and on the divergent diagnosis rates between sexes. Future directions include scrutinizing the interactive development of social and physical milestones and dimensional analyses using other diagnostic tools such as the Mullen Early Scales of Learning or Autism Diagnostic Observation Schedule-2.

Inter-day Reliability of Leg muscle Size and Quality estimates from Ultrasound in Children with Cerebral Palsy

Presenting Author: Junsoo Lee, Bachelor; University of Georgia

Poster Number: 24

Lee, Junsoo; Vogler, Suzanne; Colquitt, Gavin; McCully, Kevin, K; and Modlesky, Christopher M;

Background

Children with cerebral palsy (CP) have muscles that are smaller and weaker, have a high degree of fat infiltration, and have architectural differences relative to typically developing children. Ultrasound is commonly used to examine muscle size and quality. Unfortunately, studies determining the inter-day reliability of muscle size and quality estimates from ultrasound in children with CP are lacking. This study aimed to determine the inter-day reliability of ultrasound estimates of the size, fat concentration (i.e., echo intensity (EI)), and architecture (i.e., pennation angle) of the gastrocnemius (GA) and tibialis anterior (TA) in children with CP.

Methods

Fifteen children with spastic CP (age 5-11 y, I or II on the Gross Motor Function Classification System) participated in this study. Cross-sectional area (CSA) and EI of GA (25, 50, and 75 % of muscle belly length) and TA (20, 40, and 60 % of tibia length), belly length of GA, and pennation angle of GA and TA were assessed using ultrasound. The tests were repeated four weeks later. Image collection and processing were completed by one researcher. Agreement of muscle estimates was determined using





paired t-tests. The reliability of muscle estimates was determined using the intraclass correlation coefficient (ICC).

Results

There were no significant test-retest differences for any muscle estimates. The reliability of CSA estimates for GA and TA ranged from good-to-excellent (ICC = 0.86 to 0.97, $p < 0.001$). The reliability of EI estimates for GA and TA were excellent (ICC = 0.95 to 0.98 and 0.91 to 0.97, respectively, $p < 0.001$). The reliability for muscle belly length and volume estimates for GA was excellent (ICC = 0.99 and 0.96, respectively, $p < 0.001$). The reliability for pennation angle estimates for medial and lateral GA estimates was moderate-to-excellent (ICC = 0.57 to 0.94, $p < 0.05$). The reliability for pennation angle of TA estimates was poor (ICC = 0.24, $p = 0.235$).

Conclusions

Ultrasound can be used to detect changes in the size and EI of the GA and TA in children with spastic CP. Reasonable estimates of pennation angle are possible for the GA, but not the TA.

Influential Factors that Affect Food Allergy Families' Engagement with Research

Presenting Author: Tricia Lee, MD; Emory

Poster Number: 50

Christopher Young, Shanel Tague, MPH, Sydney Warner, Brian Vickery, MD, Tricia Lee, MD

Little is known about the influential factors that contribute to food allergy (FA) families' engagement with research. Patients with IgE-mediated FA completed a survey during their clinic visits. The outcome measure was defined as enrollment into the Food Allergy Research and Education (FARE) Patient Registry. Survey results were analyzed using descriptive statistics. The mean age of the 56 participants was 6.6 years. 23.2% declined to join the Registry with top reasons to include "time restraint" and "need to discuss with other family members." The mean age of patients who joined the Registry was 7.45 years whereas for those who declined was 3.83 years. Of those who declined: 54% were White, 31% were Black and 15% were Asian; but Asians had the highest declination rate of 66% and Blacks had the lowest at 16.7%. 50% of the wheat allergic patients declined whereas other specific food allergies had lower declination rates with the next highest being 20%. In patients with only one food allergy, 61.5% joined the registry, whereas those with 3 or more food allergies, 84.6% joined. Of the patients who had epinephrine previously administered or taken to the ER, 81.8% joined. The majority of patients were willing to join the Registry when personally invited during clinic visits. Families who declined participation had younger children and majority were white. Those families with currently more burden from the FA diagnosis may contribute to participation in a registry.

Identification and CAR T-cell targeting of protein tyrosine kinase 7 (PTK7) for neuroblastoma

Presenting Author: Jasmine Lee, B.S.; Emory University





Poster Number: 25

Jasmine Y. Lee^{1,2}, Hunter C. Jonus¹, Arhanti Sadanand¹, Gianna M. Branella^{1,2}, Victor Maximov¹, Suttipong Suttapitugsakul³, Matthew J. Schniederjan⁴, Jenny Shim¹, Andrew Ho¹, Kiran K. Parwani^{1,2}, Andrew Fedanov¹, Adeiye Pilgrim^{1,2}, Jordan Silva^{1,2}, Robert

Background

High-risk neuroblastoma (HR NB) is an aggressive childhood cancer with 5-year survival of <50%. Antibody-based immunotherapy targeting the cell surface disialganglioside GD2 improved patient survival, but half of HR NB patients relapse after standard treatment, highlighting a need for new therapeutics.

Methods

To determine NB cell surface antigen expression, mice bearing patient-derived xenografts were treated with chemotherapy. Tumors were digested for cell surface glycoproteomics performed by LC-MS, which resulted in multiple potential immunotherapy targets. A CD28-based chimeric antigen receptor (CAR) was developed against the prioritized candidate, PTK7, and used in downstream analysis for the feasibility of targeted immunotherapy using $\alpha\beta$ and $\gamma\delta$ T cells against NB preclinical models.

Results

Glycoproteomics identified PTK7 to be consistently and highly expressed, which remained after chemotherapy. A pediatric-specific tissue microarray showed minimal PTK7 expression in normal tissues. We found ab and gdPTK7 CAR T cells to be specific against PTK7-expressing NBs in vitro. CD69, an early activation marker, increased on PTK7 CAR T cells co-cultured with SK-N-AS NB cells but not above baseline with SK-N-AS cells with PTK7 knocked out. ab PTK7 CAR T cells induced cytotoxicity in IMR5 NB cells as early as 4 hours, which further increased to an average of 29, 63 and 74% at 1:1, 5:1, 10:1 E:T ratios after 12 hours. PTK7 CAR T cell-mediated tumor death was not observed in PTK7 negative CMK cells. PTK7 CAR modified gd T cells also showed significant cytotoxicity advantage compared to unmodified gd T cells. Unmodified gd T cells induced ~40% target cell death, which increased to ~85% with CAR modified cells. In vivo, PTK7 CAR T cells significantly regressed the growth of an aggressive NB metastatic model.

Conclusion

We show NB expresses PTK7, which is an attractive target for immunotherapeutic intervention. CAR T cells targeting PTK7 effectively control NB growth. PTK7 should be further investigated as a NB target, and future investigations will focus on optimizing a CAR T cell product candidate, which will include establishing the safety and efficacy of PTK7 targeting T cells.

EFFECT OF ATTENDANCE AT EMORY UNIVERSITY GENETICS ANNUAL METABOLIC CAMP ON BLOOD PHENYLALANINE LEVELS IN WOMEN WITH PKU





Presenting Author: Daniel Litton, BA in Human Health from Emory University; Emory College of Arts and Sciences

Poster Number: 128

Danny Litton, Teresa D. Douglas, Rani H. Singh

Background: Phenylketonuria (PKU) can cause toxic high phenylalanine (phe) in the blood. High phe levels in mothers with PKU during pregnancy can lead to maternal PKU syndrome in their infants. Emory University Genetics Annual Metabolic Camp was developed as a supportive and instructive method for reducing incidence of maternal PKU syndrome in infants, and it provides week-long fun yet educational activities that teach women with PKU to manage their medical diet and blood phe. **Hypothesis:** PKU participants with multiple attendances at Metabolic Camp (1995 – 2019) have better blood phe and tyrosine (tyr) levels (umol/L) upon camp arrival each year compared to one-time participants. **Methods:** Blood phe and tyr data of 72 consented campers collected from day one of most recently attended camp served as a diet compliance proxy. Preliminary data was divided into three groups by age during attendances: (1) under 18, (2) 18 or older, and (3) repeat across age division. Two-sample unmatched t-tests compared blood data from one-time attendees to repeat-attendees within Groups 1 and 2. Simple linear regression on Group 3 evaluated blood phe and tyr association with number of attendances. **Results:** Participants were aged 12-59 yrs (Median:18). Cohort phe range: 49-1477 with mean±SD of 699±408. Group 1 mean phe was 674±340 for one-time attendees and 642±335 for multi-time attendees, while Group 2 mean phe was 841 ± 494 for one-time attendees and 743 ± 480 for multi-time attendees respectively. T-tests and linear regression of blood phe and tyr showed no significant difference or association. **Conclusion:** Multi-camp attendees from 1995-2019 did not reveal statistically lower blood phe levels than one-time attendees although a trend is observed. Further analysis will include dietary phe and medical food intakes. Results will inform on optimizing camp curriculum to benefit consistent dietary management.

Active Joint Acoustic Sensing: A Digital Biomarker of Inflammatory Achilles Tendon Involvement in Entesitis Related Arthritis

Presenting Author: Miguel Locsin, M.D.; Emory University

Poster Number: 88

Goossens, Quentin; Locsin, Miguel; Moise, Emily; Ponder, Lori A; Inan, Omer T; and Prahalad, Sampath

Background: Entesitis Related Arthritis (ERA) is a subtype of Juvenile Idiopathic Arthritis (JIA), a chronic pediatric rheumatologic condition involving entesitis. The diagnosis of ERA is currently challenging as it relies on subjective patient reports and clinical examinations. This study proposes active joint acoustics (AJA), a novel non-invasive and convenient sensing technology, to offer the potential to objectively identify Achilles Tendon (AT) entesitis in patients with ERA.

Methods: We recruited 20 JIA patients who met the inclusion criteria of three subgroups; ERA with symptomatic AT entesitis (sxERA, n = 6), ERA with asymptomatic ATs (asxERA, n = 6), and JIA (non-ERA) with asymptomatic ATs (asxNERA, n = 8). AJA were recorded from each AT; a skin mounted vibrational





motor was used to excite the AT while the modulated acoustic signal was recorded using a skin mounted accelerometer. A 235 Hz burst train excitation signal was used and the AJA response signals were filtered and segmented into individual bursts after which 26 temporal waveform features and the first three principal components (PC) were extracted from the preprocessed AJA signals. Logistic regression machine learning classifiers were trained and validated using leave-one-subject-out cross-validation (LOSO-CV) to differentiate sxERA from asxNERA and sxERA from asxERA, each using the most salient waveform features and PCs separately. Overall accuracy, sensitivity, and specificity were calculated on a subject level using LOSO-CV.

Results: Differentiating sxERA from asxNERA using the waveform feature-based model yielded an overall classification accuracy of 86%, 83% sensitivity and 88% specificity. The PC-based model yielded an overall accuracy of 71%, 67% sensitivity, and 75% specificity. Differentiating sxERA from asxERA yielded an accuracy of 75%, 83% sensitivity and 67% specificity for both the waveform feature- and PC-based models.

Conclusion: Both comparisons yielded a relatively high accuracy, sensitivity, and specificity in this clinical pilot study, suggesting potential of using AJA as non-invasive and convenient screening tool for AT enthesitis in patients with ERA. Overall, the sxERA and asxERA comparison yielded lower accuracies, suggesting that chronic tendon inflammation can affect the recorded AJA signals. Future studies utilizing MRI can be used to further validate and refine the presented AJA technology.

GLP-1 Receptor Agonists - A Potential New Medication for Pediatric Non-Alcoholic Fatty Liver Disease

Presenting Author: Ana M Ramirez, MD; Emory University

Poster Number: 77

Choi, Erika; Ramirez Tovar, Ana; Arora, Shruti; Soler Rodriguez, Dellys; Fadoju, Doris; He, Zhulin; Vos, Miriam

Background

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in children in the US, rising alongside an increase in obesity and type 2 diabetes (T2DM). Untreated, NAFLD leads to end-stage liver disease and is one of the leading causes of liver transplantation in adults. GLP-1 receptor agonists (GLP-1 RA) in adult populations with T2DM have been shown to improve non-alcoholic steatohepatitis through improvement in insulin resistance, the common mechanism behind the development of NAFLD and T2DM. Currently, no medications are available for managing NAFLD or obesity in the pediatric population. We assess the effects of GLP-1 RA on markers of NAFLD and insulin resistance to address the critical, unmet need for a pharmacotherapeutic agent for pediatric NAFLD.

Design/Methods

Fifteen patients from a T2DM clinic were identified and fulfilled the following inclusion criteria: diagnosed with pre-diabetes or T2DM, prescribed a GLP-1 RA in the prior 12 months, evidence of NAFLD indicated by elevation of alanine aminotransferase (ALT) to twice the upper limit of normal (>50 for





males, >44 for females). Six patients were excluded due to either never starting the medication, documentation of inconsistent use, or not having a follow-up ALT. Nine patients were included. The average change between baseline and the first measurement after starting a GLP-1 RA was calculated for ALT, A1c, and BMI.

Results

Participants' ages ranged from 14 to 17. ALT decreased by an average of 60% or 98 points within an average of 109 days. A1c decreased by an average of 2.2 points within an average of 114 days. BMI decreased by an average of 5% or 2.4 points within an average of 105 days. The most dramatic effect was seen within the first 180 days of starting the GLP-1 RA.

Conclusions

This case series highlights the potential use of GLP-1 RA in the management of pediatric NAFLD. There was a steeper reduction of ALT and A1c compared to BMI, suggesting that improvement in NAFLD may be independent of weight loss. More randomized, robust, placebo-controlled studies are needed to evaluate the effects of GLP-1 RA.

Obesity's Impact on CAR T cell's Anti-tumor Function

Presenting Author: Jessica Maaskant, B.S.; Emory University

Poster Number: 129

Maaskant, Jessica; Evans, Alysa; Lin, Heather; Chvatal, Stacie; Ross, Anthony; Raikar, Sunil; Henry, Curtis; Rafiq, Sarwish

Background

Obesity is becoming increasingly prevalent in the US at alarming rates, especially considering its correlation with cancer and therapeutic response rates. B-cell acute lymphoblastic leukemia (B-ALL) is one of the most common forms of cancer in pediatric patients, and obese patients with B-ALL have inferior survival to their lean counterparts in both pediatric and adult populations. Chimeric antigen receptor (CAR) T cell therapy is an emerging immunotherapy used on relapsed and refractory blood cancers, with CD19-directed CAR T cells being FDA approved for pediatric B-ALL. Data suggests that CAR T cell treatment may be less effective in obese patients; however, the impact of adiposity on this therapy remains unclear.

Methods

To address this question, we manufactured CAR T cells derived from lean and obese mice and performed flow cytometry to immunoprofile the cells and in-vitro cytotoxicity assays against CD19 target cells. To induce obesity, mice were fed a high-fat diet (60%fat) for a minimum of 2 months and compared with control diet mice (10%fat). We measured cytotoxicity using two measures. First, we used a luciferase assay to quantify how much luciferase is secreted by living B-ALL tumor cells after exposure



to CAR T cells. Second, we used the Axion Maestro TrayZ and got impedance-based measurements of adherent targets after exposure to CAR T cells.

Results

Murine CAR T cells derived from obese donors were equally viable and had similar transduction efficiencies (20-50%) to their lean counterparts. The lean mouse T cells appear to have higher levels of CD69, PD-1, and Lag 3 premanufacturing, while the obese mouse T cells appear to have slightly elevated Tim3 post-manufacturing. The obese CAR T cells performed worse than the lean CAR T cells in both luminescence and impedance-based cytotoxicity assays. These cytotoxic differences appear independent of the T cells' CD4:CD8 ratios.

Conclusion

Preliminary evidence suggests adiposity may play an important role in CAR T cell function against CD19 targets. This data establishes a need to further investigate the mechanisms by which obesity may impact CAR T cell immunotherapies and the potential need to optimize this treatment for diverse populations.

Title: Early life pain alters the microglial and Cox2 response to an immune challenge in adult male and female rats

Presenting Author: Melani Macik, B.S. Neuroscience; Georgia State University

Poster Number: 130

M. Macik, M. Gomez, H. Harder, M. Pandit, A.Z. Murphy

Background: Premature infants often enter the neonatal intensive care unit (NICU) due to serious health problems. The average stay for NICU infants is 25 days, where they will experience between 10-18 painful procedures per day. Due to the vulnerable state of NICU infants, doctors will frequently withhold anesthesia or other pain-relieving drugs. Early life pain (ELP), such as that imposed by procedures in the NICU, has been shown to disrupt central nervous system (CNS) development in animal models; this can affect all neurons and glial cells, including microglia. Microglia function as the immune cells of the brain, controlling the brain's responses to illness and injury. As part of these responses, the production and release of prostaglandin E2 (PGE2) is critical. The enzyme Cox-2 is the rate limiting step in the synthesis of PGE2; as such, Cox-2 expression provides a useful proxy measure for prostaglandin activity. The present study explores the long-term influences of ELP on microglial and Cox2 response to illness in male and female adult rats with the hypothesis that exposure to ELP influences immune response later in life. Methods: At birth, half the rats were injected with the mild inflammatory agent Carrageenan (CGN); the control group was only handled. When the rats reached adulthood, ThermoChron iButtons were surgically implanted to track body temperature. Two weeks later, all rats were injected with Lipopolysaccharide (LPS) to trigger an immune response. Sickness behavior and core body temperature data were recorded. Rats were sacrificed at 2 hours post-LPS or peak fever, and Cox-2 and microglial marker Cd11b were labeled via immunohistochemistry. Critical areas for immune function—the preoptic area of the hypothalamus and periaqueductal gray—were key areas of focus. Results and Conclusions: ELP rats showed a potentiated fever response to LPS, and we predict that Cox-2 and Cd11b will also be





altered in ELP rats. These results would suggest early life pain endured by NICU infants has long-term consequences affecting immune function at a molecular level.

Single Cell Transcriptomic Analysis of Rectal Healing Profiles in Perianal Fistulizing Crohn's Disease.

Presenting Author: Sushma Maddipatla, Master's; Emory University

Poster Number: 131

Maddipatla, Sushma Chowdary; Murthy, Shanta; Dodd, Anne; Washburn, Savannah; Peliá, Ranjit; Anbazhagan, Murugadas; Kolachala, Vasantha L; Geem, Duke; Gibson, Greg; Qiu, Peng; Cutler, David J; Matthews, Jason D and Kugathasan, Subra

BACKGROUND: Perianal fistulizing (PAF) disease is a rectal complication of Crohn's Disease (CD), present in ~25% of CD patients worldwide, often requiring more aggressive and combined medical and surgical interventions. There is a unmet need to further define and promote the mucosal healing profiles of these patients based on cellular mechanisms driving their phenotype. To this end, we have used single-cell RNA-sequencing (scRNA-seq) to reveal the cellular behavior of PAF in these patients while identifying factors associated with healing or worsening disease.

METHODS: Rectal mucosal biopsies from 6 non-inflamed treatment naïve CD (TN-CD) lacking PAF (endoscopically normal) and 11 treated PAF-CD (5 healed and 6 unhealed) were obtained. Biopsies were digested by cold protease to produce a single cell suspension that was processed for 10x 3' scRNA-seq. Reads were mapped to human reference genome (GRCh38) by Cell-Ranger, and the count matrices generated and analyzed with Seurat. Cell-type annotations, proportions, differential expression analysis and STRING pathway analysis were performed.

RESULTS: From 17 patients, 114596 cells were annotated to three major compartments with 12 epithelium, 1 stromal, and multiple immune subtypes. In comparison with healed, unhealed PAF-CD had fewer epithelial cells but had higher proportions of M-cells and immune subtypes particularly B, plasma, and NK cells. Compared to healed, unhealed PAF-CD highlighted enrichment of genes involved in MHCII, IFN-gamma, TNF-alpha, ECM, and IL-1B pathways. Unhealed PAF-CD compared to TN-CD patients without PAF revealed increased gene transcripts associated with TCA cycle. Interestingly, TN-CD patients exhibited increased signatures for IL-4, -13, and -17, along with IFN-alpha and -beta when compared to healed PAF-CD.

CONCLUSION: Rectal mucosal healing during PAF was accompanied by re-establishment of epithelial subtypes and a decrease in the abundance of immune subtypes. Similarities were found between TN-CD patients and unhealed PAF-CD with increased IL-4/13/17 signatures when compared to healed PAF-CD. These signatures link them with pathways known to promote epithelial-to-mesenchyme transition and might give indications of potential PAF-CD formation in some of these newly diagnosed patients. Current studies are focused on longitudinal profiles of these patients with the role of their epithelial subtypes in the healing process.



Exploring the Genetic Interaction between *Slc25a1* and *Tbx1* in Congenital Heart Disease: Unraveling a Shared Pathway in 22q11.2 Deletion Syndrome

Presenting Author: Adam Malik, None; Emory University

Poster Number: 132

Malik, Adam; Sohani, Fateema; Gayle, Ashley; and Kwong, Jennifer

As outlined by the CDC, congenital heart disease (CHD) is a widespread birth condition that affects 1 in every 100 infants annually in the United States and is considered “a leading cause of birth defect-associated infant illness and death” (1). DiGeorge syndrome, also known as 22q11.2 deletion syndrome (22q11DS), is a prevalent cause of CHD characterized by hemizygous microdeletions on the long arm of chromosome 22. As of yet, no cure has been identified. *Tbx1*, a T-box transcription factor that resides within the 22q11.2 microdeleted region, has been well established to regulate cardiac development and contribute to the CHD associated with 22q11DS. However, hemizygous loss of *Tbx1* alone is not sufficient to recapitulate the full spectrum and severity of 22q11DS-associated cardiac malformations, suggesting that additional factors may contribute to cardiac pathology in 22q11DS. Our laboratory has recently identified *Slc25a1* (the mitochondrial citrate carrier) as another 22q11DS deleted gene that regulates cardiac development, but the mechanisms by which loss of *Slc25a1* causes CHD is not known. This study aims to investigate the potential genetic interaction between the *Slc25a1* and *Tbx1* genes and to determine if they function along a shared pathway in contributing to the emergence of CHD. Through use of *Slc25a1* and *Tbx1* knockout mouse models, we will examine heart development to determine the outcome of transheterozygotic loss of *Slc25a1* and *Tbx1*. Discovering a link between these two genes through a shared pathway holds a variety of implications; namely, it would establish these genes as co-effectors of heart morphogenesis and provide insight on the molecular mechanisms behind CHD to inform future treatment methods and possibly a cure.

(1) <https://www.cdc.gov/ncbddd/heartdefects/data.html#References>

An Educational Intervention for Caregivers of Children with Motor Delay Delivered on a Social Media Platform: First Results

Presenting Author: Larken Marra, Ph.D. Kinesiology; Emory University

Poster Number: 78

Marra, Larken; Kjeldsen, William; Pinson, Lisa; Murphy, Melissa; Denbo, Jennifer; Byrne, Rachel; Maitre, Nathalie

Background: Children born with motor delays often miss critical opportunities to improve their motor trajectory due to delays in obtaining specialized care. It may be possible to improve parent self-capacity and motor outcomes for children by empowering parents through knowledge of motor development, principles of infant motor learning, parenting and parental self-care. To address this, we designed a program based on caregiver-skills models and delivered on a social media platform over 9-weeks. Here we report on caregiver characteristics and perception of the program.





Methods/Study Design: Randomized trial with waitlist control. Included: parents of children with motor delay < 3 years of age. Exclusion: Non-English speaking or non-U.S. resident. Parents completed mother-infant bonding (MIB), maternal self-efficacy (MES), and caregiver knowledge (CK) of motor skill development questionnaires. Motor delay of the child was quantified using DAYC-2 motor scales. For those who completed the study to date, subjective impression of the intervention was obtained.

Results: 59 consented and 48 completed initial assessments. Most participants were mothers (91.7%) and Caucasian (79%), with 79% having a 4-year college degree or higher. Their children at study start had a mean age of 15 months (SD 9); 44% born preterm with mean DAYC scaled scores of 84.5 (SD 13.4) and 69.1 (SD 15.9) in fine and gross motor domains respectively. Mean MIB and MSE scores were 2.69 (SD 3) and 72.7 (SD 6.5), indicating well-bonded parents who had moderate self-efficacy. Mean CK scores, 20.9 (SD 1.8), revealed a general understanding of motor skill development, with gaps in how infants learn, positive parenting strategies, and parenting self-care. Analysis of the program feedback revealed three themes that parents saw of value in the intervention: more effective parental support for children, tailored parental support by study team, and sense of belonging to a community.

Conclusion: Parents of children with motor delays who chose a social media support program may be well-bonded with their children but had opportunities to increase their self-efficacy and knowledge of infant learning. Opportunities for future improvement of the program include limiting repetitive content, enhancing the quality of embedded videos, and increasing participant interaction on the platform.

The Impact of Elevated Cortisol Levels on Placental Function and Immunity

Presenting Author: Tameyah Mathis-Perry, B.S.; Morehouse School of Medicine

Poster Number: 133

Tameyah Mathis-Perry, Nia Thompson, Erica L. Johnson PhD

Background: There is increasing awareness that the deep racial inequities that exist today are the direct consequence of structural racism and discrimination (SRD). SRD refers to macro-level conditions that limit opportunities, resources, and well-being of individuals and populations based on race/ethnicity. Due to SRD, African American (AA) women are more likely to experience persistent stressors and the lasting impact of the stress of racism (weathering) precipitates a chronic state, that affects biological processes in the body and explains how socially structured stress increases disease vulnerability. This chronic stress may also be associated with higher rates of placental dysfunction among AA. Recent reports suggest that elevated levels of the stress hormone (cortisol) early in gestation is associated with higher levels of inflammatory mediators and an increased risk of preterm birth. Unfortunately, there is limited research further examining the impact of maternal stressors on placenta function during pregnancy. In this study, we propose to investigate the impact of elevated and persistent cortisol levels on placental immunity and hormone metabolism.

Methods: We will culture the trophoblast cell lines, BeWo and JEG-3. Cells will be treated with different concentrations of hydrocortisone (0.05 to 5 μ M). qPCR and western blot will be used to measure the





expression of 11 β -HSD2 [cortisol metabolizing enzyme], the glucocorticoid receptor, the mineralocorticoid receptor, and inflammatory cytokines (IL1 β , IL-6, and TNF- α). We will also measure apoptosis using a caspase 3/7 assay.

Results: Data collected will illustrate the impact of elevated cortisol (hydrocortisone) at the maternal-fetal interface. We will demonstrate if elevated cortisol impacts the expression and activity of the placental 11 β -HSD2, an enzyme that converts active cortisol to inactive cortisone. We will also demonstrate whether elevated cortisol levels creates a pro-inflammatory cytokine response and induces placental apoptosis.

Conclusion: There has been a gap in research between the linkage of maternal stressors and the impact it has on the offspring. Filling this gap is important because it will allow for early identification of maternal stressors and how to clinically treat high stress levels to prevent adverse pregnancy outcomes such as preterm birth.

Infected Naïve CD4+ T Cells in Children with HIV Can Proliferate and Persist on ART

Presenting Author: Maud Mavigner, PhD; Emory SOM

JFF 2017 Characterization of SIV latency in rhesus macaque infant naïve CD4+ T-cells

Poster Number: 51

Katusiime, Mary Grace; Guo, Shuang; Neer, Victoria; Patro, Sean; Wu, Xiaolin; Horner, Anna; Chahroudi, Ann; Kearney, Mary and Mavigner, Maud

Background

Pediatric HIV remains a major public health issue with 1.7 million children living with HIV (CLWH) worldwide. The key obstacle to cure HIV infection is a reservoir of latently infected CD4+ T-cells that persist despite long-term antiretroviral therapy (ART). Although HIV primarily infects memory CD4+ T-cells, recent studies suggest that naïve CD4+ T-cells represent a significant contributor to the reservoir. Here, we characterized HIV persistence in naïve CD4+ T-cells from CLWH on long-term ART.

Methods

The cohort consisted of 8 children aged 5-11 years who initiated ART at a median of 4 weeks of age (range 0-39) with suppressed viremia for a median of 8.5 years. PBMC were sorted into naïve (CD45RO-CD28+CD27+CD95-CCR7+CD45RA+) and memory (CD45RO+CD95+) CD4+ T-cells. Multiple displacement amplification (MDA) was used to amplify genomic DNA from the sorted cells. Probe-based PCR methods were used to estimate the frequency of infection of each cell population and the proportion of proviruses with intact sequences. Proviral integration site analysis (ISA) was performed on the child naïve CD4+ T-cells with the highest frequency of infection.

Results





FACS sorting resulted in purities of a median 96.6% (range 93-100%) for memory and 97% (range 96.5-100%) for naïve CD4+ T-cells. HIV-infected naïve CD4+ T-cells were detected in all 8 children at a median of 37.5 infected cells/million (range 6-231), a mean of 11-fold lower than infected memory CD4+ T-cells in the same children. Of the 201 HIV detected in the naïve CD4+ T-cells of the 8 children, 4 were predicted intact. ISA identified 8 clones of infected cells in the naïve CD4+ T-cell subset, none of which were found to carry intact HIV proviruses.

Conclusions

We found that infected naïve CD4+ T-cells persist after 5-11 years of ART in early-treated children with perinatal HIV. Some infected naïve CD4+ T-cells can proliferate into clones of infected cells and a significant proportion of proviruses detected in naïve CD4+ T-cells are predicted to be intact. Our results demonstrate that naïve CD4+ T-cells are an important HIV reservoir in perinatally infected children on ART.

Understanding Priorities and Needs Before Implementing an Early Literacy Program in the Community

Presenting Author: Adriana Mendez, MA; Emory University

Poster Number: 27

Mendez, Adriana; Guerra, Karen; Yohannes, Millena; Reid, Nina; Corea, Mario; and Pickard, Katherine

Background: Reading fluency is a critical academic skill that predicts lifelong outcomes. However, disparities exist in reading attainment and are apparent as early as 4th grade, when only 21% of Latino children read at a proficient level compared to 46% of their non-Latino, White peers. Later reading skills are associated with several pre-literacy skills that develop earlier in life. Thus, caregiver-mediated interventions that teach caregivers evidence-based, language-promoting strategies across naturalistic home routines can be leveraged to support the language developed of young Latino children and may offset these well-documented disparities in reading skills. However, culturally adapted and responsive caregiver-mediated programs are limited.

This study aims to (1) understand caregivers needs related to the language and literacy development of their children and (2) understand perspectives for how to best implement a culturally adapted and responsive caregiver-mediated program. These aims are completed from the outset in equal partnership with a community non-profit, LaAmistad.

Methods: 101 mothers completed a needs assessment of sociodemographic information, child development, and family needs. Non-profit staff and caregivers then completed semi-structured interviews or focus groups about the development and implementation of a birth-to-five (B-5) program supporting early language development in the community.

Results: 35% of families reported having at least one child with delayed language. 60.3% of mothers reported desiring strategies to support their child's early reading. Deductive content analyses revealed that both staff and parents desired a B-5, caregiver-mediated program. Staff described family-level characteristics to consider, specific inequities faced by Latino families, and suggestions to develop a



culturally responsive program. Caregivers described barriers and inequities they face related to their child's learning and how a B-5 program could be responsive to their needs and values.

Conclusions: This community represents a group of children who are at elevated risk for early literacy challenges given systemic barriers and already known family history of language delays. Furthermore, results revealed that families and staff both desire and find value in an early literacy program that is responsive to structural inequities. Ongoing work continues to organize a community advisory board to oversee the implementation of a pilot B-5 program in the community.

ENaC as a Novel Therapeutic Target for Control of Infection in CF

Presenting Author: John Moran, BS; Emory University

ENaC as a Novel Therapeutic Target for Control of Infection in CF

Poster Number: 134

Kopp, Benjamin; and Moran, John

Background: Cystic Fibrosis (CF) is a genetic disorder that leads to progressive dysfunction in multiple organ systems due to mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. CFTR modulators have significantly improved disease outcomes, however CF patients continue to suffer from chronic bacterial infections and inflammation. Our group has determined that this incomplete bacterial clearance is due in part to macrophage dysfunction from defective CFTR. We showed that two CFTR-dependent mechanisms, reactive oxygen species (ROS) production and autophagy, were reduced in human CF peripheral blood monocyte-derived macrophages (MDMs) exposed to bacteria. In addition to chronic airway infections, poor mucociliary clearance is a hallmark of CF lung disease. This is caused by over expression of the epithelial sodium channel (ENaC) which leads to sodium hyper-absorption and dehydration of airway surface liquid. CFTR is expressed in macrophages and regulates their function, however the presence and role of ENaC in CF macrophages is unknown.

Methods: ENaC expression was characterized in human immune cells isolated from CF and non-CF blood donors. MDMs from donors were co-cultured with bacteria, with/without CFTR modulators under the following conditions: +/- Amiloride (ENaC inhibitor); +/- Capsazepine (ENaC activator) or novel ENaC inhibitors.

Results: Baseline expression of ENaC in human CF MDMs, lymphocytes, and granulocytes was increased at both the transcript and protein level relative to non-CF controls and persisted after exposure to bacteria. Inhibition of CFTR in non-CF MDMs resulted in ENaC overexpression. CFTR modulator (Trikafta) treatment reduced but did not eliminate ENaC overexpression in CF MDMs. Interestingly, ENaC inhibition with Amiloride increased CFTR expression. Amiloride treated CF MDMs also showed normalized ROS production, improved autophagy, and decreased pro-inflammatory cytokine production. Finally, results from an ion channel microarray indicated that sodium channel expression in CF MDMs normalized after Amiloride treatment with minimal effect on other ion channels.



Conclusions: ENaC is overexpressed in CF immune cells and is associated with abnormal macrophage function. ENaC modulation in immune cells is a novel therapeutic target for infection control in CF, either in combination with CFTR modulators, or as a sole agent for patients not currently eligible for CFTR modulators.

Arginine Replace Therapy (ART) , Clinical Outcomes, Mitochondrial Function and Oxidative Stress in Children with Sickle Cell Disease (SCD) and Vasoocclusive Pain Episodes (VOE): A Randomized Controlled Trial

Presenting Author: Claudia R Morris, MD; Emory University

Poster Number: 160

Morris Claudia R; Bakshi Nitya; Leake Deborah; Gillespie Scott; Brown, Lou Ann; Harris Frank; Hatabah, Dunia; Khemani, Kirshma; Locke, Alexis; Korman, Rawan; Rees, Chris A, Griffiths, Mark; Reyes, Loretta; Kumari, Polly; Shiva, Sruti; Dampier Carlton

Introduction: During SCD-VOE, patients develop an acute arginine deficiency. We have previously demonstrated that intravenous (IV) ART improves mitochondrial function, while the precise mechanisms remain unclear.

Objectives: To determine the role of IV ART in management of SCD-VOE

Methods: Prospective single-center double-blind randomized controlled trial (RCT) of IV ART (TID, up to 7 days) in children with SCD age 3-21 years hospitalized for VOE, randomized into 1 of 3 arms: 100 mg/kg/dose ART, standard dose (SD); loading dose: 200 mg/kg followed by SD; placebo. Demographics, total parenteral opioid (TPO) use (morphine equivalents, mg/kg), time-to-crisis-resolution (time-of-study-drug-delivery to last IV opioid in hours) and mitochondrial function were obtained before treatment and at discharge. The primary outcome measure was TPO use.

Results: 1,548 patients were screened, 266 were eligible, 114 consented, & 108 were randomized. Mean age is 12.7±3.8years; 48% male; 72% Hb-SS; 68% Hydroxyurea use. While statistically insignificant, there was a clinically relevant decrease in TPO & time-to-crisis-resolution in both ART arms versus placebo. The placebo group required 45% higher TPO & experienced >15 hours longer mean time-to-crisis-resolution versus the combined ART groups when adjusted for hydroxyurea use, continuous age and sex. Among children <17 years, the placebo group (n=33) required 80% more TPO compared to combined ART groups (n=57; p=0.075). Notably mitochondrial complex-IV & -V activity increased significantly after ART versus no change in placebo (p<0.001); protein carbonyl levels decreased after ART (p<0.001), suggesting a decrease in oxidative stress that increased in the placebo arm (p=0.02). Greatest mitochondrial improvement occurred with the arginine loading dose arm.

Conclusion: ART increases mitochondrial activity and decreases oxidative stress in children with SCD-VOE. Acute improvements in Complex IV & V function and decreased oxidative markers with ART are consistent with arginine-induced reductions in mitochondrial oxidant generation. Given emerging data supporting a link between mitochondrial function and pain, improved mitochondrial activity may



mechanistically contribute to decreased pain and ultimately less opioid requirement with IV ART, as well as have further implications for improved metabolism and oxidative signaling in SCD.

Assessment of Disaster Preparedness at the Household Level in a Pediatric Cardiology Clinic Population

Presenting Author: Matthew Mosgrove, M.D.; Emory University School of Medicine

Buchter Resident Research Award, 2022

Poster Number: 89

Mosgrove, Matthew; Greenky, David; Iannucci, Glen; Philipsborn, Rebecca; Bohling, Amy; Steigerwald, Samantha; Herron, Benjamin; Jergel, Andrew; and Murray, Brittany

Background:

Natural and human-provoked disasters pose serious health risks to children, particularly those with underlying medical conditions. The American Academy of Pediatrics (AAP) provides preparedness recommendations for families, but little is known about recommendation adherence among children and youth with special healthcare needs (CYSHN). This study aimed to assess household-level disaster preparedness in families with at least one child who attended pediatric cardiology clinic with a focus on CYSHN.

Methods:

Over 4 months, caregivers of children seen in a pediatric cardiology clinic were recruited in clinic to complete an electronic survey. Participants self-reported child medical history information as well as their households' implementation of AAP recommended disaster preparedness items. Families received a link to AAP resources on household disaster preparedness and were offered a child ID card. Data were analyzed using descriptive statistics with Fisher's exact and Wilcoxon rank sum tests.

Results:

The survey was completed by 121 caregivers, 68 (56%) of whom indicated that their child has a cardiac condition. There were 62 (51%) female and 63 (52%) white children of respondents with a mean age of 7.8 years. Of children with a cardiac condition, 41 (60%) regularly use medication, 14 (20%) use electronic equipment, 13 (19%) require a special diet, and 5 (7%) use oxygen. The average preparedness item completion rate was 70% for household preparedness, 40% for reunification preparedness, and 27% for community preparedness. Households of children with medical needs had similar rates of preparedness compared to overall rates. Of all respondents, 30% had previously received disaster preparedness resources, 66% would like resources on discussing disaster preparedness, and 90% intend to talk with their household about disaster preparedness after completing the survey.

Conclusions:





These results demonstrate a gap between AAP recommendations and family adherence to household-level disaster preparedness. Both families of CYSHN and those without were not well prepared for disaster, but families were interested in the topic. The rate of families that received resources compared to those that would like resources highlights a need for intervention. Pediatric subspecialists may consider asking about disaster preparedness and providing disaster preparedness resources tailored to the needs of their patients.

Understanding the impact of ECMO on long-term cognitive and physical functioning amongst Single Ventricle patients who underwent Stage 1 Palliation.

Presenting Author: Ishika Mukherjee, Bachelor in Science; Major: Neuroscience and Behavioral Biology
Minor: Global Health, Culture, and Society; Emory University

Poster Number: 135

Mukherjee, Ishika; Gleason, Shelly (MPH); and Aljiffry, Alaa (MD)

Abstract: Understanding the impact of ECMO on long-term cognitive and physical functioning amongst Single Ventricle patients who underwent Stage 1 Palliation.

Authors: Mukherjee, Ishika; Gleason, Shelly (MPH); and Aljiffry, Alaa (MD)

Background: Univentricular patients are at increased risk of mortality. Of these, patients who undergo extracorporeal membrane oxygenation are at higher risk of neurological complications. We aim to describe the short-term outcomes and long-term behavioral outcomes of univentricular patients that required ECMO in the immediate postoperative period after stage I palliation.

Methods: Single-center retrospective study with a prospective limb at an academic quaternary children's hospital. All patients who underwent stage I palliation between January/2010 – December/2017 were included and stratified into ECMO and non-ECMO groups. Patient characteristics and Functional Status Scores were collected. BRIEF-II assessment was performed for the enrolled patients. Analysis was performed using appropriate statistics with a significance level set at $p = 0.05$.

Results: in the study period, we had a cohort of 200 patients. Among those, 50 (25 %) required ECMO postoperatively. Of those, 34% survived to discharge, and 8 (47%, $p < 0.001$) had neurological complications. Among the enrolled cohort, ECMO patients had prolonged hospital length of stay (57 [49; 79.2] $p = 0.05$), prolonged CICU length of stay (42 [23.8; 49.2] $p < 0.05$), and neurological complications 62.5% $p < 0.001$ when compared to non-ECMO patients. 25 % of ECMO patients had unfavorable outcomes based on FSS. There is an increase in T scores in Global Executive Functioning, Emotional regulation, and Behavioral regulation among the ECMO group ($p < 0.05$).

Conclusion: Univentricular patients who require ECMO postoperatively are more likely to have challenges in executive functioning, emotional regulation, behavioral control, behavioral awareness, and behavioral tendencies when compared to non-ECMO patients.



Trends in Pediatric Gunshot Wound Cases During the COVID-19 Pandemic

Presenting Author: Makda Mulugeta and Gabrielle Bailey, Bachelors of Science; Children's Healthcare of Atlanta

Poster Number: 136

Mulugeta, Makda; Bailey, Gabrielle; Blackwell, Laura; and Reisner, Andrew

Background: Firearm injuries are the leading cause of death and injury in children. Literature indicates the incidence of pediatric gunshot wounds increased during the COVID-19 pandemic, but it has yet to reach a consensus regarding the pandemic's impact on mortality or demographics affected. It is essential to examine trends in pediatric firearm injuries during the pandemic to understand factors exacerbating this crisis. This study examines incidence, mortality, and demographic trends in pediatric gunshot wounds before and during the COVID-19 pandemic.

Methods: A retrospective cohort of patients 0-20 years-old ($\bar{x}\pm s=9.74\pm 4.725$) presenting to the ED from January 2014 to December 2022 with gunshot wounds who were entered into the state-wide Trauma Registry based on National Trauma Data Standards were analyzed in this study (n=633). Patients were separated into "pre-pandemic" and "pandemic" groups based on the U.S. COVID-19 State of Emergency Declaration date, March 13, 2020. Race was populated from the Trauma Registry. Majority are male (76%), Black (74%), and ≤ 15 years-old (92%). Mortality rate is 6%.

Results: Of 633 patients, 299 were injured pre-pandemic (6-year period), and 334 were injured during the pandemic (2-year period). Incidence increased linearly over time ($R=0.966, R^2=0.933$); the highest was in 2022 at 124 patients, a 6% increase from 2021 and a 343% increase from 2014.

The pandemic was not associated with mortality ($\chi^2(1)=0.034, p=0.853$), nor with gender ($\chi^2(1)=0.250, p=0.617$). It was associated with White or Black race; the pandemic saw a 29% increase in Black patients and a 37% decrease in White patients ($\chi^2(1)=12.256, p<0.001$). No difference in age was noted before and during the pandemic ($Z=-.967, p=0.333$), nor between the 8-year period ($H(8)=8.609, p=0.376$).

Conclusions: The incidence of pediatric gunshot wounds steadily increased over time rather than sharply increasing during the pandemic. Although mortality, age, and gender were not significantly impacted by the pandemic, race was. During COVID-19, more Black patients and less White patients were injured than in years prior. Further studies are warranted to understand these trends and their implications.

Comparative Single-Cell RNA-Seq Analysis between Patient-Derived Mucosal Epithelium and their Intestinal Organoids

Presenting Author: Shanta Murthy, M.S.; Emory University

Poster Number: 137

Murthy, Shanta; Maddipatia, Sushma Chowdary; Anbazhagan, Murugadas; Pelia, Ranjit Singh; Dodd, Anne; Kolachala, Vasantha L; Geem, Duke; Cutler, David J; Matthews, Jason D; and Kugathasan, Subra





Background: In vitro organoids of intestinal epithelium have revolutionized studies of IBD and offer insight into the disease's molecular and cellular basis. To comprehend the properties of intestinal epithelium within IBD, we used a comparative analysis of cell subtypes and transcriptomes from epithelial cells freshly isolated from patient biopsies and corresponding in vitro counterparts once grown into organoids.

Methods: Rectal biopsies obtained during colonoscopy from consented patients at Children's Healthcare of Atlanta were immediately processed for single cell RNA sequencing (scRNA-seq) and organoid culturing. Biopsies were cold protease digested and single cells encapsulated in a 10X Chromium, with libraries prepared in 3' chemistry. TrypLE digested organoids were similarly processed after being grown from isolated crypts in Matrigel and IntestiCult media for 3 passages. CellRanger converted sequenced reads mapped to GRCh38 were analyzed using Seurat v4.3.0. QC metrics of mucosal epithelial and organoid cells were compared along with their cellular subtypes.

Results: Comparison of scRNA-seq data from fresh in vivo epithelium (14,239 cells) to cultured organoids (16,598 cells) from the same intestinal site revealed striking differences at transcriptome and subtype levels. Organoids depicted strong inverse correlations between percentage of mitochondrial and ribosomal transcripts and expressed 2 times the number of features per cell than mucosal epithelial cells. Twelve subtypes of mucosal epithelium were present; however, in organoids stem (LGR5/SMOC2+) and proliferating (TOP2A/MKI67+) subtypes were predominant, without discernable bona fide goblet (MUC-2/SPINK4+), tuft (LRMP/SH2D6+), BEST4+ (BEST4/OTOP2+), or EEC (CHGA/CHGB+) cells as observed in the mucosa. Complexity analysis described by ratios of UMI and feature counts revealed mucosal epithelial cells with broader, significantly different complexity profiles than organoids. Re-analysis of published data of intestinal organoids grown in differentiating media demonstrated profiles closer to mucosal epithelium, but still lacking multiple epithelial subclusters.

Conclusions: In vivo mucosal epithelial cells can be bioinformatically distinguished from in vitro organoids, portraying unique activity and gene expression per cell along the crypt axis that is not replicated in vitro. Absence of clearly differentiated subtypes and the abundance of organoid transcriptomes suggests loss of spatial and chemical context from the crypt-mesenchyme axis in vivo still limits cells in culture.

Social Disability and Loneliness at School in Early School-Aged Children with and without Autism Spectrum Disorder

Presenting Author: Harshini Murthy, B.S.; Emory University

Poster Number: 138

Murthy, Harshini; and Edwards, Laura

Background: Social inclusion is positively associated with positive social interactions and academic achievement (Wentzel et al., 1995; Frederickson et al., 2002; Siperstein & Parker, 2008). Children with autism spectrum disorder (ASD) may be at increased risk for social isolation than their typically developing (TD) peers (Howlin et al. 2004; Mazurek and Kanne 2010; Rotheram-Fuller et al. 2010).





Classroom contextual factors affect the academic outcomes of children with ASD (Sutherland et al., 2008), and likely also influence social inclusion or isolation.

Objectives: (1) Investigate the relationship between social disability and loneliness in a school-aged sample of children with ASD and their TD peers; (2) Explore the effects of classroom contexts on this relationship.

Methods: This study includes children who previously participated in baby sibling research once they turn 5 years old. 40 (20 ASD) participant families will be enrolled by June 2023. Caregivers complete the Social Responsiveness Scale (SRS-2) as a measure of child social disability; children complete the Loneliness and Social Dissatisfaction Questionnaire (LDQ). Parents and teachers provide information about the child's classroom environment. Multiple regression will be used to determine the effect of social disability on loneliness and investigate any moderating effects of classroom characteristics on this relationship.

Results: In a preliminary sample of TD (n=49, Mage(SD)=5.29(0.50) years), ASD (n=9, Mage(SD)=5.56(0.53) years), and children with other communication disorders (CD) (n=8, Mage(SD)=5.75(0.89) years), 56% of ASD, 33% of CD and 12% of TD children were enrolled in inclusive classrooms. Analysis of parent-reported child loneliness and social disability suggests a positive significant relationship between social disability and loneliness in school, $r(63) = .77, p < .001$, and within the ASD sample $r(9) = .75, p = .020$.

Conclusions: Analyses suggest that caregivers of children with higher degrees of social disability perceive that their children experience greater loneliness in school. Teacher reports of classroom characteristics will allow for further investigation of the potential moderating effects of classroom contexts. These findings may inform educational design and decision-making to optimize the social and academic outcomes of children with ASD.

The Impact of Face Masks on Emotional Inference in Children: A Meta-Analysis

Presenting Author: Sathvika Narasimhan, Undergraduate Student; University of Georgia

Poster Number: 139

Sathvika Narasimhan

Background

With the advent of the COVID-19 pandemic in early 2020, many safety regulations including mask-wearing became widespread in public settings. Most individuals', including children's, interactions with others in these settings began to involve face coverings. With these practices and the numerous unknowns that exist with mask-wearing, it is important to consider not only how this may impact children both socially and emotionally, but also how this affects their ability to interpret facially expressed emotions. Some studies have begun to study these effects from various experimental lenses, but it is important to compile and analyze results collected from different methodologies to wholly comprehend the effect mask-wearing has on emotion identification in children.





Methods

Research papers pertaining to the subject of emotion identification of masked faces in children were sorted through. Key terms used for the search were: “emotion comprehension”, “children”, “infants”, “masks”, and “emotional literacy”. Data sources for the study include Google Scholar, PubMed, and Web of Science. Articles were included if experimental subjects included individuals sixteen years and below, had a large sample size, and maintained the use of a control group. Data collected consisted of various controlled trials with participants of both genders.

Results

Four studies were included in this analysis which revealed several key findings. Emotions were better identified in unmasked models and masked models that stated their emotions (both explicitly or implicitly) compared to silent masked models. Older children (6 to 8 years) were better able to infer emotion in masked models compared to younger children and toddlers (3 to 5 years) despite having similar performances when unmasked.

Conclusion

Face masks can impact the inference of facially expressed emotions at any age, but have a more significant impact the younger the subject is. This is likely due to age-related development of emotional comprehension with older children and adults being better able to use situational cues to infer emotion. Results suggest that children can be better supported in emotional identification by providing verbal cues to represent emotion and will naturally be able to utilize cues, aside from facial expressions, to infer emotion as they grow older.

Preterm infant cortical responses to mother’s voice in the NICU predict later emotional connection with mother

Presenting Author: Mary Lauren Neel, MD, MSCI; Emory

Thrasher Early Career Award, 2019-2022

Poster Number: 52

Neel, Mary Lauren; Srinivas, Rachelle; Kjeldsen, Caitlin; Jeanvoine, Arnaud; and Maitre, Nathalie

Term-born infants have an auditory preference for mother’s voice. In hospitalized preterm infants, even limited exposure to mother’s voice correlates with physiological improvements. Preference for mother’s voice in the preterm period and possible later implications are unknown. We aimed to quantify preterm infant cortical responses to mother vs stranger voice and later associations with infant response to mother.

In this pilot prospective cohort study, we used time-locked high-density EEG at 34-36 weeks corrected age (CA) to measure infant responses to 4 randomly presented recorded voice conditions: mother vs stranger and infant- vs adult-directed speech (IDS vs ADS). Stranger voice was randomly provided by another participant’s mother. To determine preterm cortical frequency bands, we compared average





amplitude of responses to mother vs stranger conditions for significance across 1-20 Hz. We then tested for main effect of mother vs stranger on EEG global field power (GFP, a global estimate of brain activity) and used univariate analysis of variance to test if mother/stranger response differences were driven by infant response to IDS. Finally, we used linear regressions to test associations between response to maternal IDS vs ADS and standardized 3-4 month CA dyadic interactions (Welch Emotional Connection Screen (WECS)).

Thirty-three infants (mean birth GA=28 weeks) were tested at both timepoints. Significant spectral amplitude differences to mother vs stranger were present across 3-9 Hz. Infants had stronger average GFP responses to maternal compared to stranger's voice (138.3 uV (SD 107.3) vs 7.0 uV (SD 13.9); $p=0.042$), driven by response to maternal IDS vs all other conditions ($p=0.02$). There was no difference for stranger's voice between IDS and ADS ($p>0.5$). Mean ratio of maternal IDS to ADS response magnitude was 1.16 (SD 1.1). Higher response to maternal IDS/ADS was associated with later increased WECS baby emotional attraction [$R=0.234$ ($p=0.029$)], even when controlling for birth GA ($p=0.03$).

We show for the first time that hospitalized preterm infants have larger cortical responses to mother vs stranger's voice. More importantly, their ability to differentiate mother IDS vs ADS in the NICU predicts infant connection to mother at 3-4 mo CA. Opportunities abound for developmental interventions leveraging mother IDS.

Impact of follow-up adherence on disease activity in childhood-onset systemic lupus erythematosus (cSLE)

Presenting Author: Meghan Nelson, DO; Department of Pediatrics, Emory University School of Medicine

Poster Number: 65

Meghan Corrigan Nelson, DO, Colleen Mosley, MS, D. Sofia Villacis-Nunez, MD, Kelly Rouster-Stevens, MD, MS, and Amit Thakral, MD

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, with a potential for significant disease damage, morbidity, and mortality. In comparison to the adult population, childhood onset SLE (cSLE) tends to be more aggressive given the higher preponderance of renal and neuropsychiatric disease and increased disease activity. There is a paucity of literature examining relationship between disease activity, rheumatology follow-up visits, and health care utilization. The objective of this study is to determine whether adherence with outpatient clinic visits would affect disease activity in patients with childhood-onset systemic lupus erythematosus (cSLE).

Methods: 41 children <18 years of age at time of diagnosis with SLE who met Systemic Lupus International Collaborative Clinics (SLICC) criteria and not evaluated in clinic within the previous 120-day period were identified as eligible for inclusion. Patients were continuously searched between December 2021 – July 2022 for eligibility evaluation. Through retrospective chart review, we assessed disease activity (SLE Disease Activity Index) at the last clinic visit. The patients were stratified into two cohorts of lower and higher disease activity, with SLE disease activity index (SLEDAI) ≤ 3 and SLEDAI ≥ 4 ,



respectively. Descriptive statistics and Willcox Rank Sum (numerical variables) and Fisher's test (categorical variables) were used to compare these two groups.

Results: Clinical, epidemiological and serological data were compared between the two groups, with observed statistically significant differences to include current use of high dose prednisone associated with higher SLEDAI scores ($p=0.019$). In nonparametric analysis, time to follow up ($p<0.001$), hospitalizations ($p=0.017$) and Emergency Department visits (ED) ($p<0.001$) were found to be associated with higher SLEDAI scores.

Conclusion: Our findings suggest that cSLE patients with higher disease activity are at risk for increased health care utilization with respect to ED visits as well as hospitalizations in the setting of follow-up nonadherence. While further studies are required to enhance our understanding of this association, this links the importance of disease-related outcome and routine outpatient visits in this particularly vulnerable patient population.

Adaptive Significance of Visual Attention to Bodies in Infants with and without Autism Spectrum Disorder

Presenting Author: Christopher Nicholson, B.S.; Emory University

Poster Number: 140

Chris Nicholson, Warren Jones, Laura Edwards, Miriam Lense

Background: Communication to infants occurs multimodally through speech, gesture, and facial expressions. Parents' use of co-occurring gestures with speech facilitates language development, including in children at risk for autism spectrum disorder (ASD). Children with ASD have impairments in both gesture and language development. While previous research has shown that gestures modulate social visual engagement in typically-developing (TD) infants and infants with ASD, little is known about the adaptive significance of visual attention in clips with gestures. We investigated the relationship between visual engagement and adaptive functioning, as measured by cognitive and developmental assessments, in infants with and without ASD.

Methods: Eye-tracking measures of SVE were collected from infants while they watched videos of a caregiver engaging them naturalistically, using either infant-directed speech or song, with or without gestures. Infants were eye-tracked at 12 months (Speech: $n_{TD}=55$, $n_{ASD}=21$; Song: $n_{TD}=108$, $n_{ASD}=39$), with eye-tracking data quantified as the percentage of time infants spent fixated on regions of interest within videos (i.e. eyes, mouth, body, and object). Infants were evaluated for ASD at 24 months by expert clinicians using gold-standard assessments. Correlations were calculated between body-looking in 12-month eye-tracking data and 24-month assessment data.

Results: Between the TD infants and infants with ASD, different eye-tracking measures at 12 months were predictive of different clinical measures at 24 months. Both groups had correlations between body-looking in speech and song videos and assessment scores, but of all significant correlations, the TD infants had correlations in videos with gestures only and the infants with ASD had correlations in videos



without gestures only. Additionally, all of these correlations in the TD group were negative, while all of these correlations in the ASD group were positive.

Conclusions: Attention to the body has different adaptive value in children with and without ASD. This difference may reflect different ways infants with ASD learn about gestures; for instance, infants with ASD who look at bodies more may have greater understanding of the context in which gestures occur, which is reflected in greater developmental scores. Eye-tracking measures may be a useful tool in predicting later developmental trajectories in children at 12 months.

AI-Based Approach to Monitor Progression of Anorexia nervosa

Presenting Author: Navya Nori, High School (current); Milton High School

Poster Number: 141

Nori, Navya

Every hour, a person dies as a result of an eating disorder. Anorexia Nervosa, a type of eating disorder, is the third most prevalent chronic illness among adolescents and young people. Current efforts to prevent this condition simply provide emotional support, and do not act in real time, monitor progression, or track a patient's physiological manifestations. A comprehensive approach tracking both emotional and physiological needs called SupportED was designed to combat this problem. Given the alarmingly high presence of body dysmorphia content from teens on social media platforms, three artificial intelligence (AI) models were developed to monitor social media activity for warning signs of this illness. These models were trained on Twitter data and score a user's post captions for indicative words or phrases of an eating disorder, classifying a case of Anorexia by the DSM-5 criteria for this mental illness. To assess the physiological effects, a laboratory experiment was conducted by culturing *Clostridium sporogenes*, a common gut bacteria, in staggered dilutions of a growth medium to determine at what carbohydrate starvation level this microorganism perishes.

The lab results demonstrate that each concentration of the growth medium yields a correspondingly staggered amount of bacterial decline (cells/mL). However, at around 50% of the undiluted broth, bacterial growth decreases significantly. For the computational monitoring of emotional warning signs, the most significant words showing Anorexia were "skinny," "weight," and "eat." Both of these results were incorporated into a mobile application, SupportED. If the app detects that the user's posts suggest warning signs of Anorexia, it sends a survey asking what food the user consumed in the past day. It then calculates the carbohydrate quantity in the food consumed and divides that by the recommended number of sugars for that individual in 24 hours calculated from BMI. If this number is considerably below 50% (threshold determined through experimentation), the app sends a notification to the supporter, or trusted individual's connected account. Overall, it was shown that using bacterial growth analysis and AI modeling, a comprehensive approach could be designed to reduce the impact of Anorexia Nervosa.



AI-Based Approach to Predict High-Risk Pregnancies

Presenting Author: Navya Nori, High School (current); Milton High School

Poster Number: 142

Nori, Navya

According to the World Health Organization, approximately 300,000 women died during pregnancy and childbirth in 2017. In 2022, 2.4 million newborns were lost due to largely preventable causes. While these numbers are drastically higher in developing areas, the US has the highest maternal and perinatal mortality rates among all developed nations. These statistics reflect inequities in access to health services and medications, but resources could be allocated optimally if patients with higher-risk pregnancies could be identified. Given that the factors which contribute to a risky pregnancy are largely predictable with artificial intelligence (AI), this work proposes a low-cost and personalized tool to calculate pregnancy risk and make timely recommendations for women and their children in developing areas.

The research question in this study investigates which factors are the best predictors of a risky pregnancy. It was hypothesized that chronic conditions, as well as age, would have the highest risk. Publicly available deidentified datasets from the UCI machine learning repository were used to train three AI risk prediction models. The first set contained age, sex and, clinical information, while the other contained vitals and lab values such as blood sugar and systolic/diastolic blood pressure. The models developed were of three types – a Generalized Linear Model (GLM), which assumes a linear function for the factors, a Gradient Boosted Machine (GBM) which uses a nonlinear decision tree-based approach, and Multi-layer Perceptron which is a deep learning based network. The most important features from the first GBM model were chronic conditions such as diabetes, hypertension, and obesity; the nonlinear interactions between features were seen to be very important and drastically amplified overall risk. While models trained solely on clinical factors performed with an AUC of approximately 60%, models trained with lab values had an AUC of 88%. All the models could distinguish between high-risk pregnancies (cases), and normal pregnancies (controls), with high accuracy and precision. The linear model was used to build an app that clinicians can use to easily compute risk scores throughout the pregnancy and come up with personalized intervention plans.

Establishing the mitochondrial citrate transporter as a regulator of cardiac morphogenesis.

Presenting Author: Chiemela Ohanele, BA; Emory University

Poster Number: 28

*Chiemela Ohanele**; *Jessica N. Peoples**; *Anja Karlstaedt*; *Ashley Gayle*; *Nasab Ghazal*; *Fateemaa Sohani*; *Milton E. Brown*; *Michael E. Davis*; *Victor Faundez*; *Jennifer Q. Kwong*

Background:





Congenital heart disease (CHD) results from structural and functional defects of the heart that arise during embryonic development. CHD represents the most common type of birth defect and in the United States alone, affects ~1% of births per year. One common genetic cause of CHD is 22q11.2 deletion syndrome (22q11.2DS), where ~75% of 22q11.2DS patients present with CHD. SLC25A1, which is found in this deletion region, codes for a citrate carrier protein that is found in the inner mitochondrial membrane. In developing mouse models to study the in vivo functions of the mitochondrial citrate carrier (SLC25A1), a mitochondrial inner membrane transporter responsible for mitochondrial citrate export, we uncovered an unexpected embryonic-lethal knockout model that suggested roles for mitochondrial function in heart development.

Methods and Results:

H&E stained hearts from E18.5 Slc25a1 knockout embryos display a striking array of cardiac malformations including persistence of an expanded zone of trabeculated myocardium, reduced compact myocardium, and ventricular septal defects. Analysis of mitochondrial structure and function by electron microscopy and respiration assays reveal that loss of Slc25a1 causes mitochondrial ultrastructural defects and depresses mitochondrial function. Lastly, NanoString transcriptomics analyses of metabolism-related genes revealed that Slc25a1 deletion altered expression of oxidative phosphorylation, glycolysis, lipid metabolism, and hypoxia-related genes in a dosage-dependent manner.

Conclusions:

Our results highlight a novel role for SLC25A1 in mitochondrial citrate transport and the transcriptional control of metabolic networks in the developing heart, while pointing to a new role for SLC25A1 in the metabolic maturation of the developing myocardium.

Accurate Dosing Weight: When the 10% really matters

Presenting Author: Evan Orenstein, MD; Emory University

Poster Number: 54

Thompson, Sarah A; Kandaswamy, Swaminathan; and Orenstein, Evan W

Background: Inaccurate dosing weights can lead to medication and blood transfusion dosing errors. Dosing weights in the electronic health record (EHR) may differ from the most recently recorded weight for appropriate reasons (e.g. edema, newborns) or inappropriate (e.g. forgot to update). We aimed to reduce the proportion of medications that were administered where the dosing weight was $\geq 10\%$ different from the recorded weight through an interruptive alert that would fire upon chart open for hospitalized children when (1) the dosing weight and most recently recorded weight were $\geq 10\%$ different and (2) it had been at least 7 days since the last dosing weight update.

Methods: We developed a candidate alert design to reduce weight discrepancies based on heuristic design. We then adopted in situ usability testing to iteratively improve design of the alert. The clinical decision support (CDS) was implemented and evaluated using a pre-post design. Our primary process





measure was medication administrations while the dosing and most recently recorded weight were $\geq 10\%$ different. We also followed balancing measures including (1) number of alert firings per week and (2) alert acceptance rate (i.e. users acting on alert and changing dosing weight). Metrics were compared pre- vs. post-implementation using X2 tests.

Results: The proportion of medication administrations with difference $\geq 10\%$ between their recorded weight and dosing weight decreased from 12.7% (51,951/410,328) in the baseline period to 8.7% (9,057/103,878) in the intervention period ($1 < 0.001$). Balancing Measures: On a per patient level, the alert fired for an average of 119 distinct patients per week during the background period and for average of 106 distinct patients/week during the first six weeks of intervention. Alert acceptance rate (i.e. opening the flowsheet to update dosing weight) was 15% (109/724).

Conclusion: User-centered design of an interruptive alert improved the accuracy of dosing weights during medication administrations without substantial alert burden. In-situ usability testing is an effective approach to rapidly obtain feedback from frontline users and iterate on the design to effect desired behavior changes. Running interruptive alerts in the background prior to implementation can ensure appropriate targeting as designed.

Improving Clinical Evaluations for Non-Accidental Trauma using Clinical Decision Support

Presenting Author: Evan Orenstein, MD; Emory University

Poster Number: 53

Swaminathan Kandaswamy, Sarah Thompson, Edwin Ray, Reena Blanco, Keisha Fraser Doh, Tim Chang, Stephen Messner, Evan Orenstein

Background: Non-accidental trauma (NAT) is a leading cause of injury and death during early childhood. Many cases of NAT are missed or diagnosed late. In this study, we aimed to improve recognition of fracture-related NAT (long bone and skull fractures) through design and implementation of clinical decision support (CDS) for providers in the emergency department (ED).

Methods: We developed three interruptive alerts for fracture (Long Bone, Skull, and outside hospital). Fractures were identified based on identification of patterns in the radiology reports consistent with a fracture using regular expressions. Recommendations for skeletal survey, social work consult, and labs/imaging for other evaluation were included in the alert based on literature and local leadership consensus. Our primary process measure was missed evaluations. At Children's Healthcare of Atlanta (CHOA), the child advocacy and trauma teams screen all potential traumas and highlight potential NAT cases for manual review. Even if a case is not identified as NAT, the team nonetheless flags whether all recommended evaluations (e.g. skeletal survey, social work consult) were performed based on the documentation. We utilized descriptive statistics to compare missed evaluations pre- and post-implementation.

Results: Pre-intervention (1/1/2022 to 10/19/2022), there were 68 missed evaluations (7.56 per month) retrospectively identified by child advocacy team, compared to 13 missed NAT evaluations (3.25 per month) post intervention (10/19/22 to 2/28/23). Of the 13 post-intervention cases that were missed, an



alert fired on 7 cases (54%) but providers did not place skeletal surveys in all 7 cases. Of the remaining 6 (46%), it did not fire in 2 cases as there was no fracture (1 eye injury, 1 hemorrhage), 3 cases where either a social work consult or skeletal survey was already ordered but NAT was missed anyway, and 1 case was initially misidentified as a motor vehicle collision (a suppression criteria for the alert).

Conclusions: Recognition of NAT is challenging for physicians. While guidance exists for specific injury types by age to evaluate for NAT, often these guidelines are not followed. Standardization of subsequent evaluation may help reduce missed cases of NAT. Preliminary data suggests that a CDS based intervention may improve outcomes.

Translating Machine Learning Research into Implementation: Visual Analytics Tool for Model Evaluation, Threshold Selection, and Explainability

Presenting Author: Evan Orenstein, MD; Emory University

Poster Number: 55

Braykov, Nikolay; McCarter, Andrea; Kandaswamy, Swaminathan; and Orenstein, Evan

Background: While predictive analytics has the potential to transform many aspects of healthcare, substantially more predictive models are developed than are ever implemented and used in clinical settings. One reason for this gap is that data scientists work in silos, separated from stakeholders for whom the model is intended, as well as from the engineers who implement it. Effective model implementation requires these stakeholders to collaborate throughout the development lifecycle, iterate through multiple experiments that vary feature sets and model parameters, and understand: (1) clinical trade-offs in threshold selection (e.g., increased sensitivity leading to reduced specificity), (2) feature importance to avoid overfitting and demonstrate face validity to clinicians, (3) model accuracy vs. model complexity (i.e., a less performant model that is more easily incorporated into the electronic health record (EHR) vs. a more performant model that requires a greater technical investment). These gaps in traceability and explainability of models often lead to implementation delays and failures.

Methods: We developed a novel model evaluation dashboard optimized for making implementation decisions in cross-functional healthcare settings. The dashboard, developed in RShiny, aims to reconcile 3 critical audiences necessary for effective implementation: (1) clinical stakeholders, (2) data scientists, and (3) electronic health record (EHR) analysts and data engineers who convert retrospective models into prospective implementations.

Results: We developed a tool that allows users to select the outcome of interest (e.g. critical or suspected sepsis) and presents performance of multiple models for comparison using area under the receiver operating characteristic (ROC) or precision-recall curve (PRC). The user can drill into a single model to see additional statistics such as decile plots and lift plots. The threshold selection tab allows the user to visualize the relative frequency of false positives and negatives as they vary the threshold while also summarizing sensitivity, specificity, and accuracy. Finally, the explainability tab provides references to model coefficients or shapley values so clinicians can quickly see which variables contribute most to the model prediction.





Conclusion: A reusable tool to visualize predictive model performance can bring clinical stakeholders, data scientists, and EHR analysts and engineers together for implementation decision-making.

The Scope of Practice of an Outpatient Pediatric Palliative Care - Oncology Clinic

Presenting Author: Hee Su Park, BS, BA; Emory University School of Medicine

Poster Number: 29

Park, Hee Su; DeGroot, Nicholas; Lange, Anna; Kavalieratos, Dio; and Brock, Katharine

Background

Pediatric palliative care (PPC) improves end-of-life outcomes for children with cancer. Though PPC visits are the 'intervention' in studies focused on end-of-life care, the content of PPC visits within pediatric oncology is poorly understood. This study aimed to understand the scope of PPC practice that occurs during PPC visits for children with cancer and their families.

Methods

This was a retrospective cohort study of patients 0-27 years with cancer seen in PPC clinic within an academic pediatric oncology center between 2017-2022. During each PPC visit, documenting providers chose the domains discussed or managed (Goals of Care, Symptom Management, and Care Coordination with respective subdomains). Data was abstracted from the electronic health record, PPC clinic database, and Cancer Registry. The differences in frequency and type of domains addressed were analyzed by visit type, diagnosis group, and proximity to the end-of-life.

Results

There were 1,911 outpatient PPC visits across 351 patients. The mean domains discussed per visit (10.2) did not differ between initial visits (10.2) and follow-ups (10.2). Mean domains were higher in visits <90 days compared to visits 91+ days from end-of-life (12.4 vs. 10.5; $p < 0.0001$). Pain (87% vs. 66.5%; $p < 0.0001$) and hospice collaboration (53.3% vs. 19.8%; $p < 0.0001$) were particularly discussed <90 days from end-of-life. Compared to brain tumor or leukemia/lymphoma visits, solid tumor visits addressed more symptom management domains including pain (80.1%; $p < 0.0001$), depression (18.9%; $p < 0.001$), and fatigue (33.6%; $p < 0.0001$). Goals of care subdomains were more frequently discussed in follow-ups compared to initial visits, notably around accommodating to the disease (93.7% vs. 87.4%; $p < 0.0001$), advance care planning (16.4% vs. 8.9%; $p < 0.0001$), and code status (6% vs. 3%; $p = 0.01$).

Conclusions

The scope of PPC practice is wide and varied. Each visit encompasses many domains with the most common being care coordination with oncology teams, helping patients/families cope with the disease, and management of symptoms. Patients with solid tumors had the highest number of domains addressed during visits, notably around symptom management. Across all diagnoses, more domains were discussed near the end-of-life, indicating the crucial role that PPC plays during this time.



$\gamma\delta$ T cell trafficking: efforts to direct the migration of genetically engineered immunocompetent cells to sites of pediatric hematopoietic malignancy

Presenting Author: Kiran Parwani, BA; Emory University

Poster Number: 30

Parwani, Kiran K.; Branella, Gianna M.; Spencer, H. Trent

Background:

$\gamma\delta$ T cells are attractive alternatives to $\alpha\beta$ T cells as anti-cancer immunocompetent cell sources, especially because third-party donors allow for off-the-shelf therapeutic product manufacturing. However, we show human $\gamma\delta$ T cells do not migrate to the mouse bone marrow (BM), which is the site of many pediatric hematopoietic malignancies. For this study, our goals were to i) better understand human $\gamma\delta$ T cell migration in mice and ii) develop engineering strategies to overcome limited migration to the BM.

Methods:

To determine if $\gamma\delta$ T cells can be directed to the BM, NSG mice were conditioned with chemotherapies shown to induce BM inflammation, busulfan or incomplete Freund's adjuvant (IFA), or radiation prior to administering $\gamma\delta$ T cells, and blood and BM were evaluated by flow cytometry (FC). To mechanistically differentiate homing and migration, mice were conditioned with radiation and injected with cell tracker-stained red blood cells and followed by FC. The phenotype of $\gamma\delta$ T cells in BM versus blood was also determined.

Results:

$\gamma\delta$ T cells remain in circulation after retro-orbital infusion and do not migrate to the BM. Unlike busulfan or IFA, radiation increases the percentage and number of $\gamma\delta$ T cells in mouse BM, in a dose-dependent manner. The percentage of $\gamma\delta$ T cells in the peripheral blood remains unchanged after radiation. Interestingly, the phenotype of $\gamma\delta$ T cells in BM is identical to those in circulation, and peripheral blood flowing into the BM increases with radiation.

Conclusions:

We demonstrate radiation enhances migration of $\gamma\delta$ T cells to BM. The mechanism of increased migration is not a homing phenomenon but is instead the result of increased blood flow through the BM, which is caused by a breakdown of the blood-BM barrier. This is important because it has been postulated that BM inflammation enhances $\gamma\delta$ T cell homing; however, we show mechanical breakdown is the mechanism for the increased trafficking. Directing these cells to the BM remains a crucial development for treating hematopoietic malignancies, and based on these studies, our focus is on engineering specific chemokine receptor expression in $\gamma\delta$ T cells, which will enhance BM homing.



Invitro monitoring of T lymphocyte proliferation in response to nanoparticulate vaccine candidates against H1N1 flu and Neisseria gonorrhoea pathogens

Presenting Author: Dedeepya Pasupuleti, MS Chemistry; Mercer University

Poster Number: 31

Pasupuleti, Dedeepya; Bagwe, Priyal; Vijayanand, Sharon; Zughaier, Susu M; and D'Souza, Martin. J.

T lymphocyte (T cell) proliferation is essential in pediatric patients to neutralize an infection and develop adaptive immune responses against specific antigens. Many pain-free vaccination strategies have been explored and developed since the onset of the recent COVID-19 pandemic. One common goal is to make universally available stable vaccines capable of developing a robust adaptive immunity against several disease-causing pathogens. However, to test the effectiveness of these vaccines in the development of adaptive immunity, it is imperative to estimate the ability of these vaccines to induce T-cell proliferation against the specific antigen during the formulation stages.

To estimate T cell proliferation capability of different vaccine candidates, we adopted Carboxyfluorescein in succinimidyl ester (CFSE) assay. We optimized the assay to suit our vaccine formulations: BSA microparticles (MPs) loaded with inactivated Neisseria gonorrhoea and PLGA nanoparticles (NPs) loaded with inactivated H1N1 virus.

The DCs – T cells overlay assay was optimized to yield significant T lymphocyte proliferation. The proliferation was analyzed using Flow Cytometry analysis. Proliferation across treatment groups was compared using T-test (non-parametric) for statistical representation.

Our results indicated that the T lymphocytes treated with Neisseria gonorrhoea + adjuvanted MPs proliferated to generate a daughter cell population with lower dye intensities as days passed. Compared to day 1, the parent population (high intensity of CFSE dye) diminished significantly, and the daughter population (low-intensity CFSE dye) increased significantly by day 7. Also, this group showed a significantly higher number of proliferated cells than the blank and no particle cells only (dendritic cells and CFSE stained T cells) groups, meaning more proliferated daughter T cells are present in the vaccine + adjuvant treatment group.

Similar results were observed with the H1N1 flu PLGA nanoparticles by day seven in terms of generation and in the number of daughter T cells generated indicating the vaccine formulations are capable of inducing T cell proliferation against specific antigens.

Our future studies include continued optimization of the DCs to T cells ratios, the number of particles introduced per treatment group for improved proliferation, and the effect of cytokine IL2 on the proliferation rates of the optimized CFSE assays.

Body Mass Index Versus Mid-Upper Arm Circumference: Can We Replace The Gold Standard?

Presenting Author: Kanan Patel, MS, RD, CSP; Children's Healthcare of Atlanta

Poster Number: 144





Patel, Kanan; Martin, Malia; Cook, Maegan; Batchelder, Dinisha; Bai, Shasha; Kirchner, Kevin; and Linnemann, Rachel

Background: For people with cystic fibrosis (PwCF), body mass index (BMI) has been established as the gold standard for nutrition assessment because optimal BMI correlates with better lung function, measured according to forced expiratory volume in 1 second (FEV1). Although, as in the general population, BMI use in PwCF has limitations because it does not distinguish lean body mass from fat mass [1]. Mid-upper arm circumference (MUAC) is an established measure of pediatric nutrition status and predictor of fat mass [2]. In 2021, our care center included MUAC measurements in nutrition assessment in children with CF. The objective of this study was to compare BMI and MUAC nutrition assessment methods.

Methods: An institutional review board–approved, single-center retrospective analysis was performed on 87 patients. Data were collected on BMI, MUAC, and FEV1 from April 2021 to March 2022. Correlation was assessed between BMI Z-scores and MUAC Z-scores, between MUAC Z-scores and FEV1, and between BMI Z-scores and FEV1. Subsequent-visit BMI, MUAC, and FEV1 measurements were obtained in 34 patients.

Results: BMI and MUAC Z-scores had a statistically significant positive linear correlation. MUAC Z-scores identified more patients as malnourished than BMI Z-scores. At the baseline visit, MUAC Z-score identified 11 of 75 children (15%) who were identified as well-nourished per BMI Z-score as having mild or moderate malnutrition (Cohen kappa statistic=0.46, 95% CI, 0.26-0.65). Of the three values (BMI, MUAC, FEV1), FEV1 at baseline remained the best predictor of FEV1 at the subsequent visit.

Conclusions: Based on our review, more patients were identified as malnourished according to MUAC than BMI, but because of the small sample size and retrospective nature of this review, a larger, multicenter study on MUAC as a nutrition assessment method in children with CF is necessary to determine correlation between MUAC and lung function.

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Characterizing the Temporal Relationship Between Infant Eye Contact and Caregiver Greeting in Infants Later Diagnosed with Autism

Presenting Author: Hely Patel, Bachelor of Science in Neuroscience and Behavioral Biology with Honors; Emory University

Poster Number: 143

Patel, Hely; Ford, Aiden; and Shultz, Sarah





This study explores caregiver greeting, a ubiquitous, exaggerated expression used by caregivers to initiate social interaction with their young infants (Stern, 1974). The greeting behavior establishes infant-caregiver interactions by designating the infant as the caregiver's interactive partner (Stern, 1974). Despite the key role of the greeting behavior and evidence that caregiver greeting differs in dyads with an infant later diagnosed with autism (Ford ... Patel et al., submitted) – a neurodevelopmental disorder characterized by social-communicative disabilities – the infant behaviors that may prompt caregiver greeting are unknown. This study investigates whether infant attention to the eyes of their caregiver – a critical cue that signals infant social engagement and a cue known to differ in infants later diagnosed with autism – may play a role in eliciting caregiver greeting. This hypothesis was tested in a prospective, cross-sectional sample of 33 infant-caregiver dyads with a neurotypical infant (NT) and 31 dyads with an infant later diagnosed with autism (AUT), all infants aged 3.5-5 months. Peristimulus time histograms were generated to characterize the temporal relationship between infant attention to the eyes and caregiver greeting. Results show that in the NT group, eye-looking is not related to greeting, suggesting that caregivers may use other infant cues to initiate the greeting or rely on successful previous experiences to drive this behavior. In the AUT group, there is a significant increase in eye-looking before and after the greeting, indicating that caregivers in this group rely on cues from their infant – in this case attention to the eyes – to perform their greeting and that caregiver greeting captures the attention of AUT infants in this age range. While greeting is still cued by infant attention in AUT dyads, the lack of relationship between infant attention to the eyes and caregiver greeting in NT dyads may suggest that NT infants may have progressed beyond the need for greeting by 3.5 to 5 months and are ready for more complex caregiver behaviors. These findings offer novel insight into the role of greeting through development and into how the dynamics of infant-caregiver interactions may differ in autism.

Positive Bacterial Blood Cultures and Time to Positivity in Children: Should Empiric Antibiotics be Reconsidered Sooner?

Presenting Author: Pratik Patel, MD; Emory University School of Medicine

Poster Number: 66

Patel, Pratik; Locsin, Miguel; Xiang, Yijin; Lu, Lydia; Fernandez, Alfred; and Jaggi, Preeti

Background: Evaluation for bacterial bloodstream infections (BSIs) is often associated with prescribing empiric antibiotics while awaiting blood culture results, typically 48 hours. We examined characteristics associated with positive cultures treated as BSI vs contaminant in children and BSIs associated with early (< 24 hours) time-to-positivity (TTP).

Methods: In a retrospective study of children (≤ 21 years) at our pediatric healthcare system, we abstracted demographic, clinical, and blood culture data from the electronic medical record for all initial positive bacterial blood cultures from March 2021 to June 2022. We excluded fungi and cultures collected within 14 days of a previous positive. TTP was calculated from time/date of collection to Gram stain report. Host status was categorized as previously healthy, immunocompromised (IC), and chronic condition/s (CC). A BSI was defined as a positive culture treated as bacteremia. BSI cultures were categorized as Gram-positive definite (GPD) pathogens, other Gram-positive (OGP), Gram-negative (GN),





or polymicrobial (PM). Characteristics associated with prolonged TTP for BSIs were identified using mixed-effects logistic regression.

Results: There were 1068 positive cultures identified in 896 patients, with 756 (71%) treated as BSIs and 702 of those (93%) positive in < 36 hours. Positive cultures drawn with adequate blood volume, in the setting of fever, from IC and CC children, and positive within 24 hours were significantly more likely to be treated as BSIs (all $p < 0.05$). The most common BSI was a GN pathogen (34.3%). On multivariate analysis, cultures collected from patients with fever, more than 1 positive culture, and positive with GPD, GN, and PM pathogens were associated with early TTP ($p < 0.01$).

Conclusions: We found that 93% of clinically significant BSIs in children were identified by 36 hours with BSIs with pathogenic organisms (GPD, GN, PM) associated with TTP < 24 hours. Reassessment of the need for empiric antibiotics after 24-36 hours should be considered.

Breathe easy: The potential of intranasal microparticulate vaccines for COVID-19

Presenting Author: Smital Rajan Patil, Bachelor of Pharmacy; Mercer University

Poster Number: 32

Smital Rajan Patil, Sharon Vijayanand, Tanisha Arte, Martin D'Souza

Background: The SARS-CoV-2 virus continues to cause havoc with more than 512 million COVID-19 cases and 6.23 million deaths worldwide, pertaining to the need for yearly vaccination. Despite the rapid development and approval of COVID-19 vaccines, the need for cold-chain storage impedes the global distribution of vaccines in developing countries. Moreover, approved vaccines utilize invasive, non-patient compliant, intramuscular route. Thus, there is an urgency for a globally available, non-invasive vaccination strategy for mass immunization against COVID-19. We utilized the spike receptor-binding domain as the vaccine antigen. We developed a stable microparticulate vaccine that enhances the immune response of the spike protein, avoiding cold-chain storage. Further, we tested a patient-compliant intranasal route of vaccine delivery. The intranasal route is promising as it allows the vaccine to interact with the mucosal layer activating mucosal immunity at the entry sites of the virus. Here, we compared non-invasive routes like intranasal with the invasive intramuscular route.

Methods: We formulated microparticles in a polymer matrix with double-emulsion method following lyophilization. For in vitro studies, immunogenicity of the MPs was assessed for nitrite levels: innate immune marker. We evaluated the expression of autophagosomes and the co-expression of antigen-presenting molecules and their co-stimulatory molecules using flow cytometry. For in vivo studies, mice were immunized with prime and two booster doses, both intramuscularly and intranasally. Serum and lungs were tested for RBD-specific antibodies. Secondary lymphoid organs were tested for RBD-specific cellular responses.

Results: Vaccine MPs induced extremely significant nitrite levels ($****p < 0.0001$) in APCs, indicating innate immune response. MPs expressed very significant levels ($**p < 0.01$) of autophagosomes and extremely significant ($****p < 0.0001$) co-expression of antigen-presenting molecules and co-stimulatory



molecules in APCs: connecting links between innate and adaptive immunity. Humoral, mucosal, and cellular responses were comparable in both intramuscular and intranasal groups.

Conclusion: Our intranasal vaccine is a non-invasive strategy enabling mass immunization and can potentially confer protection at the virus entry sites.

Two for one: The innovative bivalent vaccine against COVID-19

Presenting Author: Smital Rajan Patil, Bachelor of Pharmacy; Mercer University

Poster Number: 33

Smital Rajan Patil, Sharon Vijayanand, Tanisha Arte, Martin D'Souza

Background: Cross-protective vaccines against emerging strains of SARS-CoV-2 are in dire need to avoid repeated vaccination against COVID-19. Although spike protein is immunogenic, current vaccines raise concerns regarding efficacy against emerging strains due to high mutation rates of spike protein. Here, we compared an adjuvanted-bivalent vaccine (spike and nucleoprotein) as microparticles delivered using 3D-printed dissolving films, microneedles, and nasal drops via the buccal, transdermal, and intranasal route. We hypothesize that a vaccine administered through these non-invasive routes can induce robust immune responses against emerging strains. A bivalent vaccine would ensure a cross-strain specific, durable immune response against both spike and nucleoprotein: spike binds to target cells, and more conserved nucleoprotein is involved in viral replication. The advantages of non-invasive vaccine delivery strategies are ease of use and early mucosal immunity induction at infection entry sites.

Methods: Antigen/adjuvant microparticles were formulated using the double emulsion method. These microparticles were incorporated in a polymer base to formulate microneedles, a film-based vaccine. For nasal drops, the vaccine microparticles were resuspended in an appropriate buffer. These formulations were tested in vivo for the presence of humoral, cellular, and mucosal immune responses. We tested for antigen-specific antibodies and mucosal responses in sera and lungs using binding assays. We also tested for antigen-specific cellular responses in secondary lymphoid organs using flow cytometry. Further, we tested the presence of humoral, cellular, and mucosal responses against variants of concerns such as delta and omicron to test cross-reactive immune responses.

Results: We successfully formulated non-invasive formulations such as microneedles, dissolving films, and nasal drops. In vivo testing indicated significant antigen-specific antibodies and mucosal markers in sera and lungs. This bivalent vaccine also induced significant antigen-specific cellular response levels in secondary lymphoid organs. We also observed antibody and cellular responses against the delta and omicron variants of SARS-CoV-2.

Conclusion: These vaccination strategies will be critical in developing a universal vaccine against COVID-19. Non-invasive vaccines are appealing, especially to pediatric and geriatric populations. Therefore, this vaccine is a promising patient-compliant alternative against emerging strains of COVID-19.



Delayed Viral Rebound Following Antibody Administration In Infant Macaques

Presenting Author: Jenna Powers, BS, MD Candidate; Emory University

Poster Number: 34

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

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

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

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

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

Acute Kidney Injury and Outcomes in Infants, Children and Adolescents, Supported with Extracorporeal Life Support for Cardiopulmonary Failure

Presenting Author: Joshua Qian, MD; Emory University

Poster Number: 35





Joshua Qian; Kasey Keane-Lerner; Paola Rodriguez Morales; Rebecca Shamah; Tawanda Zinyandu; Joel Davis; Joshua Rosenblum; Heather K. Viamonte; Asaad G. Beshish

Background: Extracorporeal Life Support (ECLS) provides life-sustaining support for patients with cardiopulmonary failure that is refractory to conventional treatment modalities. It is reported that 60–70% of pediatric patients receiving ECLS support develop acute kidney injury (AKI). In critically ill children, AKI is associated with increased mortality and longer ICU length of stay. We sought to describe our center's experiences and outcomes for AKI in patients requiring ECLS.

Methods: Retrospective single-center study at an academic children's hospital. Patients 0–18 years of age who required ECLS due to cardiopulmonary failure between January 2014 and December 2019 were included. An internal ECLS database was reviewed for patient characteristics, clinical variables, and outcomes. AKI was defined per the Kidney Disease Improved Global Outcomes (KDIGO) staging system. Statistical analysis was performed with a significance level of $p=0.05$.

Results: During the study period, there were 313 ECLS runs in 291 patients. The median age was 3.6 months (IQR 0.2, 46.8) with a median weight of 4.6 kg (IQR 3.2, 16.7) and an even distribution of males and females. 215 (68.7%) runs were VA-ECLS and 98 (31.3%) were VV-ECLS. Primary indications included pulmonary (42.2%), ECPR (22.4%), and cardiac (35.5%). Median time from admission to ECLS initiation was 68.5 hours (IQR 72, 200) and median duration of ECLS was 118 hours (IQR 72, 200) with a mortality rate of 39.3%. The 227 patients (72.5%) that developed stage II & III AKI were more likely to be younger and more likely to experience hemorrhagic complications ($p = 0.03$). The AKI group had significantly higher mortality rates (44.9% vs 24.4%, $p = 0.0009$). The odds of mortality in patients with AKI was 2.53 (95%CI 1.45, 4.41) times those without AKI ($p = 0.001$). This remained true after adjusting for age, body surface area (BSA), indication, and mode of ECLS (OR = 2.35, 95%CI 1.32, 4.20, $p = 0.004$).

Conclusion: Most patients that required ECLS developed stage II & III AKI. Those with AKI had twice the mortality rate compared to those without AKI. Further multicenter and prospective evaluation of this modifiable risk factor is imperative to improve outcomes.

Suppression of HIV-1 reactivation from latently infected CD4+ T cells by pyrrolopyridine-based allosteric integrase inhibitors

Presenting Author: Lindsey Ramirez, B.S Biology; Emory University

Poster Number: 36

Lindsey, Ramirez; Tung, Dinh; Christina, Gavegnano; Zahira, Tber; Franck, Amblard; Joella, Xu; Lynn, Meng; Uk-Il, Kim; Raymond, F Schinazi; Kyung-Jin, Kim; Mamuka, Kvaratskhelia; and Baek, Kim

HIV-1 integrase (IN) dimers bind to host LEDGF/p75 protein during viral integration. Transcription activator LEDGF/p75 tethers the IN-proviral DNA complex (pre-integration complex) for integration specifically to transcriptionally active regions of the chromosomes. New Allosteric IN (ALLINI) class inhibitors target non-catalytic sites of HIV-1 IN; LEDGINs are ALLINI compounds that can also inhibit IN binding to LEDGF/p75 are reported to interrupt the integration site preference of HIV-1. The Debyser group reported LEDGINs CX014442 and GS-9822 retarget HIV-1 integration site profiles to





transcriptionally non-active regions of the chromosomes which reduced viral transcription activation from latently infected HIV-1 CD4+ T cell reservoirs. LEDGINs indicate potential utility to reduce HIV-1 reactivation from latently infected T cell reservoirs as a “Block and Lock” strategy, yet no ALLINI /LEDGIN compounds have been clinically developed. Recently, we characterized antiviral efficacy and MOA of a pyrrolopyridine based ALLINI STP0404. Based on outstanding preclinical efficacy, animal safety, and phase 1 trial data STP0404 became the first-in-human ALLINI. We previously reported STP0404 binds the LEDGF/p75-binding site of IN dimer and blocks IN-LEDGF/p75 binding with ~190nM IC50. Moreover, we developed the pyrrolopyridine ALLINI derivative, EKC110, which inhibits the Y99H/A128T STP0404-resistant mutant virus and possibly elevates its genetic barrier, compared to parental STP0404. Here, we report using cellular reactivation assays STP0404 suppresses HIV-1 reactivation from latently infected CD4+ T cells in three different reactivation conditions, 1) IL15, 2) PMA/Ionomycin, and 3) latency reversing agents. Next, we examined STP0404 anti-reactivation activity from CD4+ T cells latently infected with Y99H/A128T mutant HIV-1. Also, we tested whether the second-generation pyrrolopyridine, EKC110, suppresses HIV-1 reactivation from the CD4+ T cells latently infected with wild type virus or Y99H/128T STP0404 resistant virus. HIV-1 reactivation was quantified by p24 ELISA for produced viruses as well as vRNA/vDNA copy numbers in the reactivated cells. Collectively, this study supports the use of our pyrrolopyridine ALLINIs as “Block and Lock” agents to reduce HIV-1 reactivation from latently infected T cell reservoirs

Dissecting PGE2/PTGER4 Signaling and Gene Expression in the Intestinal Epithelium Using Patient Derived Organoids

Presenting Author: Amanda Randunne, Bachelor's of Science; Emory University

Poster Number: 145

Amanda Randunne, Murugadas Anbazaghan, Jason Matthews, Subra Kugathasan

Background: The fate of intestinal epithelial cells is tied to their crosstalk with the mesenchymal stromal cells (MSC) that produce and release molecules that control the epithelium. Disruption of this crosstalk is thought to occur during inflammatory bowel disease and affects the epithelial stem cell's ability to differentiate and promote healing. Studies have shown that prostaglandin E2 (PGE2), a metabolite released from MSC, stimulates intestinal stem cells to differentiate into wound associated epithelium involved in restitution. Herein, we are using patient derived intestinal organoids to model the behavior of the epithelium in response to PGE2. The membrane receptor PTGER4 has been shown to be genetically linked to IBD and is stimulated by PGE2 to produce rapid swelling of intestinal organoids. In this study, we leveraged this organoid swelling phenomena to investigate pathways thought to mediate signaling downstream of PTGER4.

Methods: Organoids were maintained in Matrigel and propagated in Intesticult media after epithelial crypt extraction from patient rectal mucosal biopsies. After 2 or 3 passages, the organoids were used for experimentation. We tested the effect of the inhibitors (1-10 μ M range) of CFTR, PPQ102; PP2A, LB-100; HDAC4, LMK-235; PTEG4, L 161982; PTGER2, PF 04418948; PKA, H 89 dihydrochloride; and γ -secretase, DAPT on the organoid swelling during PGE2 stimulation (1 μ M, 24hr) using light microscopy and ImageJ.



Results: Swelling of intestinal organoids mediated by PGE2/PTGER4 signaling caused most of the organoids in culture (80%) to gain a 20-30% increase in size that could be blocked by PTGER4 but not PTGER2 inhibition. Neither HDAC4 nor CFTR inhibition during PGE2 treatment had a major effect on swelling but γ -secretase inhibition cut the number of swollen organoids in half and decreased the size of the PGE2-swollen organoids by 18%. Blocking PP2A showed a 40% decrease in the number of swollen organoids and 14% decrease in size. Interestingly, inhibition of PKA reduced the number of swollen organoids but increased the size of the swollen organoids by 21% than PGE2 alone.

Conclusion: We show that PGE2/PTGER4 signaling controls organoid swelling through the Notch pathway and is regulated by PKA and PP2A, kinases known to control beta-catenin localization.

Caregiver Measures of Stress in Recollection of Childhood Seizure Events

Presenting Author: Caroline Ray, MD; Emory University School of Medicine

Poster Number: 90

O'Banion, David; Ray, Caroline; and Diaz, Ana

Background: Everyone can recall seeing their first seizure. Most patients having a seizure do not remember the event but can develop chronic psychological sequelae. Now, consider the caregiver who witnesses their child seizing. Little is known about the impact of a child's serious health events on the mental and physical health of caregivers. In epilepsy, it is possible that a single seizure event is traumatic enough to induce PTSD symptoms in a caregiver; therefore, we would expect health implications for the caregiver and repercussions on the family and child from that caregiver suffering from PTSD.

Methods: During the clinical history in the routine visit in child neurology clinic, we will collect measures of autonomic responsivity in the caregivers of children who have had a seizure-like event. For the first 2 minutes, a quiet baseline recording is obtained followed by a recording during the caregiver's recollection of the seizure event. Data points from recordings will then be analyzed and compared to a control group of non-seizure presentations. We will have 30 participants in each group for a total number of 60 participants. We will then conduct a follow up interview by phone using a standard PTSD symptom scale to assess for the development of PTSD symptoms remote from the event.

Results: Project is currently enrolling with preliminary results available for consideration of statistical methods. Skin conductance values will be compared with maximum values minus average baseline value reporting the caregiver's response and in similar studies have found to be predictive of PTSD development.

Conclusions: Conclusions to report the likelihood of PTSD development in caregivers that witness the event. Aim is to encourage early intervention for these caregivers. Trauma informed care practices may need to be considered in routine epilepsy clinics.



Uremic Milieu Impairs Platelet Mitochondrial Bioenergetic Profile in Children with Chronic Kidney Disease

Presenting Author: Loretta Reyes, MD; Emory University Department of Pediatrics

Poster Number: 56

Reyes, Loretta; Khanna, Anjali; Wilkerson, Alexandria; Li, Haiyan; Harris, Frank; Morris, Claudia; Shiva, Sruti; and Smith, Matthew

BACKGROUND: Chronic kidney disease (CKD) results in decreased kidney function, accumulation of uremic metabolites and increased oxidative stress. Mitochondria are sensitive to physiologic stresses and respond dynamically to maintain bioenergetic levels related to systemic cellular functions. Mitochondrial dysfunction contributes to the pathogenesis of various kidney diseases. Circulating platelets in peripheral blood have fully functional mitochondria and increasing data suggests that platelet mitochondrial bioenergetics may represent a surrogate marker of systemic mitochondrial function in systemic diseases. We sought to identify differences in the platelet mitochondrial bioenergetic profile in children with mild, moderate and severe CKD, and to determine corresponding metabolic alterations.

METHODS: Children were classified as mild, moderate, or severe CKD based on their CKD stage (1-5). Platelets were isolated by differential centrifugation of whole blood and isolated, intact platelets were seeded in a multi-well plate format on the Agilent Seahorse extracellular flux analysis platform which measures mitochondrial bioenergetic function. Extracellular oxygen tension was measured in real time with subsequent serial additions of pharmacologic modulators (oligomycin, FCCP and rotenone/antimycin A) that enable calculation of parameters of mitochondrial respirometric function. A separate sample of whole blood was centrifuged, and plasma collected for measurement of uremic metabolites and markers of oxidative stress via ELISA. Statistical analyses were conducted via Agilent Wave Platform and GraphPad Prism.

RESULTS: Significant differences were observed in the platelet mitochondrial bioenergetic profiles of children with different CKD stages. Basal and maximal oxygen consumption were lower in severe CKD compared to mild and moderate stages ($p < 0.0001$), as was the spare respiratory capacity ($p < 0.0001$) indicating reduced energetic reserve capacity. Non mitochondrial respiration was also reduced in severe CKD compared to mild and moderate stages ($p < 0.001$) reflecting suppressed overall metabolism. Uremic markers (TMAO, IS) and markers of oxidative stress (NOX4) were increased in severe CKD compared to mild and moderate stages.

CONCLUSION: In children with CKD, severe CKD was associated with accumulation of uremic markers and markers of oxidative stress. Children with severe CKD also demonstrated significant mitochondrial dysfunction in circulating platelets suggesting reduced metabolic adaptability in the uremic milieu.

Optimizing a Pulmonary Arterial Stenosis In Vitro Model for Congenital Heart Disease Modeling

Presenting Author: Maher Saadeh, BS in Biomedical Engineering; Georgia Institute of Technology & Emory University





Poster Number: 37

Saadeh, Maher; Tomov, Martin; Serpooshan, Vahid; and Bauser-Heaton, Holly

INTRODUCTION: Pulmonary artery stenosis (PAS) affects 1 in 2000 live births worldwide, with several causes, most commonly by genetic mutations that lead to or are associated with other congenital heart diseases (CHD). Despite its prevalence, long-term treatment strategies for patients with PAS remains ineffective due to its heterogeneous etiology. Current pulmonary artery models, in vivo and in vitro, are ineffective in uncovering this mechanism in PAS because they either are unable to recapitulate the phenotype or the micromechanical environment. Recently, researchers have used extrusion bioprinting to develop arterial structures to ameliorate these challenges; however, it is difficult to recapitulate complex anatomical structures with high precision.

METHODS: To address these limitations, we propose to develop a high-throughput 3D bioprinted in vitro macrovascular arterial model utilizing digital light processing (DLP) bioprinting. This novel bioprinted model methodology will be a bilayer cellularized in distinct layers with endothelial cells (EC) and smooth muscle cells (SMC) sourced from human primary cells. Multiple bioink types and printing parameters were tuned to optimize SMC and EC viability, orientation, and functionality. Scanning electron microscopy and compression testing was done to characterize the mechanical properties of our various models. Our hypothesis is that utilizing DLP bioprinting in tandem with other methodologies will enhance in vitro arterial modeling.

RESULTS: Full endothelialization and SMC phenotype of the arterial structure was confirmed using immunofluorescent staining. Encapsulated SMC functionality was confirmed with calcium fluorescent probing and measurement of light intensity changes.

CONCLUSION: This work represents a new and substantive departure from conventional in vitro vascular modeling, for it will allow us to broaden the ability to model complex anatomical macrovascular structures found in multiple CHD related PAS. This fundamental knowledge from our vascular mimics can then be applied to facilitate uncovering pathological cell signaling and translational advancements in treatment of PAS via surgical and transcatheter intervention methods.

Inactivation of monkeypox and vaccinia viruses for safe use on molecular, antigen, and drug-discovery assays

Presenting Author: Courtney Sabino, Biology; Emory University

Poster Number: 57

Courtney Sabino, Heather. B. Bowers, Anuradha Rao, Julie A. Sullivan, Morgan Greenleaf, Wilbur Lam1, Raymond F. Schinazi1, Leda Bassit

Introduction: Recent human Monkeypox virus (MPXV) outbreaks have been occurring worldwide, including in the USA, prompting a need for better detection methods and antiviral treatments. The Emory University/RADx/ITAP team conducts studies on the limit of detection, sensitivity, and specificity of newly developed rapid diagnostic tests for several viruses, one of which is MPXV. Our center's work





contributed towards Cepheid being granted Emergency Use Authorization for their Point-of-Care Mpox Molecular Test-Xpert Mpox. In addition, drug discovery studies are currently being conducted to find novel therapeutics to help combat recent outbreaks and prepare for future ones. To perform these downstream diagnostics and novel anti-MPXV (and vaccinia-VACV) drug screen assays, studies are needed to prove that available inactivation reagents can successfully inactivate lab-cultured, highly infectious viruses and positive clinical samples. Doing so would allow for subsequent transport of the inactivated virus from the BSL3 to the BSL2*/2, where downstream assays can safely and swiftly be executed for diagnostic testing and drug discovery investigations.

Methods: Several reagents and five commercially available lysis buffers were tested using a new inactivation method and highly concentrated lab-cultured viruses in the BSL2* (VACV) and BSL3 (MPXV) for their potential inactivation of both VACV and MPXV. These lysis buffers from Roche, Qiagen, and Applied Biosystems were selected for study as they are readily available and commonly used in the lab setting. The protocol started with mixing and incubating the undiluted virus with each buffer. Then, to prevent the potential cytotoxic effects of buffers on cells used in assays, the mixture was centrifuged at high speed (+21,000xg) to result in a viral pellet, which was resuspended in fresh media. These resuspended pellets were inoculated into Vero cells for observation of cytopathic effects, and infectivity was measured by ELISpot assays. The cells were monitored over several days until collection and imaging.

Results: All five commercial lysis buffers showed complete inactivation (no cytopathic effect and no cells showing infection by ELISpot) for both viruses. With safety being of the utmost importance regarding BSL2* and BSL3-level pathogens, it is crucial to safely test for inactivation to transport VACV and MPXV to BSL2.

Professional Development Curriculum to Promote Well-being Amongst Pediatric Cardiology Fellows.

Presenting Author: Anne Sadler, MS; Emory University

Poster Number: 39

Sadler, Anne; Border, William; and Rodriguez, Zahidee

Project objective/background: Trainees have unique stressors like increasing responsibilities, leadership, career transitioning, ambiguity, and the logistics of navigating a career in medicine, both emotionally and operationally. Professional development can enhance competence, and effectiveness, thus alleviating some elements of burn-out (emotional exhaustion, depersonalization, and personal efficacy). Burnout can further be examined by domains of workplace culture (workload, control, reward, community, fairness, values). We pose a framework that intersects workplace culture with concepts of a healing culture, to yield a novel design for a professional development curriculum to promote wellbeing.

Methods/approach: Based on focus groups of pediatric cardiology fellows and early career faculty, 13 didactics were offered during normal curricular hours for pediatric cardiology fellows to voluntarily participate in between May 2021 and January 2022. Topics were chosen to be specific to the three pillars of burnout. Depersonalization was broadened to include identity to career. Healing culture





concepts gave a framework to address workplace culture domains (Table 1). Following completion of the program, fellows volunteered to participate in a standardized interview until reaching saturation.

Preliminary Results: Of 19 pediatric cardiology fellows, 15 completed interviews. Figure 1 is a Sankey diagram of which didactics were most impactful. Demystifying career transition and identity was the most impactful theme among all fellows (career depersonalization, n=25). PGY5 and PGY6 fellows reported some impact from topics surrounding emotional exhaustion (n=10), and the least from accomplishment (n=5). However, PGY4 fellows found them equally impactful. Within each of the three themes, the impact of specific didactics varied (Figure 1).

Conclusion: The stress profile of pediatric cardiology fellows may change during training. Professional development activities can be curated to target specific burnout themes and overall foster wellbeing.

A group coaching pilot to study the feasibility and impact of cognitive-emotional skills in pediatric cardiology fellows.

Presenting Author: Anne Sadler, MS; Emory University

Poster Number: 38

Sadler, Anne; Border, William; and Rodriguez, Zahidee

Project objective/background:

Physician trainees experience unique stressors contributory to burnout, including increasing responsibility, accelerated mastery of knowledge and skills, financial stress, comparison, and the perception of powerlessness. Various wellness initiatives have mixed results, however, there is no standardized curriculum or intervention. Coaching has been reported to positively impact trainee wellness by shifting perspective and meaning-making through examining values, beliefs, and attitudes in the face of challenges. We piloted a group coaching program to study the feasibility and preliminary impact on pediatric cardiology fellow wellness.

Methods/approach:

We conducted a prospective observational study of 15 voluntary, one-hour workshops during curricular time facilitated by a physician-coach from August to December 2022 for 15 pediatric cardiology fellows. Each workshop had one central theme and utilized facilitated discussion, self-reflection prompts, and live coaching. Workshops were recorded when appropriate and self-study modules were available. The first session was introductory, and the remaining topics covered were story versus fact, feelings, processing pain, intentional models and ladder thoughts, ambiguity, emotional adulthood, hidden expectations, boundaries and perfectionism, imposter syndrome, self-worth, self-confidence, arrival fallacy, purpose and agency to overcome moral injury, and becoming future you. Pre- and post-surveys were optional and included: Neff's Self-Compassion Scale – Short Form (SCS-SF), Perceived Stress Scale (PSS), non-proprietary single-item substitute for Maslach Burnout Inventory Emotional Exhaustion (MBI:EE) subscale and Clance Imposter Phenomenon Scale (CIPS). Unpaired t-test analysis with 95% confidence interval (CI) assessed the program's effect on these metrics.





Results:

12 of 15 pediatric cardiology fellows completed a post-survey. Fellows engaged the most with live session compared to recorded or self-study participation options (Fig 1). Perceived stress and emotional exhaustion trended down while self-compassion trended up, although not statistically significant (Table 1). Imposter syndrome significantly increased mid-year (CI [-41.5, -23.3], Table 1). Feedback about the emotional impact was largely positive, with fellows reporting they are better equipped to process emotions (Fig 2).

Conclusion:

Pediatric cardiology fellows self-reported community and normalization of their training experience, and learned self-reflection, self-compassion, and processing emotion through a group cognitive-emotional coaching pilot that occurred during an established curricular training period. Next steps include increasing numbers and a control group.

Feature Sensitivity during Infant-Directed Speech and Song and Its Relationship with Mouth-Looking and Language Outcomes during the First Year of Life in Autism and Typical Development

Presenting Author: Manash Sahoo, B.S. Psychology; Emory University

Poster Number: 146

Sahoo, Manash; Alviar, Camila; Edwards, Laura; Jones, Warren; Klin, Ami; and Lense, Miriam

Background: Over the first year of life, infants engaged with infant-directed speech (ID-speech) gradually shift their gaze from the eyes to the mouth of the caregiver, as the mouth contains audio-visual cues that support language development (Tenenbaum et al., 2015). Previous research has identified a positive relationship between mouth-looking and later language outcomes for typically developing (TD) infants, but not for infant siblings with high likelihood of developing autism (Chawarska et al., 2022). Infant-directed song (ID-song) extends the audio-visual features of ID-speech, capturing attention of TD and ASD infants longer than ID-speech (Macari et al., 2022). However, how TD and ASD infants allocate visual attention to the face during ID-speech and ID-song, as well as their sensitivity to features in relationship with language development, is unknown.

Methods: TD (N=136) and ASD (N=64) infants were eye-tracked longitudinally at 3, 4, 5, 6, 9, and 12 months, while watching videos of caregivers singing (ID-song) or speaking (ID-speech). Expressive language (EL) was assessed at 24 months and ASD infants were median split into higher (ASD-HighEL) or lower (ASD-LowEL) language groups. Mixed-effects models assessed mouth-looking as a function of age, group, and communicative context. Follow-up models examined sensitivity to clip features such as tempo, rhythmicity, positive affect, and audiovisual synchrony (AVS) within each group.

Results: Mouth-looking was higher in ID-song vs ID-speech ($\beta = 0.075$, $p < 0.001$), and increased with age across groups. This increase was slower for the ASD-HighEL group than TD or ASD-LowEL (β 's > 0.06 , p 's < 0.05). Sensitivity to features also varied across groups: while slower tempo, increased rhythmicity,



higher smiling and mouth audiovisual synchrony all increased mouth-looking in TD, only tempo and rhythm were predictive for ASD-HighEL, and tempo and smiling for ASD-LowEL.

Conclusions: Over the first year of life, infants with and without ASD allocate more facial visual attention to the mouth, though this effect is attenuated in ASD-HighEL infants. This effect is greater during ID-song compared to ID-speech potentially due to the features associated with song. Individual differences in feature sensitivity may impact response to early language intervention and suggest differing mechanistic processes to be targeted.

Clinical Outcomes of Children and Adolescents with Paroxysmal Nocturnal Hemoglobinuria

Presenting Author: Nabil Saleem, MD; Children's Healthcare of Atlanta

2022 Buchter Resident Research Award

Poster Number: 91

Saleem, Nabil; Graciaa, Sara; McElfresh, Patricia; Arnold, Staci; Schoettler, Michelle; Briones, Michael; and Chonat, Satheesh

Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare, acquired disorder of the bone marrow causing intravascular hemolysis (IVH). PNH exists as a spectrum, ranging from asymptomatic, small PNH clone size (subclinical PNH), to moderate clone size in patients with another bone marrow disorder (BMD-PNH), to large clone size leading to significant IVH (classic-PNH). We conducted a retrospective-prospective cohort study to characterize the clinical features and treatment of pediatric PNH.

Eighteen patients with PNH were identified in our cohort, of which 50% were males. Median age at diagnosis was 14.66 years. Time from symptom onset to diagnosis ranged from 0 to 46.93 months (Median = 1.45 months). Five patients had classic-PNH (28%) and 13 had BMD-PNH (72%). Ten patients had concurrent severe aplastic anemia (SAA) throughout the course of their disease, one had moderate aplastic anemia, and one had myelodysplastic syndrome. Four patients developed clinically significant IVH after immunosuppressive therapy for SAA due to increasing PNH clone size. Of 5 patients with classic-PNH, 100% were treated with complement inhibitor therapy (C3, n=1 or C5, n=4). Thromboses of the hepatic veins (Budd-Chiari syndrome) were noted in 2 of our patients with classic-PNH. Of the 13 patients with BMD-PNH, 6 received immunosuppressive therapy, 8 received complement inhibition, and 7 underwent bone marrow transplant. One patient with BMD-PNH died. All patients with classic-PNH achieved transfusion independence during complement inhibition, compared to 6 out of 8 (75%) of patients with BMD-PNH on complement inhibition. One patient developed Neisserial gonococcal sepsis, but no meningococcal infections nor deaths due to complement inhibition were noted. Extravascular hemolysis (EVH) with positive direct antiglobulin test was noted in 42% of all patients being treated with terminal complement inhibition.

In the largest single-center pediatric cohort of patients with PNH to date, time from symptom onset to diagnosis remains a challenge, likely due to non-specific presenting symptoms. Complement inhibition used in 72% of our patients was a safe and effective strategy at mitigating IVH and avoiding thrombosis,



though C5 inhibition can result in EVH. Additionally, our data support the use of complement inhibition to reduce transfusion need in patients with BMD-PNH and IVH.

Uncovering the presence of live SARS-CoV-2 Virus in Fecal specimens

Presenting Author: Mohammad Salman, Bachelor of Science (BSc); Emory University

Poster Number: 147

Salman, Mohammad; Ingersoll, Jessica; Schoof, Nils; Bowers, Heather; Wang, Ethan; Piantadosi, Anne; Rao, Anuradha; Lepene, Ben; Pengbo, Liu; Lam, Wilbur; Moe, Christine; Schinazi, Raymond; and Bassit, Leda

Background

SARS-CoV-2 RNA has been found in the stools of patients with COVID-19 who have had gastrointestinal symptoms, including nausea, vomiting, and diarrhea, which are common in up to 15% of the cases. Therefore, we aimed to investigate whether SARS-CoV-2-positive stools and wastewater are viable and can be cultured in Vero or Caco-2 cells. Aim 1. We tested eight clinical stool samples and four positive wastewater samples for SARS-CoV-2 for their potential to have infectious virions. Aim 2. We spiked lab-propagated SARS-CoV-2 (USA-WA-1, Delta, or Omicron) into negative human stools to test the recovery of the virions from the stool samples to infect permissive cells after three different incubation temperatures.

Methods

Samples were filtered using 0.22 µm filter tubes to remove debris. RT-PCR for N1 and N2 genes, ddPCR, and sequencing were performed. In addition, infectivity foci forming assays and ELISpot readout was conducted in three cell types.

Results

None of the wastewater samples were culturable. One of seven clinical stool samples was sequenced of Delta sub-lineage AY.25 (1.25 x 10⁶ GE/ml) post-filtration, with a Ct of ~24. However, no increase in SARS-CoV-2 RNA levels was observed in the infectivity assays. In contrast, infectious virus was recovered from stools spiked with SARS-CoV-2, including wild type (WT), Delta, and Omicron. In addition, WT and Delta were contagious to susceptible cell types under different incubations. In contrast, infectious Omicron was present only in Vero cells after being recovered from stool kept at -80oC, immediately after spiking, or in Vero-TMPRSS2 cells after being held at 4oC.

Conclusions

SARS-CoV-2 genome sequencing from a positive clinical stool indicates the existence of the intact virus in this sample. In addition, infectious SARS-CoV-2 was recovered from spiked stool samples, suggesting the possibility of viable virions in the wastewater or stool specimens.



Predictors of Social Attention in Inclusive Preschool Classrooms for Children with and without Autism: The Role of Eye-Tracking Measures of Social Visual Engagement and Teacher-Implemented Classroom Supports

Presenting Author: Brooke Schirmer, B.S.; Marcus Autism Center - Emory

Poster Number: 148

Schirmer, Brooke; Morgan, Lindee; Edwards, Laura A.; Wedderburn, Quentin; and Siller, Michael

Background: Children with autism spectrum disorder (ASD) show characteristic deficits in social attention and interaction (Bauminger-Zviely & Shefer, 2021; Sigman et al., 1986). Preschool classrooms provide unique opportunities for scaffolding social attention and engagement (Feuerstein & Landa, 2020). Moments of social attention to peers or teachers may emerge because of generalized behavioral tendencies of the child (Constantino et al., 2017), classroom interventions/supports implemented by the teacher, or both.

Methods: Participants were children enrolled in an inclusive preschool program serving children with and without autism; ASD: $n=14$, $\text{Mage}(\text{SD})=43(13)$ months; TD: $n=18$, $\text{Mage}(\text{SD})=48(10)$ months. Eye-tracking measures of SVE were collected while children viewed videos of naturalistic social interaction, and quantified in terms of percent gaze allocation to the faces in these scenes. Classroom videos were recorded once per week, for five weeks. For each child and recording day, a 5-minute segment of indoor free-play was randomly selected for observational coding. Social attention was coded using rating scales capturing children's visual attention to the faces and actions of peers and teachers (Morgan et al., 2018). Classroom supports were coded using two rating scales of the Classroom Assessment Scoring System (Pianta et al., 2008) capturing the teachers' active facilitation and supportive language use. Parents completed the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), a quantitative measure of social disability.

Results: Data were analyzed using mixed models for longitudinal data (SAS Proc Mixed). Social attention was specified as the outcome. Predictors included (1)SVA, (2)social disability, (3)ASD diagnostic classifications, (4)classroom supports, and (5)demographic characteristics. Results from the final multi-predictor model show that children's classroom social attention was independently predicted by (1)SVE, $F(1,85)=13.2$, $p<.001$, and (2)the interaction between social disability and classroom supports, $F(1,85)=8.9$, $p<.01$. Visual analyses of the interaction term indicate that the association between classroom supports and classroom social attention was stronger in children with higher levels of social disability.

Conclusions: Automated measures of SVE predict classroom social attention in children across a range of social disability. These findings suggests that teachers allocate their attention and supports to children who need them most, and the supports that they offer impact different children in different ways.

Adherence to Resuscitation Ergonomics Amidst High Rates of PICU Staff Turnover

Presenting Author: Ila Sehgal, DO; Emory University School of Medicine





Warshaw Pediatric Fellow Research Award 2022

Poster Number: 67

Sehgal, Ila; Edwards, Nicole; McGough, Jennifer; Colman, Nora; and Hebbar, Kiran

Background: Each year in the United States, there are more than 6000 pediatric in-hospital cardiac arrests (IHCA). Most children who have an IHCA will not survive. Variability amongst hospital survival rates exists which indicates an opportunity to improve survival rates by decreasing errors and optimizing resuscitation performance utilizing simulation.

Resuscitation ergonomics focuses on improving patient outcomes by optimizing the interaction of the environment with human factor driven behaviors. In 2021, the Children's Healthcare of Atlanta (CHOA) PICU utilized simulation during mock codes to identify latent safety threats. Failure mode and effects analysis (FMEA) was performed, and system improvements were embedded into an interdisciplinary team training education initiative.

During the pandemic, we experienced high rates of staff turnover leading to an influx of staff with variable to no resuscitation training. We sought out to study the optimal number of trained staff on a resuscitation team needed to maintain high quality resuscitation ergonomics during an IHCA as defined by a checklist we created using resuscitation science literature, FMEA testing at CHOA, and American Heart Association recommendations.

Methods: Demographic data was collected for all clinical staff who work in the pediatric ICU including completion of team training in 2021 and full-time equivalents. We collected a post-arrest survey after each IHCA in the PICU assessing maintenance of resuscitation ergonomics. We divided our data into three groups based on the percentage of team-trained staff present at an IHCA: Low (25%), moderate (26-50%), and high (>50%)

Results: Total compliance scores were calculated by summing the 15 measure items from the best practices checklist for each cardiac arrest event and summarized using means and standard deviations

Pairwise evaluations for differences in mean total compliance scores between simulation categories were evaluated using Cohen's d differences which looks at effect size differences between groups which can be small, moderate or large. Compared to low simulation training care teams, moderate and high simulation training care teams had more mean items endorsed, which corresponds to moderate (Cohen's d=0.57) and moderately-large (Cohen's d=0.74) effect size differences.

Conclusion: Higher percentage of team trained staff correlates with higher compliance of resuscitation ergonomics best practices.

Painless Delivery of a Microparticulate Zika vaccine Through Buccal and Intranasal Administration

Presenting Author: Sarthak Shah, MS; Mercer University

Poster Number: 40





Shah, Sarthak; Patel, Parth; Kale, Akansha; Uddin, N. Mohammed; D'Souza, Martin

Background: Zika virus is considered a travel-related infectious disease in the United States. Once this virus enters the human body, people from different age groups, including the pediatric population, are affected. In newborns, this viral infection causes microcephaly, but in adults, muscular paralysis occurs. This results from the demyelination of the myelin sheath, and this condition is named Guillain-Barré syndrome. Currently, no FDA-approved treatment or vaccine is available, which raises the possibility of a future reemerging of this viral infection. To help fill this void, we developed an inactivated Zika virus microparticle (MP) vaccine that can be administered via painless routes. We formulated an intranasal (IN) vaccine and an orally dissolving film (ODF)-based vaccine for buccal mucosa delivery. Methods: We developed this vaccine via a double emulsion solvent evaporation method. In-vitro microparticle characterization included: morphology, polydispersity index, and zeta potential. In-vitro ODF characterization included: diameter, weight variation, thickness, disintegration time, and pH test. This vaccine was evaluated via both routes (IN and ODF) with and without adjuvant MPs of aluminum hydroxide (Alum) and monophosphoryl lipid A (MPLA) to Swiss Webster mice using one prime dose and two booster doses with a two-week dosing schedule. Results: MP size ranged from 573.4 ± 10.18 nm, polydispersity index 0.294 ± 0.133 , and zeta potential was -22.6 ± 0.503 mV. The MPs had a donut-like arrangement and were spherical in shape morphologically. The average ODF with an adjuvant parameter had the following dimensions: diameter 4.08 ± 0.07 mm, thickness 0.27 ± 0.07 mm, weight variation 8.98 ± 1.37 mg, disintegration time 203.4 ± 75.6 s, and pH 7.89 ± 0.12 . We found a significant humoral response of IgM, IgG, IgA, IgG1, and IgG2a antibody titers than the unvaccinated mice. In addition, there was a balanced Th1/Th2 response. MP vaccine produced a significant CD4+ helper and CD8+ cytotoxic T-cell cellular response. Conclusion: The feasibility of formulating and delivering a painless vaccine was established. Inactivated microparticulate Zika virus vaccine showed excellent humoral and cellular responses. Buccal and intranasal administration routes showed significant immune responses. This vaccine can be further investigated in clinical trials.

Clinical Features of Cannabinoid Hyperemesis Syndrome

Presenting Author: Meera Shah, MD, MPH; Emory University School of Medicine

Poster Number: 68

Shah, Meera; Jergel, Andrew; George, Roshan; Jenkins, Elan; and Bashaw, Hillary

Background: With increasing cannabis usage, it is important to understand and recognize conditions associated with its use including cannabinoid hyperemesis syndrome (CHS). CHS presents similarly to cyclic vomiting syndrome (CVS) with recurrent episodes of nausea, vomiting, and abdominal pain however CHS is associated with chronic cannabis use. This study aims to find clinical characteristics that distinguish the two entities at presentation, and to describe their management in a large pediatric center.

Methods: This study is a retrospective chart review of patients admitted to a large children's healthcare system between 2015-2022. A total of 201 CVS and CHS patients were initially identified by the electronic medical record (EMR) using ICD-9 and ICD-10 codes. Of these, 125 met inclusion criteria.





Results: A total of 125 patients were included in analysis. CHS patients were significantly older than those admitted with CVS (18.06(1.41) vs. 14.5(2.91), $p < 0.001$, Table 1). There were no significant differences in gender, race, ethnicity, or hospital length of stay between groups. CHS patients were more likely to have a positive urine drug screen (UDS) (86% vs. 2.9%, $p < 0.001$), lower potassium (3.62(0.77) vs. 3.88(0.49), $p < 0.001$), higher creatinine (0.83(0.41) vs. 0.63(0.17), $p < 0.001$), and higher glucose (112.35(36.93) vs. 104.76(51.89), $p = 0.045$) than CVS counterparts. The average systolic (SBP) and diastolic blood pressures (DBP) were significantly higher in CHS patients (SBP 124.46(10.66) vs. 115.37(9.43), DBP 75.16(9.37) vs. 69.25(8.45), $p < 0.001$ for both). Imaging was obtained in 36% of all patients and only 2.4% of patients had abnormal imaging. Finally, CHS patients who had higher SBP were significantly more likely to receive both Ativan and Haldol whereas those with lowest SBP were significantly more likely to receive neither medication (135.35(6.83) vs. 121.64(12.09), $p = 0.040$, Table 7).

Conclusions: This study is the largest existing pediatric study on CHS. This data indicates that there are clinical features including older age on admission, hypertension, THC positivity on UDS, lower potassium, higher creatinine, and hyperglycemia, that may distinguish CHS from CVS. The data also suggests that abdominal imaging may not be indicated. Early recognition of CHS may allow for earlier appropriate therapy, decreased testing, and ultimately may reduce length of stay.

Is Hyperoxia During Veno-Arterial Extracorporeal Life Support Due to Cardiopulmonary Failure Associated with Mortality in Pediatric Patients?

Presenting Author: Rebecca Shamah, BS; Emory University

Poster Number: 41

Rebecca Shamah; Joshua Qian; Kasey Keane-Lerner; Paola Rodriguez Morales; Tawanda Zinyandu; Joel Davis; Joshua Rosenblum; Heather K. Viamonte; Asaad G. Beshish

Background: Patients with cardiopulmonary failure requiring Extracorporeal life support (ECLS) are frequently exposed to supranormal blood oxygen tension. Studies suggest that hyperoxia is associated with worse outcomes in patients after exposure to ECLS, but data is limited regarding the effects of hyperoxia in pediatric patients. We investigated the association of hyperoxia with mortality and other clinical outcomes in a large volume ECLS center.

Methods: Retrospective single-center study at an academic children's hospital. Patients 0–18 years of age who required VA-ECLS due to cardiopulmonary failure between January 2014 and December 2019 were included. An internal ECLS database was reviewed for patient clinical variables, average partial arterial pressure of oxygen (PaO₂) during the first 48 hours of ECLS, and clinical outcomes. Analysis was performed using appropriate statistics with a significance level $p = 0.05$.

Results: During the study period, 229 VA-ECLS runs occurred in 209 patients. The median age was 2.5 months (IQR 0.3, 19.0), weight 4.4 kg (IQR 3.2, 10.7) with an even distribution of male and females. The majority of patients were neonates (73.4%) with cardiac being the most common indication (48.9%). Using a receiver operating characteristic curve, a mean PaO₂ of 233 mmHg in the first 48 hours of ECLS was determined to have the optimal discriminatory ability for mortality (sensitivity 36% and specificity



76%). Of the VA-ECLS runs, 68 (29.7%) had mean PaO₂ > 233 mmHg and were categorized as the hyperoxia group. Patients in the hyperoxia group tended to be older (median age 4.6 vs 1.5 months, $p = 0.019$), had a cardiac indication for VA-ECLS (60% vs 44%, $p = 0.0004$), and no expected recovery (54% vs 73%, $p = 0.049$). Multi-variable logistic regression controlling for BSA, age group, and indication assessed the association of hyperoxia with development of ECLS complications and mortality. A suggestive association existed between hyperoxia and mortality in the unadjusted analysis (OR 1.76, 95% CI 0.995 – 3.12, $p = 0.052$).

Conclusion: Hyperoxia during the first 48 hours of VA-ECLS may be associated with mortality. Prospective evaluation of this modifiable risk factor is imperative to improve the care of this cohort.

Assessing the Residual Cell Type Abundance After Cold Protease Digestion and Filtering of Human Intestinal Mucosal Biopsies for Single Cell RNA Sequencing

Presenting Author: Garima Sharma, Undergraduate; Emory University

Poster Number: 149

Garima (Jeeya) Sharma, Yeonjoo Hwang, Sushma Maddipattla, Shanta Murthy, Vasantha Koachala, Anne Dodd, Jason Matthews, and Subra Kugathasan.

Background: The intestinal mucosa is made up of many cell types, including epithelium, immune and stromal cells, that must function in a coordinated manner for homeostasis. Recent studies have used single cell RNA sequencing (scRNA-seq) technology to measure the cellular composition of the mucosa and the transcriptional states within each of the cells. However, to make this assessment, the technology relies on a small population of cells (~10,000) that are extracted from the mucosal biopsies (~250,000 cells) with protease digestion, mechanical agitation, and filtering, that could potentially leave behind certain cell types and alter downstream assessment. Thus, we tested the accuracy of scRNA-seq in detecting all the cell populations of a biopsy by comparing them to the bulk RNA sequence data from residual material/cells on the filter and the cells after filtering. Methods: Ileal biopsies were processed for scRNA-seq using cold protease digestion and standard 10x Genomics 3' chemistry while total RNA was recovered from the filter and the filtered cells (~100,000) were used for scRNA-seq. Bulk RNA was processed using mRNAseq Clontech SMARTseq v4. After alignment with STAR and further QC, the data was deconvoluted by CIBERSORTx against a single cell reference constructed from seven pediatric ileal samples from the Gut Cell Atlas (GCA) database with forty-one cellular subtypes to calculate cell type proportions. These proportions were compared to those of previously analyzed single cell data that were formatted into pseudo-bulk samples. Broadly, cell type proportions were compared across three lineages: epithelial, immune, and stromal. Results: We saw that stromal cells were not as represented in the scRNA-seq data of a healthy patient as they were in the samples from those with inflamed (diseased) mucosa. While there were discrepancies in cell proportions between residual cells on the filter and the filtrate, the prediction of cell types by the scRNA-seq analysis showed good representation of the immune and epithelial compartments. Conclusion: Our analysis shows current scRNA-seq protease digestion protocols yield different proportions of cell types depending on patient sample, and



do not adequately capture the stromal compartment, suggesting collagenase might improve the recovery of these missing cell types.

Social Determinants of Health in Infants with Cerebral Palsy or High Risk for Cerebral Palsy: Matched comparison with infants from a high-risk infant follow-up clinic

Presenting Author: Katie Shin, BS Candidate; Emory University

Poster Number: 150

Kendrick-Allwood, Salathiel; Shin, Katie; Minaz, Anmol; Walker, L. Keecia; Maitre, Nathalie L.; and Murphy, Melissa

Introduction:

Social determinants of health (SDH) affect early diagnosis and intervention of many developmental disorders. This relationship has not been well studied in cerebral palsy. Our aim was to examine the context of SDH, and behavioral health issues faced by families of children newly diagnosed with cerebral palsy (CP) or designated as high-risk for cerebral palsy (HRCP).

Methods:

We examined caregiver-reported psychological and SDH, Post-Traumatic Stress Disorder (PTSD), and Adverse Childhood Experiences (ACE) in a preliminary sample of children diagnosed with CP/HRCP (n=97), and age-matched controls (n=97) at Emory's Developmental Progress Clinic (DPC) between 11/2021–11/2022. Additional questions reviewed by a social worker (SW) asked caregivers if they needed help with access barriers (e.g., transportation, employment, housing, daycare).

Results:

Among the 194 families, depressive and PTSD symptoms were higher than for the overall US population (21% vs 8%, respectively) but no significant differences emerged between CP/HRCP and high-risk control groups. ACEs for both groups were in the higher range compared to published studies. While 27.8% of families of CP/HRCP children and 25.8% of controls reported at least 1 SDH in food, housing, income, or healthcare access insecurity; 65.4% of combined insecurities were disclosed only on repeated queries. All needs and barriers were immediately addressed by SW.

Conclusion:

In this preliminary analysis, SDH does not differ between HR/CP and comparison, but is higher than general population, suggesting that families seen at DPC are especially vulnerable to socioeconomic and psychological stressors. Given that receiving an HR/CP diagnosis adds additional burden, systematic screening and support for adverse SDH should be provided as part of the early CP detection process. Specifically asking where help is needed may be more effective at eliciting information than yes/no questions. Additional work with a larger sample and documentation of HR/CP diagnosis impact and resource support in this group over time is needed to confirm these results.



Secondhand Vape Exposure from e-Cigarettes negates CFTR Restoration and Function in Cystic Fibrosis

Presenting Author: Mahesh Shrestha, MS; Emory University

Poster Number: 151

Shrestha, Mahesh; Wisniewski, Ben; Shrestha Chandra; Bojja Dinesh; Reynolds, Susan and Kopp, Benjamin

Background: Secondhand smoke exposure (SHSe) is a major challenge for people with cystic fibrosis (CF) and other chronic lung diseases and primary smoking is known to reduce CFTR function, the causative defect in CF. We have previously reported that SHSe worsens respiratory and nutritional outcomes in people with CF by disrupting host immune responses and metabolic signaling pathways (e.g., reduced macrophage prostaglandin D2 [PGD2] signaling). Recently the use of electronic nicotine delivery systems (e-cigs) by caregivers and peers has increased rapidly and hence the number of people with CF who have secondhand e-cig vape exposure (SHVe). Primary vaping is associated with immunologic deficits in healthy people but it is unknown if SHVe similarly impacts immune function.

Methods: Human CF and non-CF peripheral blood monocyte derived macrophages (MDMs) and human bronchial epithelial cells (HBECs) were exposed to flavored and unflavored e-cig vapor. The effect of SHVe on CFTR expression and function, bacterial killing, cytokine signaling, lipid mediators of immune signaling and metabolism was measured during treatment with the CFTR modulator ellexacaftor/tezacaftor/ivacaftor (ETI).

Results: SHVe from e-cigs decreased CFTR expression and function in CF and non- CF MDMs and negated CFTR functional restoration by ETI in CF MDMs. SHVe reduced the beneficial effects of ETI on MDM-mediated clearance of bacteria. SHVe also negated the restoration of PGD2 expression in CF MDMs treated with ETI compared to unexposed controls. Flavored but not unflavored SHVe increased pro-inflammatory cytokine expression in CF MDMs and promoted glycolytic metabolism. Overall, HBECs were less impacted by SHVe compared to MDMs.

Conclusion: SHVe reduces macrophage CFTR expression and hinders functional CFTR restoration by CFTR modulators thereby reducing bacterial killing and promoting a glycolytic, pro-inflammatory state in macrophages. SHVe is an emerging public health threat that may limit therapeutic efficacy in people with CF.

Comparison of Open vs Closed Economy Treatments for Children on the Autism Spectrum

Presenting Author: Allie Silbert, Undergraduate Degree in Psychology with minors in Spanish and Health/Medical Sciences in progress; Georgia Institute of Technology and Marcus Autism Center

Poster Number: 152

Allie Silbert, Tracy Argueta, Sarah Slocum-Freeman, and Nathan Call





Background

The purpose of this study is to evaluate the rates of compliance and challenging behavior maintained by accessing a break (i.e. escape-maintained challenging behavior) from instructions between positive and negative reinforcement conditions where reinforcers are only available for compliance (i.e. open economies) or are available for free in addition to compliance (i.e. closed economies). Challenging behavior that originates from escaping instructions can be detrimental to children's social and intellectual development because it interferes with learning. The results of this study could be used to enhance effectiveness of treatments for escape-maintained challenging behavior by assessing which variation (i.e. open or closed economy) of positive and negative reinforcement is most successful at increasing compliance and decreasing challenging behavior.

Methods

This study begins with an edible preference assessment to pick a positive reinforcer and establish a strong establishing operation (i.e. EO). This is followed by a demand latency assessment. After a demand is chosen, baseline then evaluates the participants starting rate of challenging behavior and compliance in a 10 minute interval. During baseline, participants can escape a non-preferred task for 30 seconds by engaging in challenging behavior, while compliance results in praise. During treatment, participants experience combinations of positive and negative reinforcement and open and closed economies in a multi-element design. In positive and negative reinforcement conditions, participants receive a preferred edible or a break for complying with instructions. In closed economies, participants receive these reinforcers for compliance only, whereas in open economies participants also receive edibles or breaks at regular intervals regardless of behavior. Results are evaluated using a single-case ABAB design.

Results

While the results have shown all four treatments effectively reduce challenging behavior, the changes in percent compliance are variable across conditions and participants. On average, percent compliance is higher in positive reinforcer conditions when compared to negative reinforcer conditions. Amongst the positive reinforcer conditions, the closed economy results in a higher rate of compliance overall.

Conclusions

The results of this study indicate that, while all four treatments can effectively reduce challenging behavior, the most dependable for increasing compliance is positive reinforcement with a closed economy.

Adult Survival Improves Following the Formation of a Transition Program and Joint Clinic for Pediatric Liver Transplant Recipients

Presenting Author: James Stevens, MD; Emory University School of Medicine

Poster Number: 69





Stevens, James; Sadjadi, Raha; Hall, Lori; Ford, Ryan; Westbrook, Adrianna; Gillespie, Scott; and Gupta, Nitika

Background: Pediatric liver transplant recipients have a high risk of complications following transfer to adult healthcare. We previously published data demonstrating 28% mortality in young adults, with death disproportionately affecting Black patients. Formal transition processes have since been implemented, including a multidisciplinary “teen clinic” and joint pediatric-adult clinic. Our study aims to analyze outcomes following this program’s formation.

Methods: Single-center, retrospective study describing demographics, clinical characteristics, and outcomes from a tertiary university health system with affiliated liver transplant programs. Pediatric transplant recipients who completed transition between March 2015-2020 were included.

Results: Fifty-nine patients were transitioned. They were 64% female, 59% White, 32% Black. Median age at first transplant was 6.9 years, median age at transfer 20.7 years. Comparing this transition cohort (T) to a prior non-transition cohort (NT, n=64), patients who underwent transition had improved teenage medication adherence as reflected by tacrolimus medication level variability index <2.5 (68% T vs. 33% NT, p<0.01). T teenagers developed less post-transplant diabetes mellitus (8% vs. 31%, p<0.01) and had higher prevalence of employment (53 vs 31%, p=0.02). With formal transition, adult survival was 97% over a median length of follow-up of 4.4 years (mortality decreased from 28% NT to 3% T, p<0.05). Transitioned Black adults had higher prevalence of acute cellular rejection, days hospitalized, need for dual immunosuppression, and re-transplantation (each p<0.05). Documented substance use was higher in adulthood than childhood (37% vs. 10%, p<0.01).

Conclusions: After initiating a transition program for liver transplant recipients, adult survival and adolescent medication adherence improved. Further work is needed to address ongoing racial disparities and substance use.

Investigating Rurality and its Association with Initiation of Childhood Cancer Survivor Care

Presenting Author: Liberty Strange, MD, MPH; Emory University/Children's Healthcare of Atlanta

Poster Number: 70

Strange, Liberty; Lewis, Rebecca; Ji, Xu; Mertens, Ann; and Effinger, Karen

Background: Research has shown that childhood cancer survivors (CCS) are at increased risk of chronic health conditions due to their treatment. Many large pediatric cancer treatment centers have survivor programs that help screen for these chronic health conditions. These centers are typically located in metropolitan areas and serve catchment areas often including rural populations. While studies have evaluated distance from survivor clinic as a variable leading to disparate survivor care, rurality has been understudied. Our primary objective is to examine differences in survivor clinic initiation and follow up between rural and urban CCS.

Methods: This is a retrospective analysis of patients followed in the Aflac Cancer and Blood Disorders Center who were diagnosed with cancer at <21 years, completed therapy between 2009-2017, and were





alive at 2 years from completion of therapy. Sex, race, ethnicity, diagnosis, treatment, zip code, insurance, and date of first survivor clinic visit were abstracted from the medical record. Patient zip codes at diagnosis were converted to Rural-Urban Commuting Area (RUCA) codes with rural codes defined as those in which <30% of workers commute to an urbanized area. Chi-square and Kaplan-Meier analysis were performed.

Results: Within our cohort of 1182 eligible patients (52% male, 49% non-Hispanic White, 51% leukemia/lymphoma survivor), 10.4% were classified as living in a rural area. Compared with 71.0% of urban CCS, 62.6% of rural CCS attended an initial survivor clinic visit [$\chi^2 = 3.33$, p-value = 0.07]. For CCS who attended an initial survivor clinic visit, the median time to clinic visit was 30.6 months after completion of therapy for rural CCS and 31.6 months for urban CCS [p-value = 0.90].

Conclusions: Less rural survivors had an initial survivor clinic visit compared with urban survivors although this did not meet statistical significance. Survivors were seen for their initial survivor clinic visit at a median of 31.4 months from the completion of therapy with no difference by rurality. We anticipate that additional subgroup analysis, covariate analysis, and analysis of subsequent survivor clinic follow up visits may uncover a population of survivors that could benefit from future interventions to aid in improved survivor care.

Disparities in Pediatric Solid Tumor Therapeutic Clinical Trial Enrollment at a Single Institution

Presenting Author: Oludamilola Taiwo, MD; Emory University SOM

Pilot Grant: Alex's Lemonade Stand Pediatric Oncology Student Training Grant, 2022

Poster Number: 42

Taiwo, Oludamilola; Woods, William; and Hong, Andrew

Introduction: Cancer survival rates for pediatric patients have steadily increased over the last 30 years. This is partially due to new treatments and the centralization of clinical trial enrollment by organizations such as the Children's Oncology Group. However, recent studies found that differences in clinical trial enrollment rates affected survival rates and treatment outcomes. Whether these findings apply to pediatric solid tumors remains understudied. Therefore, this study aimed to determine potential drivers of therapeutic clinical trial enrollment and overall survival for pediatric patients diagnosed with nephroblastoma (Wilms tumor), neuroblastoma, or medulloblastoma treated at Children's Healthcare of Atlanta.

Methods: We conducted a retrospective cohort study of pediatric patients with a new cancer diagnosis between 2011 and 2018. We abstracted patient demographics in addition to disease and family information. We used addresses to calculate the national area deprivation index (ADI) percentile. Percentiles were placed in quartiles, with the first quartile (1st to 24th) containing the least disadvantaged neighborhoods and the fourth quartile (75th to 99th) having the most disadvantaged neighborhoods. Univariable and multivariable models were constructed to examine predictors of trial enrollment and survival rates.



Results: We found that patients who lived in rural areas were less likely to enroll in a clinical trial (OR 0.10, 95% CI 0.01 to 0.75, p-value 0.03). Furthermore, patients enrolled in a clinical trial had a higher ADI percentile, meaning they came from a more disadvantaged neighborhood (60.8 vs. 48.5, p-value 0.03). Patients from the most disadvantaged communities (fourth quartile) were more likely to enroll than those from the first quartile (OR 9.56, 95% CI 1.32 to 85.94, p-value 0.03). Regarding overall survival, patients who did not enroll in a clinical trial demonstrated a higher mortality risk (HR 4.01, 95% CI 1.36 to 12.39, p-value 0.01)

Conclusion: We concluded that disparities in pediatric therapeutic clinical trial enrollment present differently than those in the adult population. Family dynamics, health literacy, and physician bias may play a more significant role in these differences than previously suggested. Further studies in other institutions and of these underlying mechanisms will help create more equitable access to pediatric solid tumor clinical trials.

Association between Receipt of COVID-19, Influenza, and Pneumococcal Vaccination

Presenting Author: Grace Taylor, B.S Psychology; Emory University

Poster Number: 153

Choi, C.; Tippett, A.; Salazar, L.; Hussaini, L.; Reese, O.; De Castro, K.; Taylor, G.; Taylor, M.; Ciric, C. R.; Puzniak, L. A.; Hubler, R.; Valluri, S.; Lopman, B.; Kamidani, S.; Rostad, C.; McLaughlin, J. M; and Anderson E.J.

Background: COVID-19 and influenza vaccination are recommended in adults without contraindications, and pneumococcal vaccination is recommended in high-risk adults and those ≥ 65 years of age. Vaccine hesitancy threatens COVID-19 vaccine uptake. Limited data suggest that prior receipt of influenza and/or pneumococcal vaccinations may correlate with COVID-19 vaccination uptake. We evaluated correlations between the receipt of COVID-19 vaccination and receipt of flu and pneumococcal vaccinations in those ≥ 65 years of age.

Methods: Active surveillance was performed at two hospitals in Atlanta, GA from May 2021 to June 2022. Eligible subjects were at least eighteen years of age presenting with symptoms of an acute respiratory infection (ARI). Subjects were asked to provide an informed consent and participate in an interview regarding medical, social, and vaccination history. Finally, a nasopharyngeal swab was collected. Medical records were reviewed. Vaccination status was verified from an electronic vaccine registry and medical records. Participants were considered vaccinated for our study if their first COVID-19 vaccination was given greater than or equal to fourteen days prior to the onset of the ARI symptoms. Characteristics were compared using a bivariate analysis (two-tailed p-value < 0.05). A stepwise logistic regression model was generated with inclusion in the model set at 0.05. Adjusted Odds Ratios (ORs) were determined for COVID-19 versus influenza vaccinations and COVID-19 versus pneumococcal vaccinations.

Results: Of the 1,365 enrolled patients, 748 (54.7%) received ≥ 1 COVID-19 vaccination. COVID-19 vaccination correlated with older age, male, white, and comorbidities (cardiac, diabetes, chronic kidney



disease, and immunosuppression). Patients who received the influenza vaccine were 3.7 times more likely to have received a COVID-19 vaccination (OR: 3.7, 95%CI: 2.9,4.7). Patients who were age eligible for the pneumococcal vaccination were 2.9 times more likely to receive a COVID-19 vaccination (OR: 2.9, 95%CI: 1.8,4.7).

Conclusion: 55% of those admitted with ARI symptoms had received a COVID-19 vaccination. COVID-19 vaccination correlated with older age, male, white, and comorbidities (cardiac, diabetes, chronic kidney disease, and immunosuppression). Receipt of COVID-19 vaccination strongly correlated with influenza (OR 3.7, 95% CI 2.9, 4.7) and pneumococcal (OR 2.9, 95% CI 1.8, 4.7) vaccination. Opportunity exists to improve COVID-19 vaccination.

A Comparison of Postoperative Analgesia for Nuss Procedure with Cryoablation Patients Receiving Single Shot Nerve Blocks (SSRNB) with and without Patient Controlled Intravenous Analgesia (PCIA)

Presenting Author: Renee' Tolly, MD, MHA; Emory University

Poster Number: 58

Bohling, Amy; Bartels, Ashley; Dalby, Ally; Liu, Katie; Alalade, Emmanuel; Bansal, Vipin; and Tolly, Renee'

Background: The post-operative management of Nuss procedure for treatment of pectus excavatum is challenging due to inadequate pain control leading to prolonged opioid use, increased length of stay and higher readmission rates. Peripheral nerve blocks has surpassed neuraxial analgesia for post-operative pain management for Nuss procedures due to introduction of cryoablation. Our study aimed to investigate if SSRNB would be non-inferior to SSRNB with PCIA for pain management in this patient population.

Methods: A retrospective review was conducted of patients undergoing Nuss procedure with cryoablation at Children's Healthcare of Atlanta-Scottish Rite in Atlanta, GA from December 1, 2015 to May 30, 2022. The primary outcome variable was total OMEs at 6, 12, 24, and 48 hours post operative. For secondary outcomes, we expanded the variables to include numeric pain scores at 6, 12, 24, and 48 hours post-operative, post-operative day (POD) to ambulation, post operative nausea and vomiting (PONV), POD to oral intake, LOS, medication administered during the operative case and in the recovery room, type of regional, block medication and additives, and complications. Descriptive analyses were performed to calculate median, Inter Quartile Range (IQR), frequency, and percentage. To compare the differences between with and without PCIA, Fisher's exact tests were used for categorical variables, and Wilcoxon sum rank tests were used for continuous variables. A p-value < 0.05 was considered statistically significant.

Results: 6/34 patients (17.6%) received SSRNB with PCIA while 28/34 (82.4%) received SSRNB only. SSRNB with PCIA patients were administered statistically significantly more opioids at the 6, 12, 24, and 48 hours post operative (p < 0.001). There is no statistically significant difference in pain scores, POD to oral intake, PONV, medication administration during the operative case and recovery room. SSRNB only patients had a statistically significant decrease LOS (median LOS = 2 days, p value < 0.002) and were able



to ambulate earlier ($p = 0.006$). The median amount of dexmedetomidine in a SSRNB was statistically significant ($p=0.013$) with patients receiving a PCIA.

Conclusion: In patients undergoing Nuss Procedures, SSRNB only patients had statistically significant decreased OMEs administered and decreases in time to ambulation and LOS.

Inducing Stenotic Hemodynamics in an In Vitro Bioprinted Pulmonary Vein Mimic Induces Rapid Endothelial to Mesenchymal Transition (EndMT) in Endothelial Cells

Presenting Author: Martin Tomov, PhD; Emory University

Poster Number: 79

Tomov, Martin L; Chen, Huang; Avazmohammadi, Reza; Dasi, Lakshmi Prasad; Bauser-Heaton, Holly and Serpooshan Vahid

Background: Pulmonary Vein Stenosis (PVS) is an acute cardiovascular condition characterized by progressive lumen size reduction due to overgrowth of connective and fibrotic tissue in one or more of the pulmonary veins. While current clinical interventions (stenting and angioplasties) have shown promising results in treating PVS, they require multiple re-interventions that can lead to re-stenosis and diminished long-term efficacy. There is an unmet need to develop functional in vitro models of PVS that can serve as a platform to study clinical interventions, specifically addressing endothelial to mesenchymal transition (EndMT) and flow shear stress changes, which are major triggers for stenosis and restenosis. We thus hypothesize that patient-inspired 3D bioprinted tissue models can provide a unique approach to recapitulate changing shear stress and EndMT transitions and allow for analysis of the complex tissue microenvironment impacted during PVS.

Methods:

We developed perfusable in vitro models of healthy and stenotic pulmonary vein by 3D reconstruction and bioprinting of patient-inspired computer tomography and X-ray angiography data. Flow hemodynamics through bioprinted vein models were predicted via computational fluid dynamics modeling and measured experimentally using 3D ultrasound particle imaging velocimetry (PIV). These PVS models were then seeded with human endothelial cells and assayed for cell survival, growth, and cell states within the printed channels while under homeostatic flow in either healthy or stenotic bioprinted geometries.

Results:

Our work here successfully demonstrated a how to generate perfusable and cellularized biomimetic constructs that can be used to model complex biological processes. The constructs further allowed us to incorporate and quantify the effects of tissue-like geometrical, chemical, metabolic and biomechanical ques that could offer substantial insights for prevention and treatment of PVS, as well as other cardiovascular diseases.

Conclusions:





Our work demonstrates the feasibility of bioprinting perfusable, patient-inspired, cardiovascular constructs that can recapitulate complex in vivo structures, survive long-term under homeostatic flow rates, and recapitulate functional aspects of the stenosis triggers, namely EndMT cascades.

Clinical Practice Guideline Development, Implementation, and Assessment of Adherence in U.S. Pediatric Emergency Departments: A Cross-sectional Study

Presenting Author: Chidiebere Ugwu, MD; Emory University

Poster Number: 71

Ugwu, Chidiebere; Jergel, Andrew; Gillespie, Scott; Rees, Chris; and Jain, Shabnam

Background: Over the last decade, there has been an expansion of clinical practice guidelines (CPGs) to standardize and improve the care of children seen in pediatric emergency departments (PEDs). Appraisal of Guidelines for Research and Evaluation II (AGREE II) is a widely used tool to assess the quality and reporting of CPGs. However, adherence to AGREE II recommendations in CPGs developed in PEDs is unclear.

Objectives: To describe the process of CPG development, implementation, and assessment of adherence in PEDs in the United States.

Design/Method: In Oct-Nov 2022, we conducted a cross-sectional survey of CPGs developed in PEDs with fellowship programs. The survey was based on 12 questions used to assess the quality of CPG development in AGREE II with a score assigned to each institution. Participant demographics, CPG implementation strategies, barriers, and methods of assessing adherence were collected via an online survey using REDCap. Univariate analysis was used to assess associations.

Results: Respondents from 44/84 (52%) qualifying PEDs (from 28 states) completed the survey. Most respondents (n=29, 66%) were from free-standing children's hospitals and level 1 pediatric trauma centers (n=35, 79%). 43 (97%). Only 19% reported receiving formal training on CPG development; 12% reported including patients in CPG committees, and potential conflict of interest was infrequently considered (14%). Lack of time and human resources were common barriers to CPG development. Fewer than half (n=21, 49%) of PEDs had a high-quality CPG development process, often due to infrequent use of "an outlined approach for grading recommendations" (Figure). There was no association between PEDs with a development score > 9 and ED volumes (P=0.42). Educational materials were reported as the most used strategy for CPG implementation and reminders perceived to be most effective when used. Quality improvement initiatives, audits/feedback, and use of incentives (e.g. MOC credit) were commonly used to promote CPG adherence.

Conclusion: Although a vast majority of surveyed PEDs develop their own CPGs, fewer than half reported developing CPGs through a high-quality process. Including patients on CPG committees and conducting training on CPG development process may promote higher quality CPGs and further improve clinical care for ill and injured children.



Elucidating the effects of combination therapy with Venetoclax and IAP inhibitor AZD5582 in SIV-infected, ART-suppressed macaques

Presenting Author: Benedicth Ukhueduan, BS, BAS and PhD; Emory University

Emory VTP-T32 Fellowship, 2021-2023

Poster Number: 80

Authors: Benedict Ukhueduan¹, Lakshita Lopez Lopez¹, Katherine Bricker¹, Nils Schoof¹, Vidisha Singh¹, Amir Dashti¹, Maud Mavigner^{1,2,3}, Amanda Schauer⁴, Lauren Tompkins⁴, Mackenzie Leigh Cottrell⁴, Ann Chahroudi^{1,2,3} Affiliations: 1. Department of Pedi

Background: Combining the IAP inhibitor AZD5582 with the Bcl-2 inhibitor Venetoclax (ABT199) to reverse latency and enhance clearance of infected cells via apoptosis is a novel approach to cure HIV. In this pilot study, we evaluated the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of ABT199 with AZD5582 in a nonhuman primate model.

Methods: Two juvenile rhesus macaques (RMs) were orally infected with SIVmac251 and ART was initiated 4 wpi. At 112 wpi, RMs received escalating single doses of ABT199 at 2.5 mg/kg, 10 mg/kg and 20 mg/kg intramuscularly (i.m.). Next, AZD5582 was administered once intravenously at 0.1 mg/kg with 4 daily doses of ABT199 (at 15 mg/kg i.m.). PK parameters in plasma was evaluated and changes in absolute T- and B-cell counts were assessed by flow cytometry.

Results: Venetoclax was well tolerated, with only mild adverse events (AEs) at 10 and 20 mg/kg single doses and no AEs with repeated doses given in combination with AZD5582. AEs included short term injection site pain and swelling, with nausea and vomiting in 1 RM (20 mg/kg dose). Steady state C_{max} after 15 mg/kg i.m. ABT199 dose 4 (2.26 mg/ml) approximates the C_{max} in humans after 400 mg oral dosing (2.1+/-1.1 mg/ml), with similar AUC₀₋₂₄ but shorter T_{1/2} observed. Absolute CD20+ B-cell counts were used as a PD marker, with reduction of 62-91% found at 24h post ABT199 dose 1 (15 mg/kg) + AZD5582 and full recovery to baseline levels by 2 weeks post ABT199 dose 4. Absolute CD4+ and CD8+ T-cell counts also declined at 24h post ABT199 dose 1 + AZD5582, including both naïve and memory subsets, without complete recovery by 2 weeks post ABT199 dose 4.

Self-reported Comorbidities Among Adults with Congenital Heart Disease: A Report from Congenital Heart Disease Project to Understand Lifelong Survivor Experience (CHD PULSE)

Presenting Author: Romie Velani, MBBS, MPH; Emory University

Poster Number: 154

Velani, Romie; Kuo, Krisy; Claxton, J'Neka; Zindayu, Tawanda; Flores, Jessica; Ilardi, Dawn; Gaitonde, Mansi; Deshpande, Shri; Wright, Lydia; Whitehill, Robert; Spector, Logan; Knight, Jessica; Yang, Yanxu; Kochilas, Lazaros and Oster, Matthew



Background: Adults with congenital heart disease (CHD) may experience several cardiovascular and non-cardiovascular comorbidities. We aimed to understand how these comorbidities compare to similar conditions reported by their non-CHD sibling respondents.

Methods: We performed a cross-sectional study using data from the Congenital Heart Disease Project to Understand Lifelong Survivor Experience (CHD PULSE), a survey of individuals enrolled in one of the 8 US centers participating in the Pediatric Cardiac Care Consortium after intervention for CHD. We used unadjusted generalized estimating equations to compare comorbidities reported by patients with CHD and their siblings without CHD.

Results: There were 1,759 respondents with CHD and 142 siblings without CHD, with no differences between the groups by sex (56.3% vs 62% female, $p=0.26$) or age (mean 34 years vs 33.2 years, $p=0.4$). Compared to their siblings, those with CHD overall were more likely to report at least 1 cardiovascular comorbidity (45.1% vs 16.9%, $p<0.01$) and less likely to report cancer (2.8% vs 6.3%, $p=0.03$). When analyzed by CHD severity those with single ventricle were the only group more likely than siblings to report at least 1 non-cardiovascular comorbidity (77.4% vs 61.3%, $p<0.01$). Within non-cardiovascular comorbidities, those with single ventricle CHD Severity were more likely than siblings to report mental health (69.6% vs. 16.9%, $p=0.02$), liver (29.6% vs. 0.7%, $p<0.01$) and kidney (8.7% vs. 0.7%, $p=0.02$) related comorbidities.

Conclusion: Compared with their siblings, adults with CHD are more likely to report cardiovascular comorbidities, but only those with single ventricle were more likely to report non-cardiovascular comorbidities.

Congenital Diaphragmatic Hernia Outcomes in a Low-Volume Center

Presenting Author: Michael Vieth, BS in Kinesiology - Exercise Science; University of Kentucky College of Medicine

Poster Number: 43

Vieth, Michael; Schadler, Aric; Ballard, Hubert; Bauer, JA; and Thakkar, Pratibha

BACKGROUND

Congenital diaphragmatic hernia (CDH) is a condition characterized by herniation of abdominal contents into the thoracic cavity requiring surgical repair. Previous literature suggests improved outcomes at high-volume centers compared to low-volume centers. The purpose of this study was to examine CDH outcomes at Kentucky Children's Hospital (KCH), a low-volume center, compared to the Congenital Diaphragmatic Hernia Study Group (CDHSG).

METHODS

A retrospective chart review was performed at KCH from 2007-2019 for neonates with CDH and subdivided into two cohorts: those requiring ECMO and those not requiring ECMO. Demographic data and measures of mortality and morbidity were compared to the CDHSG. Measures of morbidity for the



ECMO cohort including but not limited to ECMO duration, intracranial hemorrhage, sepsis, surgical repair timing, and ventilator days were collected. Statistical analysis was performed using IBM SPSS Statistics version 28. One-sample t-tests and one-sample Wilcoxon Signed Rank test were utilized as appropriate.

RESULTS

There were a total of 27 neonates with CDH at KCH from 2007-2019; 9 required ECMO. Birth weight and gestational age were similar between KCH and the CDHSG (2.99 kg vs 2.92 kg, $p=0.655$; 37.0 weeks vs 37.4 weeks, $p=0.51$). About half of the patients were inborn in both cohorts (52% vs 56%, $p=0.676$). KCH had significantly more caucasian patients (96% vs 55%, $p<0.001$). Unadjusted mortality was similar (KCH 70% vs CDHSG 72%, $p=0.857$). Using ECMO utilization (KCH 78% vs CDHSG 52%, $p=0.118$) and need for surgical repair (KCH 95% vs CDHSG 85%, $p=0.060$) as proxy for severity, mortality was comparable. No significant difference was noted for pulmonary outcomes such as average ventilator days (KCH 43.2 vs. CDHSG 17.3, $p=0.078$) and home oxygen dependency (KCH 44% vs. CDHSG 24%, $p=0.108$). Average length of hospital stay for patients treated at KCH was similar to CDHSG (64.4 vs 49.2, $p=1.000$).

CONCLUSIONS

Our study demonstrates that outcome in CDH patients is independent of center's case volume. Management of CDH with a standardized approach in a low-volume center can yield similar outcomes. This data supports treating patients with CDH at low-volume centers versus transferring to higher-volume centers.

A Patient-Friendly, Non-Invasive COVID-19-Influenza Combination Vaccine

Presenting Author: Sharon Vijayanand, Bachelor of Pharmacy; Mercer University College of Pharmacy

Poster Number: 44

Sharon Vijayanand, Smital Patil, Devyani Joshi, Revanth Singh, and Martin J. D'Souza

Purpose:

Like influenza, SARS-CoV-2 mutants impact the efficacy of the current vaccines, which may result in a yearly vaccination requirement. This study investigates the immunogenicity of an adjuvanted microparticulate (MP) SARS-CoV-2-influenza combination vaccine administered as one oral dissolving film (ODF) via the buccal route. A mucosal vaccine can trigger localized immune responses at the mucosal sites, including the respiratory mucosa, thus making buccal vaccination a desirable and non-invasive alternative to injectable vaccines. Further, a combination vaccine eliminates separate immunizations, making this vaccination strategy highly patient-friendly.

Methods:

Inactivated viruses were used as the vaccine antigens in polymeric MPs. The vaccine MPs were prepared using a double emulsion method, freeze-dried, characterized, and assessed in vitro for immunogenicity





and cytotoxicity using cell-based assays. In vivo, mice were administered the vaccine-loaded ODFs via the buccal mucosa in three doses. The serum was collected bi-weekly for analysis, followed by sacrifice and immune organ isolation at week 12. The virus-specific serum antibody levels (IgG, IgG1, IgG2a, IgM, IgA) were assessed using an enzyme-linked immunosorbent assay (ELISA). The virus-specific secretory IgA (SIgA) in the lungs was evaluated as a mucosal immunity marker using ELISA. The CD4+ and CD8+ T-cells in the spleen and lymph nodes were assessed using flow cytometry analysis.

Results:

The vaccine MP was found to be immunogenic and non-cytotoxic to cells in vitro. Following in vivo immunization, the SARS-CoV-2-specific and Influenza-specific serum IgG and IgA levels increased significantly. Serum IgM levels were predominant in the initial weeks. The IgG subtype analysis showed an equal distribution and significantly high serum IgG1 (Th-2/antibody-mediated response) and IgG2a (Th-1/cell-mediated response) antibodies specific to both viruses. Elevated levels of SIgA in the lung supernatant and an increased percentage of CD4+ and CD8+ T-cells in the splenocytes and lymphocytes were also observed.

Conclusion:

The combination vaccine induced increased levels of virus-specific serum antibodies and cellular responses following immunization. The buccal vaccine also induced SIgA in the lung tissue, essential for neutralizing the virus at the entry site (respiratory mucosa). Thus, a combination buccal vaccine for COVID-19 and influenza can potentially cause a fundamental breakthrough in vaccine development.

Integration of Educational Videos into Well-Child Visits: Feasibility, Acceptability, and Impact on Parent Knowledge and Practices Related to Infant Fruit Juice and other Sugary Beverage Consumption

Presenting Author: Jean Welsh, PhD, MPH, RN; EMORY UNIVERSITY

Poster Number: 95

Jean Welsh, Katelyn Chiang, Aileen Rivell, Wilhemina Quarpong, Terri McFadden, Belise Livingston-Burns Welsh, Jean; Chiang, Katelyn; Rivell, Aileen; Quarpong, Wilhemina; DeSantos, Karla; Smith, Joy; McFadden, Terri; and Livingston-Burns, Belise

Background

Current dietary recommendations include a focus on minimizing sugar-containing beverage consumption (SCBs). This includes delaying the introduction of fruit juice (FJ) until >12 months, avoiding sugar-sweetened beverages (SSBs) <2 years, and limiting the amounts of both thereafter. Pediatric clinicians are a respected source of infant feeding-related information for parents but have limited time to do prevention education. We aimed to determine if targeted educational videos could be integrated into Well-Child Visits (WCV) and increase parent knowledge and compliance with SCB-related early feeding recommendations.

Methods





Participants in this study include a convenience sample of parents attending a well-child visit at a single pediatric practice Aug 2021-May 2022 (control group) or Nov 2022-April 2023 (intervention group). At the 4- and 12-month visits, parents viewed and responded to survey questions assessing their perceptions of a short (3-4 minutes) age-specific educational video on SCB-related recommendations (intervention group) or a control video. At the 6- and 15-month visits, they completed surveys on their SCB-related infant feeding knowledge and practices.

Results

Respondents in both the intervention (n=287) and control groups (n=120) were primarily women (85%) and Black/African American (92%), most (93%) were Medicaid enrolled. Nearly all (93%-97%) of the parents in the intervention group (n=251) reported that: they learned something from watching the SCB focused video, watching it was a good use of their time, the length was “about right”, and they were able to focus when viewing it during the clinic visit. 77% reported that the video changed how they think about feeding or caring for their child. A sub-sample of intervention parents also completed a feeding questionnaire at their subsequent 6-month (n=30) or 12-month (n=6) well-visit. No differences in SCB-related knowledge and feeding practices compared to the same age control group were observed with the one-time viewing of the single video.

Conclusions

Our findings demonstrate that integrating short educational videos into well-child visits is feasible, that they are well-received by parents, and that doing so may be an effective strategy for increasing parent knowledge on key infant feeding recommendations. Further research is needed to assess their impact on parent behavior.

Preconditioning with TBI vs CTX Impacts CD4+ Adoptive T Cell Therapy Efficacy

Presenting Author: Megen Wittling, Student; Emory University

Poster Number: 45

Wittling, Megen; Knochelmann, Hannah; Paulos, Chrystal

We sought to determine if differential preconditioning methods impact the efficacy of our Th17 therapy. Our team has previously found that the preconditioning method prior to CD8 T cell therapy does not appear to have a major impact on therapy response, however, our new work shows preconditioning may be important in the context of CD4 cell ACT. Using TBI (5 Gy), CTX (200 mg/kg), or no preconditioning prior to ACT of Th17 cells in our TRP melanoma model, we found that preconditioning with TBI led to better long-term engraftment in the mice. This engraftment increase was importantly linked with improved antitumor responses in the TBI treated mice with 6/6 TBI mice living >30 days, 3/6 CTX mice living >30 days, and only 1/6 mice with no preconditioning living >30 days. Also of note, the cytokine profile at day 10 post-Th17 injection varied between the various preconditioning methods, notably with increased G-CSF, IL-6, MCP-1, MCP-5, IL-5, and KC in the TBI treated mice. IL-17 and IFN- γ were greatly increased in both the TBI and CTX treated mice but were nearly absent those with no preconditioning. Our results indicate the antitumor response, engraftment in multiple organs, and





cytokine profile differ between these different preconditioning regimens and that further investigation into the optimal preconditioning regimen may be needed prior to ACT involving Th17 cells.

Differential Effects of Neighborhood Socioeconomic Status on Post-Surgical Outcomes of Infants undergoing Congenital Heart Surgery

Presenting Author: Yanxu Yang, DrPH; Emory University School of Medicine

Poster Number: 81

Yang, Yanxu; Claxton, J'Neka; Knight, Jessica; Kuo, Kristina; Taylor, Shreya; Oster, Matthew; Kochilas, Lazaros

Background:

Congenital heart disease (CHD) is the most common cause of birth defect-related death among infants. Neighborhood socioeconomic status (nSES) influences many health outcomes, but its effect on congenital heart surgery (CHS) outcomes is less well studied. Our study aims to examine the effect of nSES on survival after infantile CHS.

Methods:

This is a retrospective cohort study of infants enrolled in the Pediatric Cardiac Care Consortium (PCCC), a multi-center US-based registry of interventions for CHD after undergoing their first CHS. We included infants with available identifiers for matching with the National Death Index and maternal demographics from birth registries of Missouri, Ohio and Arkansas between 1990-2003. nSES was stratified into tertiles (low, middle, high) using a census-based score derived from maternal zip code at CHS. Mortality risk was assessed by Cox proportional hazards models.

Results:

We included 2,939 infants. Patients living in areas with low nSES had lower unadjusted 3-year survival rate following discharge after CHS (89.8%) and 92.3% for middle nSES vs patients in high nSES group (93.6%). After adjusting for covariates, infants in low nSES were not independently associated with an increased mortality risk within the first 3 years after CHS (aHR: 1.28, 95% CI:0.88-1.85, p=0.20) when compared with their counterparts from high nSES and this disadvantage persisted up to 30 years later. Stratified analysis by CHD severity revealed that the increased risk of low nSES was restricted to the mild CHDs and those with white maternal race.

Conclusion:

Low nSES at the time of the first CHS is associated with lower survival probability at early and longer-term. The increased mortality risk by low nSES applies mostly to infants with mild CHD and only to those with white maternal race. The effect of nSES has not changed significantly over time. These findings highlight the enduring effects of early social determinants of health on long-term outcomes after CHS and underline the need for additional strategies to reduce nSES disparities and improve health outcomes across the board for CHD patients in the US.





Prevalence of Food Selectivity in Autistic Children

Presenting Author: Chitrakleha Yarasani, Neuroscience and Behavioral Biology; Emory University

Poster Number: 155

Chitra Yarasani; Megan L. Alder, PhD, RN; Stormi P. White, PsyD; Destinee Rogers; Lawrence Scahill, PhD; William G. Sharp, PhD

Background: Food selectivity (FS) is the most common feeding problem in children with autism spectrum disorder (ASD) with a current estimated prevalence of 50-90%. However, there is a lack of consensus across studies, resulting in a broad range of prevalence estimates.

Purpose: The purpose of this study was to evaluate the prevalence of food selectivity in autistic children ascertained from a specialty outpatient diagnostic clinic.

Methods: Cross-sectional data were collected from a sample of 109 autistic children (Mean age= 5.3 ± 2.19 years, 78% Male). Children diagnosed with ASD within the past year were recruited from the Marcus Autism Center. Children with an untreated medical condition were referred to a hospital and were excluded. Parents completed the modified Brief Autism Mealtime Behavior Inventory (BAMBI) to record the child's mealtime behaviors. Parents completed a clinical assessment with a registered dietitian to record the child's dietary intake patterns. To examine the prevalence of FS in autistic children, parent-ratings were combined with dietary assessment data. FS was defined by the child's omission of food items across food groups and the child's willingness to try new foods.

Results: Of the 109 children, 104 (95.4%) completed parent-ratings and clinical assessments and 5 (4.6%) completed parent-ratings. The mean value for the BAMBI was 37.46 + 9.79. Based on validated thresholds, 68 (63%) had significant mealtime behaviors (modified BAMBI > 34). Of the 109 children, 35 (33.7%) omitted 1 or more food groups and vegetables were the most frequently omitted food group (N=31, 29.8%) followed by fruits (N=19, 18.3%), dairy (N=3, 2.9%), and proteins (N=2, 1.9%). Of the 103 autistic children with complete parent-rating and clinical assessment data, 47 met our FS criteria with the estimated prevalence of 45.6%.

Conclusions: Our results show a generalizable prevalence estimate of FS in children with ASD using combined parent-ratings and dietary assessment. The impact of FS on child growth and development should be explored in future studies.

Examining Relationships between Provider Fidelity, Caregiver Satisfaction, Therapeutic Alliance, and Child Skill Gain within a Parent-Mediated Intervention Delivered in an Early Intervention System

Presenting Author: Millena Yohannes, B.A.; Emory University School of Medicine

Poster Number: 156

Millena Yohannes, Katherine Pickard, Nicole Hendrix





Background

Research has shown parent-mediated interventions (PMIs) to be an effective approach to early intervention (EI) for autistic children (Nevill et al., 2018; Oono et al., 2013). Emerging research has attempted to increase access to PMIs by training community providers to deliver them within diverse community settings, including Part C EI systems (Stahmer et al., 2020; Rogers et al., 2022). This research has focused less on caregivers' experience receiving PMIs. This gap limits our understanding of whether PMIs are aligned with the needs of families underrepresented in research (Pickard et al, 2016).

Objectives

Examine caregiver satisfaction receiving PMI Project ImPACT within Georgia's EI system; determine whether intervention fidelity is associated with therapeutic alliance or caregiver satisfaction; assess the association between intervention fidelity and child skill gain.

Methods

Participants included 42 caregivers of children (12-30 months) with an autism diagnosis or increased likelihood receiving services within Georgia's EI system. Caregivers completed surveys prior to (N=42) and following (N=14) receiving Project ImPACT. Specific surveys included the Measure of Processes of Care (MPOC; King et al., 2004); parent-reported intervention satisfaction scale; and the Social Communication Checklist (Wainer et al., 2017). Providers' intervention fidelity was scored alongside their training in Project ImPACT. Correlation analyses were used to assess the relationships between these measures.

Results

Data collection is ongoing with anticipated data from an additional 20 caregivers by May 2023. In preliminary analyses, caregiver satisfaction (M=4.70/5(SD=0.33)) and therapeutic alliance (M=4.60/5(SD=0.43)) were rated highly. Intervention fidelity averaged 73.40%. Analyses between intervention fidelity, parent satisfaction ($r=0.001$; $p=.997$), therapeutic alliance ($r=-0.204$; $p=0.484$), as well as child skill gain in communication ($r=0.108$; $p=0.725$) and social engagement ($r=0.132$; $p=0.663$) did not yield significance.

Conclusions

Data collection is ongoing and the sample size is not powered to detect significant relationships. Preliminary analyses suggest that caregivers are highly satisfied with delivery of EIs services and have good rapport with their provider. Interestingly, provider fidelity to either PMI is not associated with caregiver satisfaction, therapeutic alliance, or child skill gain. These findings are important to understand what factors drive both caregiver and child outcomes in regard to the implementation of PMIs within EI systems.

Case Study of a Young Child Receiving Treatment in an Applied Behavior Analysis Clinic with Dual Diagnoses of Cortical Vision Impairment (CVI) and Autism Spectrum Disorder (ASD)





Presenting Author: Rachel Yosick, PsyD; Emory University School of Medicine

Poster Number: 59

Naresh, Aparna; and Yosick, Rachel

BACKGROUND: Current literature has discussed the relationship between the diagnoses of ASD and CVI in terms of commonalities in symptom presentation¹. Most diagnostic tools used to identify ASD as well as research-based interventions to address skill deficits include multiple items/characteristics that are directly based on an individual's visual abilities². However, there is a paucity of research examining possible needed adaptations to existing interventions for children with this ASD and CVI. In the current case study, we adapted behavior-analytic assessment and intervention procedures to more accurately identify skill deficits and improve social communication skills with a child diagnosed with ASD and CVI.

METHODS: This case involved an 8-year-old boy, "Aaron", with dual diagnoses of ASD and CVI. The outcome measure utilized was the Verbal Behavior Milestones Assessment and Placement Program (VB-MAPP) which assesses language/verbal abilities and barriers to learning. The VB-MAPP was administered at intake and mid-treatment (i.e., 3 months post-admission) to measure verbal skill development over time. Specific adaptations were made to assessment and intervention procedures in order to address Aaron's diagnosis of CVI, i.e. reduction of visual array size, specific use of light, concrete narration, simplification of the visual environment, and increasing latency to the presentation of consequences during teaching (i.e., error correction procedures, prompts, etc.).

RESULTS: Aaron's VB-MAPP score increased from 10.5 at treatment admission to 82.0 mid-treatment. This increase in VB-MAPP scores across several skill domains (i.e., requesting, labeling, listener skills, visual perceptual skills, etc.) over time likely reflects the benefits of various modifications employed during sessions. Reductions in barriers to learning (e.g., prompt dependency) were also observed.

CONCLUSIONS: Limited research exists to guide practitioners on how to modify existing behavioral interventions for children with ASD and CVI. The current case showed a significant difference in VB-MAPP scores after modifying assessment and treatment approaches. Results shed light on 1) the importance of identifying the most effective modifications/adaptations for children with ASD and CVI and 2) how to apply these modifications to assessment and intervention procedures to more accurately determine the presence of skill deficits and program for a more rapid acquisition of social communication skills.



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