

# ADVANCING NEONATOLOGY CARE IN 2021



## A MESSAGE FROM Steve Olsen, MD

Division Director, Neonatology

This year, we're excited to highlight some innovative care and scientific research taking place at the Level IV Neonatal Intensive Care Unit (NICU) at Children's Mercy Kansas City.

First, as the nation continues to deal with the impact of COVID-19, we have started to see neonates who are affected by this devastating illness. We've experienced this firsthand, treating an infant diagnosed with COVID-19 with ECMO. We've also conducted a retrospective study of COVID-19's impact on our tracheostomy and home ventilator patients.

Second, our researchers are investigating a broad range of issues critical to advancing the field of neonatology. These include:

- The DLL4 gene and its role in lung vascular and alveolar development.
- Steroid treatment response in infants with BPD.
- Timing of postnatal steroid treatment for BPD.
- Mean age of tracheostomy and decannulation of patients in our nationally recognized Tracheostomy and Home Ventilator Program.

This and the many other programs we have developed to better serve our patients, such as trauma-informed care, set Children's Mercy apart from our peers.

We invite you to review the advances in research made this year and reported in several high-impact medical journals. Our physician-scientists' passion for issues that impact our patients and their families is truly making the difference in the care we deliver.

## 2021 HIGHLIGHTS

Children's Mercy neonatologists have created a podcast called **Neonatology Review: Isolette to Crib**. The podcast features Joti Sharma, MD, MEd, and Julie Weiner, DO, as they walk through helpful information for fellows preparing for boards. The podcast also serves as a resource for others in the field. There have been **more than 7,000 interactions** with the podcast year-to-date.

We are recognized as a **Platinum Center of Excellence** by the Extracorporeal Life Support Organization (ELSO) — **one of only 10 centers in the nation to earn this distinction**. Our ECMO survival rates frequently exceed national averages.

John M. Daniel, IV, MD, MS, a Cardiac Neonatologist and Medical Director of the Neonatal ECMO Program, and Alex Oschman, PharmD, BCPPS, a Clinical Pharmacy Specialist, received funding from the National Institute of Child Health and Human Development Neonatal Research Network to serve as co-principal investigators for Children's Mercy as part of a **multicenter trial looking at the use of the drug milrinone for the treatment of pulmonary hypertension in neonates diagnosed with congenital diaphragmatic hernia**. Twelve other neonatal intensive care programs across the country are taking part in this research.

Children's Mercy has **one of the largest neonatology-led home ventilator programs in the country**. The total number of ventilator-dependent infants and children cared for at home has grown to more than 336 patients.

**Four new faculty** have joined the Children's Mercy Neonatology team: Sean Curtis, MD, Megan Tucker, MD, Mariana Theodoro, MD, and Ahmed Elsaie, MD.

Children's Mercy is **one of the few pediatric hospitals in the nation to offer a neonatal organ donation program**.

# 2021 By the Numbers

1,075 admissions

238 NICU beds in Kansas City Metro

694 NICU transports

3,641 clinic visits (special care, neonatology, home vent)

42 faculty

37 neonatologists

4 pediatricians

1 psychologist

## CLINICAL OUTCOMES

NICU CLABSI 0.406/1,000 line days

Unintended extubations 0.696 per 100 vent days

## CLINICAL EXCELLENCE SETTING NEW STANDARDS OF CARE IN NEONATOLOGY

### Utilizing ECMO to Care for a Critically Ill Neonate with COVID-19

A critically ill 2-week-old male identical twin infant born at 35 weeks’ gestation was admitted to the Children’s Mercy NICU after decompensating rapidly at an area emergency room.

After the child tested positive for COVID-19, his need for ventilator support and oxygen requirements gradually increased. Despite aggressive measures, the infant had escalating mechanical ventilation needs with concerns that he was not likely to survive without extraordinary measures.

To support his respiratory function, on hospital day 10 the decision was made to cannulate to extracorporeal membrane oxygenation (ECMO), making this possibly the first case reported in the literature of neonatal COVID-19 requiring ECMO in the U.S.

To date, the child has survived treatment, but COVID-19 has badly damaged his lungs, requiring tracheostomy and ventilator support long term.

This case has been submitted for publication.

## Impact of the COVID-19 Pandemic on Children <5 Years of Age with Tracheostomy and Home Ventilator Dependence

Researchers at Children’s Mercy looked at the ongoing impact of COVID-19 on high-risk patients with tracheostomy and ventilator dependence in a retrospective study conducted on infants who received tracheostomy at less than 1 year of age, with or without ventilator dependence at home, and currently being followed in the Infant Tracheostomy and Home Ventilator Clinic at Children’s Mercy.

A total of 68 patients were included in the study whose primary diagnosis was bronchopulmonary dysplasia. The authors concluded that having a tracheostomy with or without ventilator dependence did not seem to increase the risk of acquiring COVID-19 infection significantly in children under 4 to 5 years of age.

Akangire G, Begley A, Lachica C, Jensen DR, **Manimtim W.** Impact of the COVID-19 pandemic on children <5 years of age with tracheostomy and home ventilator dependence. *Clinical Pediatrics*. Sept. 18, 2021. <https://doi.org/10.1177/00099228211046697>.



Winston Manimtim, MD, FAAP, and patient

### Implementing Trauma-Informed Care in the NICU

Dena K. Hubbard, MD, FAAP, Neonatologist, and Patty Davis, Clinical Social Worker, are leading an initiative to implement trauma-informed care in the Children’s Mercy Level IV NICU.

This approach to treatment acknowledges care teams’ need to have a complete picture of a patient’s life experiences in order to provide healing and mitigate further trauma. Incorporating the principles of TIC into the policies and procedures of the high-stress NICU environment can improve outcomes not only for patients and families, but also staff.

Dr. Hubbard and the Children’s Mercy team have taken a multidisciplinary approach to this initiative, training every level of staff who have contact with the patient’s family, from environmental services and unit clerks to physicians, nurses, pharmacists, dietitians and developmental care

therapists. To date, staff have received more than 1,400 hours of TIC training involving awareness, sensitive practices, resilience at work and cultural humility.

Dr. Hubbard and her colleagues have been invited to present on the topic on a regional and national stage, including at the American Academy of Pediatrics and the Pediatric Academic Society meetings.

A paper entitled Trauma-informed Care and Ethics Consultation in the NICU, authored by Dr. Hubbard and her colleagues, was recently published online in *Seminars in Perinatology*. Additional IRB-approved research projects into the topic are under way.

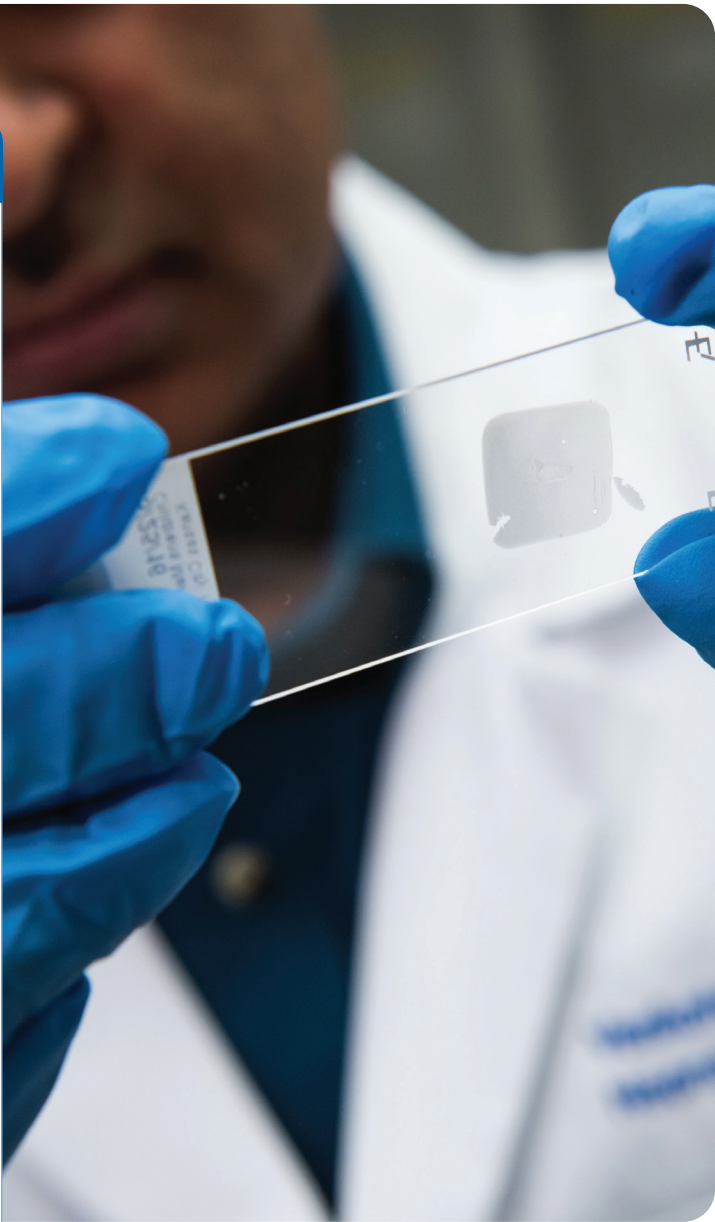


# LEADING THE WAY Through Research

## By the Numbers

- 83 published manuscripts
- 6 published book chapters
- 38 international and national presentations (8 oral and 30 posters)
- 11 invited lectures
- Faculty holds 27 leadership positions in international, national and local industry and advocacy organizations
- Participation in 35 clinical trials
- 7 retrospective IRB-approved studies
- 12 prospective studies
- 4 approved registries
- Secured \$4,749,400 in external grant funding, including \$4,199,341 in NIH grants\*

\*Please note that these amounts reflect all total active project awards during the time frame of CY 2021—due to variance of the calendar year and grant year, we are unable to provide the amount awarded each calendar year.



## RESEARCH HIGHLIGHTS

### Children’s Mercy Researcher Publishes First Study on DLL4 Gene and Its Role in Lung Vascular and Alveolar Development *JCI Insight*

Venkatesh Sampath, MBBS, MRCPCH, Neonatologist and Medical Director of the Neonatal Diseases Research Program at Children’s Mercy Kansas City, has performed novel research into the little-understood molecular mechanisms that regulate normal lung vascular growth, limiting understanding of defective vascularization in BPD.

Dr. Sampath’s research team is the first to demonstrate that the gene DLL4 regulates microvascular growth and arborization during distal lung ontogeny and DLL4 deficiency programs deviant angiogenesis, disrupting lung vascular patterning and alveolarization. These phenotypic changes occurred concurrently with altered expression signatures of lung endothelial cell fate specification and notch signaling, as well as impaired expression of AT1 lineage markers.

Dr. Sampath’s results support the “vascular hypothesis” from a lung development perspective by indicating that DLL4, an endothelial gene, is required for distal lung morphogenesis.

### Researchers Use R21 Grant to Study Steroid Treatment Response in Infants with BPD

Tamora Lewis, MD, PhD, and William Truog, MD, both neonatologists, were awarded a two-year, \$455,856 R21 grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development to assess the genomic and metabolomic markers which correlate with steroid response in a group of preterm infants who have evolving BPD.

Their project is called Less Lumping, Smarter Splitting: Genomics and Metabolomics of Systemic Steroid Response in Bronchopulmonary Dysplasia.

By better understanding steroid response variability, the team hopes to move BPD therapy into the age of personalized therapeutics in this group of infants using contemporary tools (genomics, metabolomics) to identify infants with the greatest likelihood of therapeutic benefit with the naturally associated minimization of development of adverse events by preventing steroid exposure to infants unlikely to respond. This precision therapeutics approach addresses a large gap in current knowledge and may lead directly to improved pharmacotherapy for infants with BPD.

Children’s Mercy is serving as the principal investigator for this research.





# RESEARCH HIGHLIGHTS continued

## Validating the Timing of Postnatal Corticosteroid Treatment for BPD Nationwide

*Pediatric Pulmonology*

Alain C. Cuna, MD, Neonatologist, Assistant Professor of Pediatrics, University of Missouri-Kansas City School of Medicine, conducted a retrospective cohort study of preterm infants treated with low-dose dexamethasone for BPD in the Children's Mercy NICU.

His findings led Dr. Cuna and his colleagues to conclude that among preterm infants, earlier treatment with steroids could potentially modify the disease trajectory and allow for the sicker cohort to have better outcomes compared to delayed treatment.

To validate the results in a larger patient database, the researchers worked with the Children's Hospitals Neonatal Consortium (CHNC), posing the same question regarding timing of corticosteroid treatment and outcomes, this time via a multicenter retrospective cohort study looking at data from January 2010 to December 2016 from the Children's Hospitals Neonatal Database and Pediatric Health Information System Database.

The results from this much larger database were recently published in *Pediatric Pulmonology* and mirrored the findings that Dr. Cuna identified in the initial retrospective study at Children's Mercy. In short, later initiation of treatment among preterm infants with systemic corticosteroids was associated with a higher likelihood of developing Grade 2 or Grade 3 BPD when compared to earlier intervention.

## Retrospective Study Reports Mean Age at Tracheostomy and Decannulation

*Pediatric Research*

The Children's Mercy Kansas City Infant Tracheostomy and Home Ventilator Program is the only program in the U.S. serving as a medical home for these patients in a multidisciplinary setting with other key subspecialists, including pulmonologists, gastroenterologists and otolaryngologists.

The program has collected the data necessary to systematically examine several key factors related to outcomes in this specific patient population, contributing important research to this field. Their retrospective study on tracheostomy and decannulation was one of the largest studies of its kind, a significant strength of this research.

Specific to the Children's Mercy cohort, the team found through regression analysis that they had a much higher rate of survival for the premature infants compared to term infants with tracheostomy, as well as a higher rate of decannulation. The authors postulated that the improved overall survival outcomes in these very high-risk infants are the result of consistent delivery of both primary and subspecialty care, along with a number of other factors.

The team's goal is that these insights will assist other clinicians as they provide families with counseling based on this data, helping them manage expectations for tracheostomy and home ventilator support, and aiding them in making better informed decisions on behalf of this vulnerable population.

## Children's Mercy Participates in the Neonatal Neurobehavior and Outcomes in Very Preterm Infants (NOVI) Study

*Pediatric Research*

Children's Mercy is one of eight sites across the U.S. that enrolled babies born at less than 30 weeks' gestation from 2014-2016 in the Neonatal Neurobehavior and Outcomes in Very Preterm Infants (NOVI) Study and has continued to follow them to 6 to 7 years of age. Brian Carter, MD, Children's Mercy Neonatologist and Bioethicist, serves as the site's principal investigator.

This research not only concerns neonatal-perinatal risk, but the environment of raising the child, exposure to environmental modulators and the frequency and severity of any illness or developmental impairments, as well as therapeutic services utilized.

The researchers have begun analyzing the data gathered from 587 infants born <30 weeks postmenstrual age from the sites. To date, they have published several notable papers, including one recently published online in *Pediatric Research* on the neurodevelopmental profiles of infants born <30 weeks gestation at 2 years of age. Insights from this study may have an impact on neurobehavioral screening upon discharge from the NICU and early intervention services.

The researchers anticipate additional publications and insights as the data collected from this project is analyzed.

## Examining the Role of Breast Milk in Neonatal Development

A group of researchers led by Todd Bradley, PhD, at Children's Mercy is utilizing the NICU's Breast Milk Bank to study and monitor the impact of breast milk on neonatal health. They are working to identify the cellular composition of human breast milk, determine differences in milk composition in mothers of preterm and full-term infants during early life and identify milk predictors of neonatal infection. In addition, they want to determine the levels of immunomodulatory molecules in human milk that may impact the development of the infant's immune system.

The impact of this project will uncover mechanisms of how breast milk cells contribute to neonatal immunity, which can be used as a noninvasive biomarker for neonatal health. These tools could potentially be critical for identifying and treating neonatal infections and reducing global childhood mortality caused by infections.

## Genomic Answers for Kids Advances Rare Disease Research

The Children's Mercy Research Institute has released more than 2,300 pediatric rare disease genomes through its Genomic Answers for Kids (GA4K) program, which makes it one of the largest pediatric rare disease whole genomic datasets ever publicly shared.

To date, more than 3,700 patients have enrolled in the program, which has resulted in more than 18,000 new genomic analyses and more than 600 genetic diagnoses. In addition, the program has advanced research genomic analyses for children of 350 families with more common childhood diseases: cerebral palsy and Down syndrome.

The full pediatric data repository is shared in a real-time web interface through a comprehensive process, which gives researchers and clinicians low-barrier access to processed data with disease prioritized genetic changes.

"Giving access to our data allows researchers to link their own genetic findings so they can accept or reject hypotheses on their gene discoveries," said Tomi Pastinen, MD, PhD, Director, Genomic Medicine Center, Children's Mercy Kansas City. "Data sharing is the only way we'll make headway in the quicker delivery of results that are non-diagnostic today."



The GA4K program has helped hundreds of kids, like Celia, find a genetic diagnosis.



# MEET THE TEAM

## LEADERSHIP

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