

The Alabama Center for Childhood Cancer and Blood Disorders

2021 IMPACT REPORT



Children's
of Alabama®



DIVISION DIRECTOR NOTE

At this writing, the COVID-19 pandemic is still active in Alabama. We continue to navigate the challenges of a highly contagious virus as we provide care for our pediatric hematology-oncology population.

Our work, through elite national and international consortiums, opens doors for our patients to participate in a multitude of cutting-edge clinical trials. Last year, Children's of Alabama joined the prestigious Pacific Pediatric Neuro-Oncology Consortium (PNOC), a unique clinical trials consortium focusing on personalized therapy approaches for children with malignant brain tumors. Unlike other consortia, PNOC's clinical trial portfolio includes neurosurgery trials with techniques such as convection-enhanced delivery, fluorescent agents and advanced imaging compounds.

Through these consortiums, our researchers and clinicians have the opportunity to collaborate with researchers across the world to identify improved treatment options via new trials. The PNOC, for example, is comprised of about two dozen sites across the United States, Canada, Europe and Australia.

None of this would be possible without our dedicated team and the support of the community. Your commitment and generosity keep this momentum going so that we can continue to serve our patients and their families. Thank you for your partnership.

Girish Dhall, M.D.

Benjamin Russell Endowed Chair in Pediatric Hematology & Oncology
Head, UAB Division of Pediatric Hematology, Oncology, and Blood & Marrow Transplantation
Director, The Alabama Center for Childhood Cancer and Blood Disorders at Children's of Alabama
Director, Clinical Trials Office, Children's of Alabama
Director, Neuro-Oncology Program, Children's of Alabama
Deputy Director, Neurofibromatosis Clinical Trials Consortium
Professor of Pediatrics



Girish Dhall, M.D.

WE CARED
FOR OVER
2,000
PATIENTS WITH
SERIOUS &
LIFE-THREATENING
CANCER & BLOOD
DISORDERS

ONCOLOGY

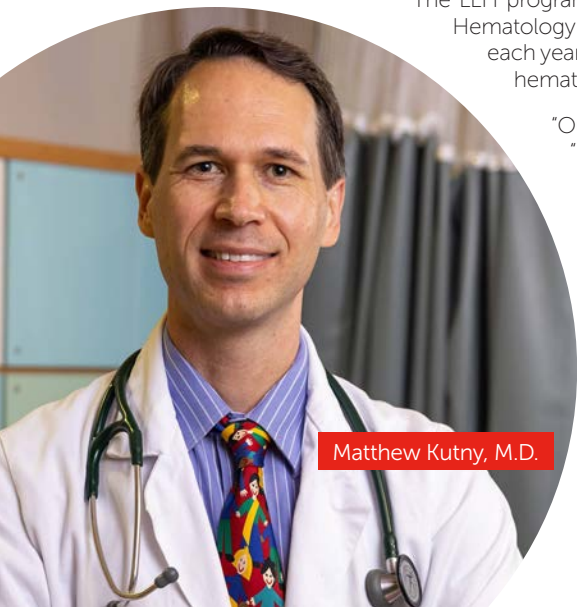
Children's of Alabama Advances Research, Clinical Trials for Leukemia, Lymphoma

The Leukemia, Lymphoma and Histiocytosis (LLH) program at Children's of Alabama has nearly doubled in size over the past decade as faculty members spearhead innovative clinical trials and research focused on improving cure rates while decreasing treatment toxicity and side effects.

The LLH program includes five physicians and four nurse practitioners within the Division of Pediatric Hematology and Oncology. LLH clinicians consult on about half of the new cancer diagnoses seen each year at Children's, said Director **Matthew Kutny, M.D.**, also an associate professor of pediatric hematology and oncology at the University of Alabama at Birmingham (UAB).

"Our faculty has expanded, but we've also gained greatly in our expertise," Kutny explained. "When children come here with a particular diagnosis, they're not just treated by a general hematologist or oncologist, but rather, through our disease-specific teams."

LLH faculty members published 34 research articles in peer-reviewed journals over the last two years and presented more than 30 times at national oncology meetings. Additionally, several members sit on national steering committees or review boards that develop pediatric cancer treatment guidelines, Kutny said. The LLH program also participates in several key clinical trial consortiums, such as the National Cancer Institute's Children's Oncology Group, including selected membership in a network studying the newest oncology treatments in children.



Matthew Kutny, M.D.

"We have providers who really understand that disease and are involved at a national level in developing the best treatments for that disease," he added.

Kutny's own research efforts include leading several national trials in myeloid leukemias as well as focusing on central nervous system disease in acute myeloid leukemia. Other notable faculty research efforts include:

- **Anna Hoppmann, M.D., M.P.H.,** and **Smita Bhatia, M.D., M.P.H.,** are studying the social determinants of health and outcomes in cancer including understanding barriers to consistent home administration of medications for many months as recommended in current leukemia treatment regimens.
- **Aman Wadhwa, M.D., M.S.P.H.,** also working with Dr. Bhatia, is examining how body composition affects childhood cancer outcomes in lymphomas, with an eye toward predicting and modifying toxicities.
- **Julie Wolfson, M.D., M.S.H.S.,** is concentrating on outcomes disparities in adolescents and young adults with cancer, an at-risk group not often incorporated into clinical trials.
- **Ana Xavier, M.D.,** is leading several national trials in difficult-to-treat lymphomas. Xavier is also focusing on reducing the burden of chemotherapy and radiation exposure in lymphoma patients.

Bringing Groundbreaking Cancer Trials to Alabama Children

Although there have been great strides in treating pediatric cancer, it remains the leading cause of death by disease among children. In addition, more than 95 percent of childhood cancer survivors have significant health-related issues because of the toxicity of current treatment options. Yet just 4 percent of government spending on cancer goes to pediatric cancer.

That's why the Sunshine Project is so important. The project, part of the National Pediatric Cancer Foundation, brings together more than 20 children's hospitals, including Children's of Alabama, with the goal of streamlining the process required to bring new, less toxic, more effective pediatric oncology drugs to clinical practice.

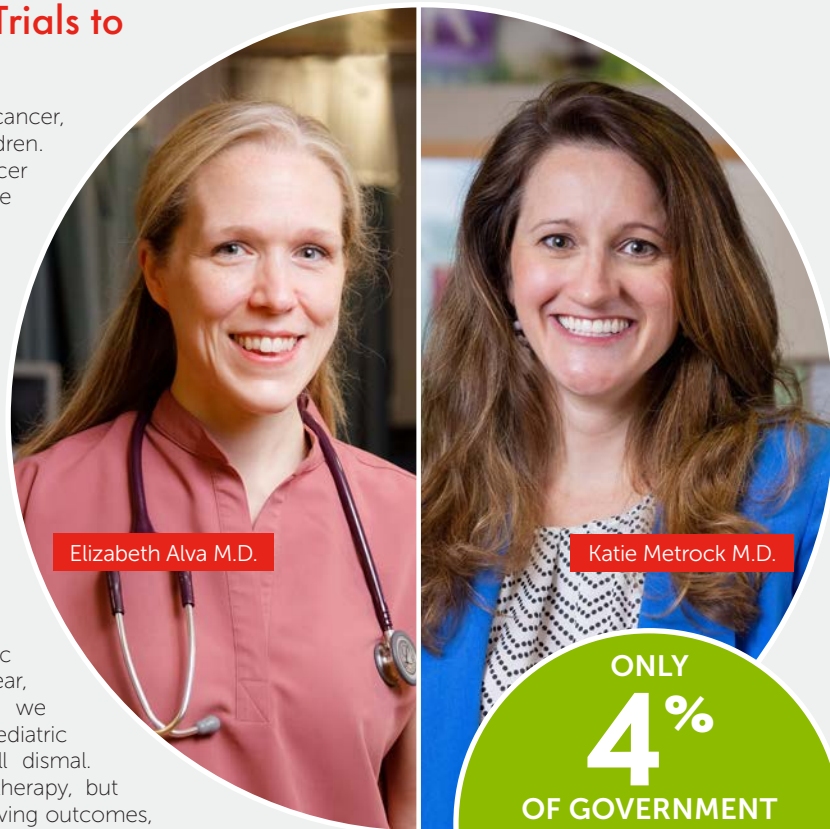
Children's joined the consortium in 2020 and is already participating in several novel studies for some of the worst pediatric cancers. The ultimate goal is to "provide hope to families," said Children's oncologist **Elizabeth Alva, M.D.**

One such trial is for patients newly diagnosed with metastatic fusion-positive rhabdomyosarcoma, which has a three-year, event-free survival rate of just 6 percent. "Traditionally, we inundate these patients with very intensive therapy," said pediatric oncologist **Katie Metrock, M.D.,** but outcomes are still dismal. Research has traditionally focused on intensifying that therapy, but sometimes that just leads to greater toxicity without improving outcomes, said Dr. Alva.

This uniquely designed study, called the EVOLUTION trial, is based on evolutionary theories around adaptation and resistance. Patients will be enrolled into one of four arms based on shared decision-making between the family and clinicians—not randomization.

The first arm is standard of care. The second arm is "first strike therapy," which Dr. Alva compares to a "meteor hitting the Earth and killing all the dinosaurs." This approach addresses the hypothesis that children relapse because once the chemo-sensitive cells are gone, a more resistant population emerges. "So the first-strike theory is to get rid of everything," she said.

A third arm focuses on maintenance, or a "second strike": providing the standard of care until the patient is in remission and then switching to a less-intense maintenance therapy to keep those resistant cells at bay while restoring quality of life.



Elizabeth Alva M.D.

Katie Metrock M.D.

ONLY
4%
OF GOVERNMENT
FUNDED CANCER
RESEARCH IS
DEDICATED TO
CHILDHOOD
CANCER

The fourth arm provides adaptive therapy. This means starting with standard chemotherapy that starts and stops based on response and adaptive timing of therapy, with a goal of increased time to progression rather than complete remission.

Children's is also participating in a phase 2 study evaluating the use of digoxin, a decades-old drug typically used in patients with heart failure, for patients with recurrent/refractory medulloblastoma. The drug was identified as potentially beneficial in laboratory and animal studies.

"It is exciting to think that there are well-known drugs that can be repurposed to help treat various cancers," said Dr. Metrock. "Our hope is that the tumors will show response to digoxin, and it could potentially be added to other up-front regimens in the future." While the drug is well tolerated in children," she said, "we haven't used it in this heavily pretreated population, so we need to see how our patients do with it."

Two other trials are exploring immunotherapy. One is testing the immunotherapy nivolumab in combination with azacitidine for children with recurrent, refractory osteosarcoma. The other is exploring a vaccine made from the patient's own cancer cells designed to trigger the immune system to target the cancer for destruction in children with high-grade gliomas.

Projects like the Sunshine Project are desperately needed, said Dr. Alva. "Unfortunately, pediatric cancer doesn't get the same degree of funding as adult cancer. It's rare, but when it strikes in a pediatric population, so many more years of life are lost."

AT OUR CENTER,
MORE THAN
300
DEDICATED PEDIATRIC
HEALTHCARE
PROFESSIONALS PROVIDED
EXCEPTIONAL PATIENT
CARE, EDUCATION
& RESEARCH

Oncolytic Herpes Virus Immunotherapy Shows Early Promise in Pediatric Patients with High-Grade Glioma

It's a pretty big deal when your research is published in the New England Journal of Medicine. But it's just as rewarding when your research holds promise for treating one of the most deadly cancers seen in children: high-grade gliomas.

"Unfortunately, outcomes are very poor for children with progressive gliomas, and we have not seen a significant improvement in outcomes for this dreadful disease in the last 30 years," said **Gregory Friedman, M.D.**, professor of pediatrics at the University of Alabama at Birmingham (UAB), director of developmental therapeutics for the Alabama Center for Childhood Cancer and Blood Disorders at UAB and Children's of Alabama and lead author of the paper, "Oncolytic HSV-1 G207 Immunovirotherapy for Pediatric High-Grade Gliomas."

"The toxicities associated with the current standard therapies are unacceptably high," Dr. Friedman said. "There is, therefore, a great need for effective and less toxic targeted therapies for these children."

Dr. Friedman's team used a genetically engineered cold-sore virus, a herpes simplex virus type-1 (HSV-1), which naturally infects cells of the peripheral and central nervous system. While the modified virus, called "G207," can't infect and harm normal cells, it can target tumor cells by directly killing the cells and stimulating the child's own immune system to attack the tumor.

Twelve patients between 7 and 18 years old with high-grade gliomas that had progressed on prior treatments received an infusion of G207 through intratumor catheters. Within 24 hours, some also received a single, small radiation dose directed to their tumors, which was designed to enhance virus replication and spread throughout the tumor.

Treatment response was assessed by imaging, tumor pathology and the patient's performance status. Eleven of the 12 patients demonstrated a response, with a median overall survival of 12.2 months; a 120 percent increase over the typical overall survival of 5.6 months in this population. To date, 36 percent of patients have survived longer than 18 months, surpassing the median overall survival for newly diagnosed pediatric high-grade glioma.

To date, immunotherapies have failed to improve outcomes in pediatric brain tumors because the tumors are "cold," with very few immune cells needed to attack the tumor, Dr. Friedman said. "Importantly, when examining matched pre- and post-treatment tissue from patients, we showed something that has not been seen before with any other therapy: that G207 dramatically increased immune cell trafficking to the tumors and turned the 'cold' tumors to 'hot' ones. This is a critical step in the development of an effective immunotherapy for children with brain tumors," he said.

G207 alone or in combination with radiation therapy was well tolerated, with no dose-limiting toxicities, grade 3/4 treatment-related adverse events, or evidence of virus shedding into the bloodstream, saliva, or conjunctiva.

"While further investigation in a phase 2 clinical trial is needed, our findings suggest that oncolytic immunovirotherapy using a modified cold-sore virus is a safe and potentially efficacious approach to target pediatric high-grade glioma," Dr. Friedman said.



Gregory Friedman M.D.

HEMATOLOGY

Asthma, Sickle Cell Disease and Trauma – Connecting the Dots

Take a child with sickle cell disease who is already at a significantly higher risk for asthma, pain, and acute chest syndrome – the leading cause of death in these children – and mix in adverse childhood experiences (ACEs) such as violence, racism, abuse, parental death or divorce. The result: sicker children who, due to toxic stress exposures, are more likely to experience poorer health outcomes.

That's what **Brandi M. Pernell, DNP**, assistant professor of pediatric hematology and oncology who works at the Children's of Alabama dedicated pediatric sickle cell clinic, found in her research.

"The literature shows that those who experience ACEs early in life have a higher risk of chronic conditions like asthma, cardiovascular disease, and obesity" – even cancer, Dr. Pernell said. But until her work, there was limited documentation in the sickle cell literature about ACEs. What is known is that acute stress is a common trigger for pain episodes in children with sickle cell disease. Pernell is now connecting the dots to show that ACEs increase asthma risk in these children which, in turn, leads to an increased risk for pain and acute chest syndrome.

Her findings highlight the need to screen children with sickle cell disease, particularly adolescents, for ACEs and, if found, implement protective factors and buffering mechanisms to address the physiologic sequelae from these toxic exposures.

She's already begun that process, teaming with the local chapter of the Sickle Cell Foundation to promote social and emotional competence and resilience among affected adolescents. That community-based approach is important, she said. "I believe we need to meet families and patients where they are," she said. And the Foundation has a different relationship with patients and families than the clinic staff. "We address the medical side, but ACEs are things happening in the home and neighborhood," said Dr. Pernell.

For Dr. Pernell, the work is more than a scientific endeavor; it's personal. She felt called to this research, she said, both as a Black woman (sickle cell primarily affects Black people) and as a healthcare provider, particularly given the events of 2020. "In the wake of COVID and the social and racial uprising prior to and throughout 2020, it just spoke to me," she said. So when she joined the University of Alabama at Birmingham faculty in 2016, this is where she focused her research. "I can relate to my patients in a way that some others can't," she said. "I've experienced some of the same things they have."

"If not me, then who?" she asked, quoting the late congressman and civil rights leader John Lewis. "If not now, then when?"



Brandi Pernell, DNP

CHILDHOOD CANCER SURVIVOR: COMING FULL CIRCLE WITH CHILDREN'S OF ALABAMA

Sarah Anne Hicks

Sarah Anne Hicks was diagnosed with leukemia and lymphoma at the age of 2. Doctors, nurses and staff at Children's of Alabama guided her family as they faced the worst time of their lives and ultimately inspired Sarah Anne to pursue a nursing career.

"When I was going through nursing school, I had an idea from the very beginning that I wanted to work at Children's in the same unit," Sarah Anne said. "That is what I do best. I wanted to give back to the hospital that gave so much to me and my family."

Today, she works alongside some of the same doctors and nurses at the hematology, oncology and bone marrow transplant unit that treated her 20 years ago.

"It was definitely a full circle moment," Sarah Anne said. "I feel super blessed to have been able to get through my illness with God, a supportive family and care team to help me. I'm so grateful to have overcome my cancer and that I'm able to help other families now. It's part of my testimony—I am doing exactly what I was meant to do."



Sarah Anne Hicks

CHILD OF CHILDREN'S

Lilianna Thompson

Lilianna Thompson was diagnosed with acute myeloid leukemia in August 2011, a few weeks after her 2nd birthday. While on a family trip to the beach, the toddler became ill with symptoms that mimicked a strep infection. Her parents, Randy and Anna, cut their trip short and Anna took Lilianna to her regular pediatrician who ran blood work on the sick little girl – twice. “They thought their machine was broken because the numbers were so high,” Anna said.

They were immediately referred to Children’s of Alabama where Lilianna was admitted on a Friday. She began treatment the next Monday. The chemo failed to put her into remission, though, so she was placed on the bone marrow transplantation list. In December 2011, she underwent a cord blood transplant, but Lilianna’s little body rejected it, so she was given more chemotherapy and underwent a procedure called a double cord blood transplant in February 2012. It was successful and she was discharged from the hospital a month later. She relapsed the next day. “After that, they gave us no hope,” Anna said, “but we refused to give up hope.”

So a new chemotherapy was tried and Lilianna went into remission immediately. She relapsed six months later but that short remission still allowed time to find a bone marrow donor that matched nine of the 10 criteria for transplant. Not an ideal match, but it was the best that could be found. “It was ‘take it or leave it,’” Anna said.

They took it and Lilianna underwent more chemotherapy and total body radiation before receiving her third transplant in January 2013. “And from there, here we are!” Anna said. “She is definitely a miracle. There’s no doubt about it.”

Lilianna has transitioned to the Taking on Life after Cancer, or TLC, Clinic. There, she is monitored for any late complications of her therapy, such as growth problems, infertility, learning difficulties or second cancers. The goal of the TLC Clinic is to support survivors like Lilianna as they thrive and grow so they can live their best lives possible. “Lilianna inspires all of us and her story gives hope to many families affected by childhood cancer,” said Kimberly Whelan, M.D., who serves as director of the TLC Clinic.



Lilianna Thompson

Arielle McFarland

Arielle McFarland is an active 19-year-old who has a severe blood disorder called sickle cell anemia hemoglobin SS. Sickle cell anemia is an inherited gene from both parents. Sickle cells are abnormally-shaped red blood cells that can stick to blood vessel walls causing blockage and preventing the cells from carrying oxygen through the body. When this happens, it causes a pain crisis.

Arielle was diagnosed with the disease by a screening at birth. “Her father and I knew we had the sickle cell gene, and there was a one-in-four chance for each pregnancy that our child could be born with it,” said Arielle’s mother Sophia McFarland.

Arielle was 6 months old when she had her first pain crisis. “She developed dactylitis, which causes swelling of the hands, and is very painful,” said Sophia. Arielle was treated at Children’s of Alabama, which would be the first of many hospital visits to come.

“It has been difficult, but everyone at Children’s has always been so sweet to us through all of this,” said Sophia. “We have always had a very good relationship with everyone on the staff.”

Arielle’s condition continues to be high risk and complex, but she manages her disease well with medication and a monthly red blood cell exchange. As for Arielle’s care at Children’s, her mom said, “The support, the attention and information they have provided us has been invaluable. They are like family to us.”



Arielle McFarland