

**How Sweet
the Sound**

Page 12

Cover story

12 **How Sweet the Sound**

Thanks to a national study led by St. Jude investigators, Elechi Madu makes a joyful noise.

Features

7 **Baby, Oh, Baby!**

Clinicians and researchers team up to help infants with ALL.

10 **Calm Within the Storm**

St. Jude interpreters help families buffeted by language challenges.

15 **A Vision of Growth**

Kay and David Dempsey help the children of St. Jude.

16 **Gratitude and Generosity**

Individuals and organizations give thanks and give generously.

18 **The Quest for CREST**

Scientists develop a novel tool for finding genetic mistakes.

20 **Hitting out of the Rough**

A young golfer undergoes four bone marrow transplants.

Highlights

2 News and Achievements

Perspective

24 **Laura Hackelton Brown**

Unwrapping the Gift



Promise

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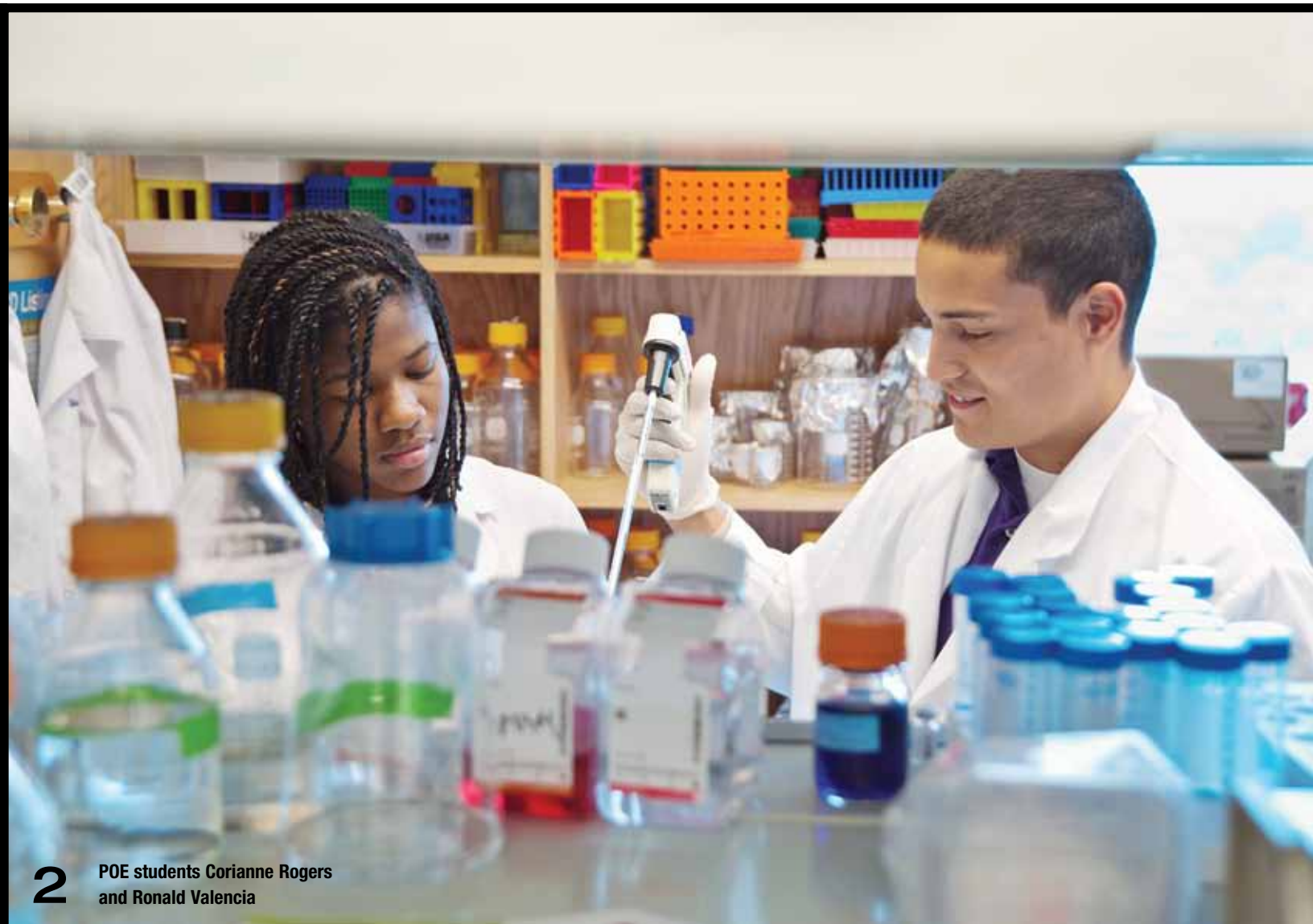
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2

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Research Highlights



Embracing the future

St. Jude Pediatric Oncology Education (POE) program director Suzanne Gronemeyer, PhD, receives a group hug from some of the 2011 POE participants (from left) Aaron Deleonguerrero, Erika Russell, Ronald Rodriguez-Santiago, Ronald Valencia, Alexandra Rivera-Santiago, Krystal Herline and Corianne Rogers.

Funded by the National Institutes of Health/National Cancer Institute, the POE program provides students with short-term internships in laboratory or clinical research.

The POE program received more than 550 applications this year for 50 openings in its summer 2011 program for students interested in making cancer the centerpiece of their professional lives.

“The success of future biomedical research depends on the availability of well-trained young investigators. There is a shortage in both the number and diversity of well-trained, competent pediatric oncology researchers, clinicians and nurses in this country,” Gronemeyer said. She recently authored a report on the St. Jude POE program, which appeared in the *Journal of Cancer Education*.

To learn more about the program, visit www.stjude.org/poe.

*“The success of future
biomedical research depends
on the availability of
well-trained young investigators.”*

A dramatic increase in transplant survival

Bone marrow transplant survival more than doubled in recent years for children with high-risk leukemia treated at St. Jude, with patients lacking genetically matched donors recording the most significant gains. The results are believed to be the best ever reported for leukemia patients who underwent the procedure.

The findings are expected to make transplantation a treatment option for more children and adolescents with high-risk forms of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) who lack genetically matched donors, either related or unrelated. The research appeared in the scientific journal *Blood*.

“This study shows that transplantation offers a real hope of survival to patients with high-risk leukemia that is not curable with intensive chemotherapy,” said Wing Leung, MD, PhD, the study’s principal investigator and chair of Bone Marrow Transplantation and Cellular Therapy. Leung linked the gains to advances in cancer treatment as well as to improved infection control and more sophisticated donor selection.

Five years after transplantation, survival was 65 percent for St. Jude patients with high-risk ALL treated at the hospital between 2000 and 2007, compared to 28 percent for similar patients who underwent treatment between 1991 and 1999. AML survival after transplantation rose from 34 percent for patients treated between 1997 and 2002 to 74 percent for the AML patients treated between 2002 and 2008.

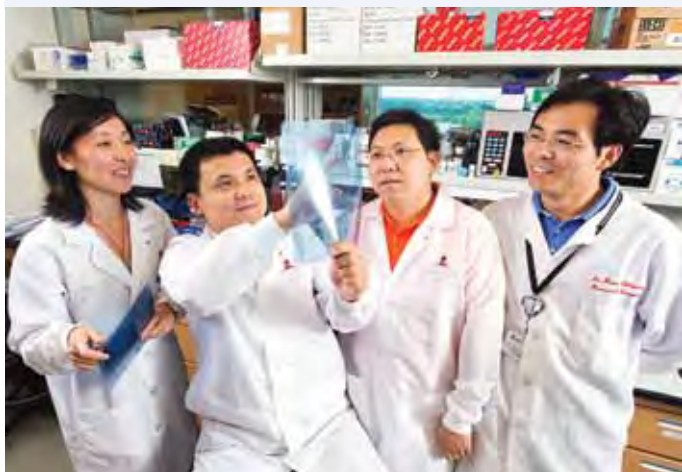
“We can now identify donors for virtually all pediatric patients who need transplants to cure their leukemia. Importantly, our transplanted patients not only have high cure rates but also excellent quality of life, resulting largely from advances in donor selection and supportive care,” said Ching-Hon Pui, MD, Oncology chair and the paper’s senior author.

The results raise hopes that the MKP-1 pathway will lead to new tools for shaping the immune response.

Regulating immune balance

St. Jude researchers are constantly seeking new ways to help patients' own immune systems effectively fight disease. Now, investigators have identified a signaling molecule that functions like a factory supervisor to ensure that the right mix of specialized T cells is available to fight infections and guard against autoimmune disease. The research also showed the molecule, phosphatase MKP-1, is an important regulator of immune balance. Scientists demonstrated that MKP-1 serves as a bridge between the innate immune response that is the body's first line of defense against infection and the more specialized adaptive immune response that follows. A report on this study appeared in the journal *Immunity*.

The results raise hopes that the MKP-1 pathway will lead to new tools for shaping the immune response, said the study's senior author, Hongbo Chi, PhD, of Immunology. Chi (seated, second from left) is joined by (from left) the study's co-first authors, postdoctoral fellows Yanyan Wang, PhD, and Gonghua Huang, PhD; and additional author Lewis Shi, MD, PhD. The findings provide new details about how dendritic cells regulate the fate of naïve or undifferentiated T cells. Dendritic cells patrol the body, ready to respond at the first sign of infection.



Star power unleashed

Amanda Koziol, whose sister is undergoing leukemia treatment at St. Jude, takes a red carpet walk past cheering doctors, nurses and other staff during Sibling Star Day. The annual event held for the brothers and sisters of patients celebrates and recognizes the important role siblings play in the healing process. This year's event, themed "Hollywood," featured arts-and-crafts, a luncheon for siblings and other special activities.

Finding order in chaos

A key finding by St. Jude researchers could lead to a new family of cancer drugs.

Investigators in the project identified the structure responsible for the versatility of a protein called p21, which belongs to a class of proteins known as intrinsically disordered proteins (IDPs). Unlike many other proteins, which form rigid 3-D shapes and bind to single partners, IDPs are unstructured, which allows them to fold, binding to different partners and performing diverse biological tasks.

Disordered proteins are often altered in cancer, affecting many regulatory and signaling pathways. Tumor suppressor proteins frequently include disordered segments. Researchers showed that p21's structural flexibility is essential to its ability to bind to and inhibit several different enzyme complexes that regulate cell division.

"Disordered proteins hold great potential for understanding the molecular basis of cancer," said Richard Kriwacki, PhD, of Structural Biology. The proteins also represent challenging new targets for small-molecule inhibitors to block their regulatory interactions.

Kriwacki is senior author of a paper on this topic, which was published in the journal *Nature Chemical Biology*.

Research Highlights

Teamwork yields targeted AML therapy

A drug that targets a molecular misstep at the heart of 15 percent of childhood acute myeloid leukemia (AML) cases has shown early promise in a safety study led by St. Jude researchers and is now being tried in newly diagnosed patients.

In eight of 11 young AML patients enrolled in a St. Jude Phase I study, cancer went into remission following treatment with a drug named sorafenib and two other chemotherapy agents. A ninth patient had a partial remission. The patients had all relapsed or failed to respond to earlier therapies. The research appeared in the *Journal of Clinical Oncology*.

If results are confirmed in larger studies, sorafenib will mark a new era in treatment of AML, said the study's first author, Hiroto Inaba, MD, PhD, of Oncology. Inaba said sorafenib is a good example of close collaboration between St. Jude researchers in the laboratory and clinic. He said work from the laboratory of Sharyn Baker, PharmD, PhD, of Pharmaceutical Sciences, provided the foundation for the Phase I study. Baker is the study's senior author.

*If results are confirmed
in larger studies,
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new era in treatment of AML.*

New target pinpointed for eye tumor

A research team led by St. Jude scientists has identified a potential new target for treatment of the childhood eye tumor retinoblastoma. The work also settles a scientific debate by showing that the cancer's cellular origins are as scrambled as the developmental pathways at work in the tumor.

Unlike other cancers that resemble a particular type of cell, researchers showed that retinoblastoma is a hybrid cell with elements of at least three different cell types. The research appeared in the scientific journal *Cancer Cell*. Researchers also demonstrated that multiple, normally incompatible, developmental pathways are turned on simultaneously in retinoblastoma cells. The study found the tumor takes over at least one pathway to fuel its own growth, making it a promising drug development target.

The study's senior author is Michael Dyer, PhD, of Developmental Neurobiology.



St. Jude more than doubles national vaccination rates

St. Jude investigators recently published results of the first study to report employee attitudes about influenza vaccine at an institution with high rates of voluntary vaccination.

More than 90 percent of St. Jude health care workers are voluntarily vaccinated against influenza each year. That number is in sharp contrast to national vaccination rates—about 44 percent of health care workers nationwide receive flu vaccinations each year. Investigators found that altruism and self-protection both play a role in the high St. Jude rates.

Scott Howard, MD (above), of Oncology and Information Sciences, receives his annual flu shot as part of the hospital's vaccination program.

The findings, published in the journal *Vaccine*, demonstrate that high rates of flu vaccination are possible without making vaccination of health care workers mandatory, said Hana Hakim, MD, of Infectious Diseases, the study's principal investigator. But she noted that the hospital's patient population and its mission make it difficult to generalize the findings to other health care settings. Jon McCullers, MD, of Infectious Diseases, was the paper's senior author.



Talking to children about prayer

Using feedback from parents of St. Jude patients, Chaplain Services has developed a book to help parents incorporate prayer into their children's hospital experience. The project began when members of the St. Jude Family Advisory Council observed that many parents acknowledged having difficulty talking about prayer with their children. To help facilitate those conversations, Chaplain Services wrote *Sometimes A Prayer* for children ages 3 to 8.

"Even under normal circumstances, prayer can be a tough concept for young children," said Brent Powell, Chaplain Services director. "After discussing the topic with parents, the chaplains agreed that the best way to help both parents and children was to properly equip the parents, since they are usually available to the children and have the most trusted relationship."

Chaplain Mark Brown (above) shares the new book with St. Jude patient Haley Hines.

The book contains concepts derived from the collective experience of pediatric chaplains and from the literature on the psychology of religious development in children.

New hope for children with solid tumors

A drug that blocks a pathway commonly disrupted in cancer has shown early promise against childhood solid tumors and is now being combined with other agents in a Phase II trial targeting rhabdomyosarcoma, the most common soft tissue cancer of childhood.

The drug is temsirolimus. In a Phase I study, a child's neuroblastoma tumor disappeared completely for about nine months in response to weekly intravenous treatments with the drug. The disease stabilized in five patients with other childhood cancers. All had undergone prior therapy that failed to eradicate their disease.

The results were published in the *Journal of Clinical Oncology*. Sheri Spunt, MD, of Oncology, was principal investigator of a multi-center trial that focused on the safety and optimal dose of temsirolimus in young solid tumor patients.

Assessing survivors' risks

The largest study yet of adult childhood cancer survivors found that, for some survivors, the first cancer was just the beginning of a lifelong battle against different forms of the disease. The work underscores the importance of cancer screenings for the estimated 366,000 Americans alive today who are childhood cancer survivors.

St. Jude investigators led the study involving 14,358 individuals enrolled in the Childhood Cancer Survivor Study. Researchers reported that nearly 10 percent of survivors developed new tumors unrelated to their original cancers. About 30 percent of those survivors developed three or more tumors. Results of the study appeared in the *Journal of Clinical Oncology*.

"These findings show that when you describe adult survivors of childhood cancer it is not sufficient to describe their risk of a first subsequent cancer, but to acknowledge that some of these patients are at risk for multiple cancers. This is the first study to more fully enumerate that risk," said principal investigator Gregory Armstrong, MD, of Epidemiology and Cancer Control.

Research Highlights

A glimpse into the immune system

St. Jude scientists have identified a key immune system regulator, a protein that serves as a gatekeeper in the white blood cells that produce the “troops” to battle specific infections.

Researchers demonstrated the protein, Tsc1, is pivotal for maintaining a balanced immune system and combating infections. Loss of the Tsc1 protein was associated with a reduction in the number of certain immune cells and a weaker immune response. A report on this work appeared in the scientific journal *Nature Immunology*.

“These findings not only advance understanding of the cell biology of the immune system but also have great potential for clinical applications in the future,” said the study’s senior author, Hongbo Chi, PhD, of Immunology.

Scientists learn how Sudemycins work

St. Jude scientists have collaborated to show that a promising family of anti-cancer drugs, known as Sudemycins, works by influencing how a cell’s machinery edits messenger RNA (mRNA).

Researchers reported that mRNAs that code for proteins made by a mechanism called alternative splicing change in response to treatment with this family of antitumor drugs. Alternative splicing determines how information encoded in DNA is packaged to produce different versions of mRNA that is then translated to produce variants of the encoded protein. The process makes it possible for a single gene to yield multiple, related proteins. Other scientists have demonstrated that alternate splicing is deregulated in many cancers.

The laboratories of Philip Potter, PhD, and Thomas Webb, PhD, both of Chemical Biology and Therapeutics, worked together to understand the biology that makes Sudemycins such promising anti-cancer drugs. Webb had previously discovered Sudemycins at St. Jude. The most recent research appeared in the journal *ACS Chemical Biology*.

*Originally created at St. Jude,
Sudemycins are toxic to cancer cells
but not to normal cells.*



Science can be fun

The St. Jude Cancer Education for Children Program visited the St. Jude Adopt-A-School, Bellevue Middle School, recently for an outreach education event. Several St. Jude staff members discussed science careers with the school’s sixth and seventh grade students. Students also participated in an educational microscope lab exercise from the Cure4Kids for Kids outreach program. Emma Delva, PhD, of Immunology (at right), assists a Bellevue student with the exercise.

Exploring the origins of devastating diseases

The enzyme ligase III (Lig3) has long been linked to fixing broken strands of DNA in the cell’s nucleus. But new work from the laboratory of Peter McKinnon, PhD, of Genetics, demonstrates that Lig3 makes its greatest contribution in the mitochondria, the energy-producing structures inside cells.

“We found that inactivating ligase III did not compromise nuclear DNA repair, but in a profound way it compromised mitochondrial DNA replication and repair. Defects in mitochondrial DNA lead to a spectrum of very different devastating childhood diseases,” explained McKinnon, senior author of a study that appeared in the journal *Nature*.

McKinnon said evidence suggests Lig3 might sometimes work cooperatively with Lig1, a related enzyme, to repair nuclear DNA damage. Efforts are underway to determine whether Lig3’s primary role is to keep mitochondrial DNA in good repair or to see that it is copied correctly.

Baby, Oh, Baby!

The tiniest patients face the biggest odds when it comes to acute lymphoblastic leukemia. St. Jude clinicians and researchers work to change that scenario.

BY ELIZABETH JANE WALKER

ANN-MARGARET HEDGES



Four-year-old Camille Davis has a precocious way with words. On this day, before scampering off to play with her three sisters, she approaches her mother, Lois.

“Mama, I’m going to give you a hug because you are so cute today,” says Camille, extending her arms for a breezy embrace.

Lois smiles when she reflects on how far her daughter has come. A little more than three years ago, doctors discovered that Camille had the most aggressive type of childhood leukemia and an extremely poor survival rate. A couple of years later, the toddler also experienced a dangerous cardiac problem that required open-heart surgery.

Although those events were incredibly stressful, Lois admits that one of the most difficult tasks she faced was closing her Internet browser and placing her trust in the scientists and clinicians at St. Jude Children’s Research Hospital.

“When we arrived at St. Jude, I started reading everything I could, whether it was from the Internet or from the library at the hospital,” Lois says. “That’s when I started getting scared and crying a lot. I thought, ‘If Camille only has a 20 percent chance to live, what are we even doing here?’”

Camille’s treatment team encouraged Lois to quit pondering the bleak survival rates for infants

St. Jude researchers and clinicians are working to eliminate the grim survival statistics for babies with acute lymphoblastic leukemia. Now 4 years old, Camille Davis (shown with her mom, Lois) has benefited from that research.



Camille's primary care team included (from left) Michelle Chandler, PNP, Corie Bounds, RN, and oncologist Sima Jeha, MD. Like other recent St. Jude patients with acute lymphoblastic leukemia, Camille received personalized chemotherapy treatments, but no cranial irradiation.

with acute lymphoblastic leukemia (ALL); instead, they suggested that she approach the challenges one day at a time.

"Soon I noticed that every week, Camille was getting a little bit better," Lois says.

Diagnosis: MLL+

The journey had begun with a small bump on the head of the 7-month-old.

"Just keep an eye on it," a pediatrician told Lois and Casey Davis. A week later, dozens of nodules appeared on Camille's scalp. MRIs, CT scans and blood work failed to produce a definitive diagnosis.

"First they said it was a brain tumor; then they said she had tumors in her belly; then they said it was lymphoma," Lois recalls.

Camille's physician arranged for the couple to take their baby to St. Jude.

"We arrived at 1:30 a.m., and they immediately started doing tests," Lois recalls. "Within 24 hours, we knew exactly what Camille had, and she had already begun receiving chemotherapy."

The Davises learned that their daughter had ALL. Although most children with that disease have a projected cure rate of 90 percent, the outlook is not rosy for the 3 percent of ALL patients who are infants. About 80 percent of those babies have an *MLL* gene rearrangement, which has a dismal outcome.

Camille had the *MLL* rearrangement. Her disease affected the central nervous system, which further increased her risk of treatment failure. Scans indicated that in addition to the bumps on her scalp, Camille had lesions that extended deep into her brain. Her spinal fluid also contained leukemic blasts.

In another cancer center, Camille would have received radiation to her brain, a treatment that would have affected her ability to learn and develop normally. But radiation was removed from ALL therapy at St. Jude when oncologist Ching-Hon Pui, MD, and his colleagues made an important research discovery. They reported that children who receive highly personalized chemotherapy treatments actually enjoy better

survival and quality of life than do children who receive a combination of chemotherapy and cranial irradiation.

Camille directly benefited from that discovery.

A team effort

As part of the hospital's Total XVI protocol, Camille received an intensive chemotherapy regimen. Some drugs were administered orally or through her central venous catheter, while others were injected directly into her cerebrospinal fluid. Infants with the *MLL* rearrangement in the Total XVI study receive a novel combination of medications, including clofarabine, a drug that was developed for pediatrics by St. Jude investigators.

Oncologist Sima Jeha, MD, worked closely with clinical pharmacists and other members of the treatment team to ensure that Camille received the optimum doses of drugs.

"Camille needed the highest doses of chemotherapy she could tolerate to clear her disease, but not so much that it would cause unacceptable toxicity," Jeha says. "You have to have a balance. We are fortunate to have the greatest pharmaceutical service in the world and to be one of the first centers to integrate pharmaceutical science into therapy."

During a visit home in April of 2010, Camille developed fluid around her heart. She and her mom quickly boarded a plane and returned to St. Jude. Soon after their arrival, Lois, pregnant with her fourth child,

was shocked to feel the first pangs of premature labor.

St. Jude nurses took care of Camille while Lois rushed to a local maternity ward. As Lois delivered a baby across town, Camille began to have trouble breathing and her blood pressure skyrocketed. She was admitted to the St. Jude Intensive Care Unit.

The day after delivering her fourth daughter, Lois returned to St. Jude. There, she witnessed Camille going into cardiac arrest.

“They administered CPR and put Camille on the ventilator. It seemed like a bad dream,” Lois says.

Cardiologists discovered that the toddler had a heart aneurysm as well as a viral infection.

“Camille needed open-heart surgery,” Jeha recalls. “As her treating physician, I had the support of experts in infectious diseases, cardiology, cardiovascular surgery and intensive care. We all worked together to decide how to time the interventions, how long to safely hold chemotherapy, and other issues regarding the management of such a high-risk child.”

Thanks to exceptional teamwork and superior supportive care, Camille recovered from her surgery and completed her chemotherapy in December of 2010. Her disease remains in remission.

The future of infant ALL

Although Camille has responded well to therapy, the prognosis for babies with ALL remains grim. Infant ALL survival rates have not kept pace with the increases experienced by some other forms of childhood cancer.

“We’ve figured out that we can get comparative results without radiation, which is a big, big step. But it’s still a bad disease,” says James Downing, MD, St. Jude scientific director, deputy director and executive vice president. “We need fundamental knowledge on the genetic lesions that underlie this leukemia before we can substantially improve the outlook for these patients.”

At St. Jude, efforts are underway to better understand the origins of infant ALL and to develop effective ways to prevent and treat it. The hospital recently recruited a new faculty member who will study the disease in the clinic as well as in the lab.

Through the Pediatric Cancer Genome Project (PCGP), St. Jude and Washington University School of Medicine in St. Louis are collaborating to learn more about infant ALL. Investigators are sequencing the entire

“If Camille only has a 20 percent chance to live, what are we even doing here?”

genome of the leukemia cells to define the total complement of mutations that drive the formation of this form of leukemia. From information gained from the project, scientists and clinicians hope to develop therapies that will substantially improve the cure rate for infant ALL.

“We chose to include infant ALL in the PCGP because it has an abysmal cure rate,” Downing explains. “We want to know

if there are no mutations, very few mutations or key recurrent mutations that underlie infant ALL. We’ve completed sequencing 22 cases thus far. Our team of scientists are working around the clock analyzing the data.”

Lois is thankful for the scientists and clinicians who are dedicated to learning more about infant ALL. In addition to assuaging her fears about Camille’s health, St. Jude staff helped alleviate Lois’ worries about health care costs. “There is no possible way with all the help in the world that we could have been able to afford all that St. Jude gave her,” Lois says.

Now, with the terrors of infant ALL behind them, Lois and Casey revel in their active, healthy—and messy—little girls.

“Mama, I cleaned my entire room all by myself. Are you so proud of me?” Camille asks, her blue eyes shining. Lois smiles. ●



Before Camille (left) underwent open-heart surgery, she joined her sisters Kelsey (center) and Chloe in welcoming their baby sister, Keeley.

Calm Within the Storm

BY CARRIE L. STREHLAU

Buffeted by unfamiliar words, limited-English-speaking families find safe haven thanks to St. Jude interpreters.



Interpreter Guillermo Umbria talks with an international family in a hospital corridor.

INTERPRETERS work like life's subtitles, serving as a calming influence when a storm of words floats around a room. At St. Jude Children's Research Hospital, medical interpreters go a step further, gathering unfamiliar words, medical terminology, clichés and colloquialisms and reassembling the dialogue to ensure that nothing is lost in translation.

When a family arrives at St. Jude for the first time, their apprehension can be overwhelming. For patients and families whose native language is not English, the anxiety is intensified by communication challenges. Medical interpreters bridge the language gap between caregivers and families, assisting with communication about admissions, procedures and treatments.

"We're of critical importance as the connection of communication between providers and patients," says Marc Friedman, Interpreter Services coordinator. "It's clinically, medically and emotionally imperative to have clear communication in these types of circumstances, and I feel like we help empower families."

Medical interpreting has been an emerging vocation for many years but is now considered an established profession, which led to the creation of a national exam and certification process in 2010. Three out of four St. Jude medical interpreters have been nationally certified within the last year. They are also trained and approved in Spanish, Portuguese, French and Catalan.

Training for medical interpreters at St. Jude is a continuous process

that consists primarily of mastering the standards of practice and demonstrating competency in a list of about 50 specific encounter types that are essential to St. Jude. The initial training process includes shadowing and observing a mentor, discussing possible situations and role playing. Trainees then interpret in the presence of a mentor before proceeding to the next competency.

"We want to be a role model for other institutions around the nation by providing the best language services possible to patients and providers," Friedman says.

Medical interpreting is not just about being bilingual. Medical interpreters have to pay attention to what is being said, the style and register of what people say.

"You need to have medical knowledge and, the other key, is

that you have to be able to hear a segment of information, convert its exact meaning into another language, and then say it in the other language—which is not typically word for word,” Friedman says. “To me, it’s like running up and down a basketball court at top speed—but it’s all happening inside your head.”

In moments of confusion or misunderstanding, medical interpreters ask for clarification.

“We also have to decode colloquial expressions and metaphors to more literal terms,” Friedman says. “If a clinician says to me, ‘We’ll have to run it up the flag pole,’ I can’t interpret that literally; I have to determine how to say what he really means. I also have to be sensitive to dialects. There are at least five different ways to say ‘bus’ in Spanish, depending on where you come from.”

Aware of not inserting their own opinions into conversations, interpreters must sometimes bite their tongues to maintain transparency. “It’s a challenge sometimes not to jump into the conversation, but we are there to negotiate meaning,” Friedman says.

Part of great medical care is ensuring clear communication, especially for these patients.

“Marc and the other medical interpreters are truly hands-on,” says Alicia Huettel, Family Centered Care coordinator. “Humanness is such a key to this process. It’s a standard of care for the team to make sure each family’s needs are being met.”

Huettel and Friedman collaborate on written translations for patients whose English skills are limited. St. Jude patients and families are encouraged to share their thoughts and views on everything from new hospital signage to universal symbols and verbiage.

“The essence of information sharing is about understanding the information and the ability to act

on that information,” Huettel says. “We’re continuously assessing the effectiveness of our patient education efforts in English and other languages so we can effectively promote the multi-directional communication between our families and staff. We include our patients and families in this process to ensure accuracy and understanding. How you ask the question, what symbol you choose, makes a difference.”

When approved on-site interpreting services are unavailable, a contract telephonic interpreting service is available through dual-handset blue phones and most desk phones in patient care areas.

“When we’re not available, or the need is for a language we’re not trained in, we utilize the phones,” Friedman says.

Before becoming a certified medical interpreter at St. Jude in 2006, Guillermo Umbria volunteered at the hospital as a medical interpreter for two years. His days now start early and can be hectic.

“First thing in the morning, we start getting calls from the clinics requesting our services,” Umbria says. “We also get calls from patients wanting to get in touch with the medical staff, Patient Services or schedulers. We not only provide language services in person, but also by phone, so it makes for a busy day.”

Mornings are usually the busiest, with interpreters visiting clinics, Social Work, Patient Services or patient rooms.

“When things slow down, usually in the afternoons and weekends, we focus on translating emails and conducting teleconference interpretations. But we never know when we’re going to get that random call or page,” Friedman says.

For Umbria, being a medical interpreter is a balance of rewards and challenges, including interpreting end-of-life conversations or

confirmations from physicians about diagnoses.

“Interpreting ‘Your child is cured; now you can make arrangements to go home’ is rewarding,” Umbria says. “It’s an honor to be a part of a patient’s journey at St. Jude.”

In the last three years, interpreting service time at the hospital rose from about 580 hours to more than 1,480 hours. Of the demand for language translations at St. Jude, 95 percent are for Spanish. The patient population also includes those who speak Arabic, French, Portuguese, Russian, Chinese, Vietnamese and Thai.

“The visible demand for interpreters is only a fraction of the total real demand. The unmet need becomes more visible as more demands are met. And, as we better meet the requests for interpreters, the demand grows,” Friedman says. “There are more than 5,000 languages on the planet, so we accomplish what is possible with the resources we have—and I’m very proud of what we do.” ●



The Badawi family from Lebanon converses in French with St. Jude interpreters. Pictured from left are Leyla and Manuelle Badawi, Marc Friedman, Irma Morales, St. Jude patient Marie Belle Badawi and Guillermo Umbria. When onsite interpreters are unable to assist with communication, families and staff can use the dual-handset blue phones located in the hospital’s patient care areas.

How Sweet the Sound

BY ELIZABETH JANE WALKER





The results of the Baby HUG study are music to the ears of Emmanuel and Pamela Madu and to other parents of young children with sickle cell anemia.

has something that you cannot fix,” Pamela says. “It was an overwhelming, indescribable feeling.”

Elechi is one of about 100,000 Americans with the disorder. Individuals with this inherited disease have red blood cells that may be shaped like crescents instead of discs. Instead of moving smoothly through the circulatory system, the sickle-shaped cells clog blood vessels, triggering episodes of extreme pain and causing other dangerous complications that range from organ damage and stroke to a pneumonia-like illness known as acute chest syndrome.

“Within a year-and-a-half, Elechi had at least six bouts of acute chest syndrome,” Pamela recalls. “It seemed like she had pneumonia back to back to back. She would get a blood transfusion and stay in the hospital for days. She was tired and exhausted all the time.”

When Elechi was 3 years old, doctors at St. Jude prescribed a drug called hydroxyurea, a cherry-flavored liquid that Elechi swallows once each day. The results have been stunning.

“Now she is full of energy,” Pamela says. “She went from being hospitalized many times in a year to having only one hospitalization in the last 2½ years. Hydroxyurea has been the answer to our prayers.”

Variations on a theme

St. Jude researchers have been studying the effects of hydroxyurea for about 16 years, according to Winfred Wang, MD, of Hematology. Soon after the U.S. Food and Drug Administration approved the drug for use in adults with severe sickle cell disease, Wang and his colleagues began to investigate the possibility of its use for children. In 2002, their HUSOFT study proved the feasibility of giving liquid hydroxyurea to infants and indicated that the drug might help preserve spleen function.

As a result of the study, the National Institutes of Health began a project to study the use of hydroxyurea

When Elechi Madu practices the violin, the 6-year-old produces the requisite squeals and squeaks of a beginning musician. But to Emmanuel and Pamela Madu, those halting melodies are sweeter than any symphony. The Madu home—once resounding with Elechi’s cries of pain—now reverberates with music, laughter and the little girl’s excited chatter about soccer and gymnastics.

The transformation occurred as a result of treatment Elechi received at St. Jude Children’s Research Hospital.

In December 2004, Emmanuel and Pamela were devastated to learn that their beautiful, newborn daughter had the most severe form of sickle cell disease. “I don’t think there’s anything as scary as knowing that your child



“Hydroxyurea has the potential to dramatically improve the quality of life for an entire generation of patients with this disease,” says Winfred Wang, MD, shown with Elechi Madu.

in young children. Wang was principal investigator of the six-year study, deemed Baby HUG, which involved 193 children at 13 centers across the country. Children were randomly assigned to receive daily doses of either hydroxyurea or a placebo for two years. Neither the families nor their clinicians knew which children were receiving the drug and which were receiving the placebo.

St. Jude Pediatric Nurse Practitioner Lynn Wynn organized the study coordinators nationwide, while Lane Faughnan, RN, served as the local Baby HUG coordinator. Wang attributes Wynn and Faughnan with helping families understand the importance of the research.

“Our patients and their families were diligent about their involvement in the study,” Wang says. “The study was demanding, because they had to be seen every couple of weeks at the beginning and every four weeks thereafter for two years. Some participants experienced some sickle-cell–related problems; we suspected and later learned that most of those individuals were on the placebo. But even those families stuck with the study instead of dropping out. Every patient at St. Jude remained in the study for the entire two years.”

Pamela says the education and personal attention she received at St. Jude helped her cope with the stresses of having a child with severe sickle cell anemia.

“My husband and I learned so much from the people at St. Jude,” she says. “It was like Biology 101 all over again. They taught me step by step everything I needed to know to take care of Elechi. I would email Lane Faughnan in the middle of the night, and she would write me back immediately. My child wasn’t a number to them—they genuinely cared about Elechi and our family.”

The couple’s experiences at St. Jude inspired Pamela and her husband to make career changes. Emmanuel is pursuing a doctorate in cancer research while Pamela completes the prerequisites for nursing school.

Command performance

As a result of Baby HUG, researchers discovered that hydroxyurea reduces the incidence of pain crises, acute chest syndrome and other symptoms, as well as the number of days children spend in the hospital. Wang and his colleagues published their findings in the medical journal *The Lancet* this summer.

“We found that it’s effective, beneficial and reasonably safe to give hydroxyurea to young children with sickle cell anemia,” he says. “We think the drug should ideally be prescribed for all sickle cell anemia patients. It has the potential to dramatically improve the quality of life for an entire generation of patients with this disease.”

Hydroxyurea works by inhibiting DNA production. Created as an anti-cancer drug decades ago, the drug is relatively inexpensive—costing about \$1 a day—and easy to administer, which makes it a viable option for both children and adults with sickle cell anemia.

Second fiddle

All St. Jude Baby HUG participants have agreed to participate in a follow-up study that should continue through 2016. Children in this study are offered the opportunity to take hydroxyurea daily. Participants who received hydroxyurea in Baby HUG received relatively low doses of the drug during that study. The current research project will address possible long-term benefits of continuing treatment with higher doses.

As part of the study, Elechi continues to make regular visits to St. Jude, where she delights the medical staff with her energy and intelligence.

A budding gymnast and soccer player, Elechi frequently emulates her older brother, Chinua. When Chinua learned to read, she quickly followed suit; when he took up the violin, she became interested in music, as well. Although she has not yet begun first grade, Elechi’s reading skills now approach a third-grade academic level. Her musical repertoire includes such standards as “Twinkle, Twinkle, Little Star” and a special song that she composed for her daddy’s birthday.

Keeping up with Elechi is both exhausting and exhilarating, but Pamela says she wouldn’t change a thing.

“I honestly don’t know where her energy comes from,” she says, laughing. “The change is so phenomenal. Now she’s growing, she’s active and she’s doing great. It’s such a blessing to our entire family.” ●

A Vision of Growth

One couple raises funds for the Pediatric Cancer Genome Project, knowing children will benefit from the growth in scientific knowledge.

BY LEIGH ANN ROMAN

Growing up in Big Stone Gap, Virginia, a little girl named Kay Isaac often heard the names St. Jude and its founder, Danny Thomas.

As a member of a large Lebanese community in the small Appalachian town, Kay remembers her mother, Rose, and her Aunt Mary urging her to pray to St. Jude Thaddeus.

"We had great respect and admiration for and knowledge of Danny Thomas," she says.

Of course, Kay knew about the establishment of St. Jude Children's Research Hospital.

"The story so impressed me as a young girl about Danny Thomas, in light of his success, dedicating his life to establishing the hospital. This is a great message for us today," she says, fighting back tears as she sometimes does when talking about St. Jude.

That young girl from Virginia is now Atlanta businesswoman Kay Dempsey, president and CEO of her own insurance brokerage firm, The Dempsey Companies Inc. Her husband, David, who successfully ran an Atlanta advertising company for many years, is semi-retired and works as a consultant in the agency.

The Dempseys are serving as regional chairs of the fundraising campaign for the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project (*see page 18 for an article about a revolutionary new tool created as a result of that undertaking*). The campaign is working to raise \$55 million for the project.



Kay and David Dempsey

"The scientists and their brilliance are astounding to us. The project is a strategic step," she says. "It is much akin to bamboo. You plant bamboo, and growth is slow in the early years. Then one witnesses an explosion of growth."

Always devoted to children's charities, Kay and David intensified their involvement with St. Jude after Kay visited the hospital in 2008.

"The moment you see the little red wagons, you are amazingly full of hope and blessings for these children," says Kay, who shares

a family connection to Michael Tamer, ALSAC's first CEO, through her aunt, Julia (Tamer) Isaac.

In addition to their support for the Pediatric Cancer Genome Project, Kay and David hosted a dinner for ALSAC CEO Richard C. Shadyac Jr. in 2009, so that he could share the St. Jude mission with potential donors in Atlanta. The Dempseys are planning a similar larger event for this fall. The couple also has made St. Jude the beneficiary of a life insurance policy and plan to leave the hospital a bequest in their will.

After learning about St. Jude research and treatment, Kay says, "You can't be a bystander."

Far from being bystanders, the Dempseys are investing in the vision of a brighter tomorrow for children.

"I have been told for many, many years that we should help others have a vision of a bigger future," Kay says. "This is what St. Jude is doing." ●

Gratitude and Generosity

From coast to coast, individuals and organizations are inspired to give thanks and give generously.

BY LEIGH ANN ROMAN

During the last seven years, a holiday tradition of gratitude and generosity has developed, thanks to a special campaign in support of St. Jude Children's Research Hospital. That tradition is the *Thanks and Giving*® campaign, an unprecedented union of corporations, retailers, celebrities and the media that asks consumers to "Give thanks for the healthy kids in your life, and give to those who are not."

The response to this call to action nationwide has raised more than \$247 million for St. Jude since the campaign was launched in 2004 by Marlo, Terre and Tony Thomas, the children of St. Jude founder Danny Thomas. The campaign occurs annually in November and December.

This year, more than 60 brands will encourage their customers to give to St. Jude through add-ons at the register or by purchasing specialty merchandise during the traditional holiday shopping season. Kmart, the lead fundraiser for the 2009 and 2010 *Thanks and Giving* campaigns, will continue its support for a sixth consecutive year. Other committed partners include CVS/pharmacy, DICK'S Sporting Goods, Kay Jewelers, Williams-Sonoma Inc., ANN INC., Domino's Pizza, AutoZone, Target, New York & Company and many more. The campaign is also excited to announce that Hammermill Paper (a brand of International Paper) and Claire's Boutiques will be new corporate partners this year.

"The money raised from our dedicated partners and their customers is crucial to our continuing search for the cures that will save the lives of precious children in communities across the country," says Marlo Thomas, St. Jude national outreach

director. "And because of their boundless support, we are able to keep my father's founding promise—that no child is ever turned away for a family's inability to pay."

Getting involved

Beginning in November, shoppers will see the *Thanks and Giving* magnifying glass logo displayed at stores across the country and online, identifying retailers who are helping St. Jude in the battle to save children's lives. Employees at these companies will join in the effort to raise as many donations as possible to support the hospital.

The comprehensive nature of the campaign, with its

Marlo Thomas celebrates the 2011 *Thanks and Giving* campaign with (from left) Cameron Palton, Kiley Farmer and Maddie Wright.





David Feldman spent the past year raising funds for St. Jude. He encouraged friends, acquaintances and strangers to donate through the *Thanks and Giving* website. "I feel like we made a difference," he says.

many and varied ways to support the children of St. Jude, makes it easy for individuals to get involved. That is just what one young couple in Missouri decided to do. On Valentine's Day 2010, David Feldman and his wife, Melissa, made a commitment to spend a year trying to make a difference in the world. They set out to use that time to raise money for St. Jude.

Feldman chose St. Jude because of the hospital's mission and because the *Thanks and Giving* website made funneling donations to St. Jude simple and seamless.

"That was one of the big deciding factors, that the *Thanks and Giving* portal was already set up," he says. "I was able to hit the ground running."

With help from friends, family and co-workers, he raised more than \$26,000 during that year. Although he hoped to raise more, Feldman is happy that his walk-a-thon, bowl-a-thon and other special events made an impact. "I feel like we made a difference," he says.

In addition to the vital commitment of corporate partners that is the foundation of the *Thanks and Giving* campaign, Feldman's experience shows the impact of individuals on the fundraising effort. The website www.tg.stjude.org offers many ways to get personally involved in the national campaign.

Donors can send e-cards in honor or memory of loved ones; they can join the campaign on Facebook; they can sign up to become online fundraisers, like the Feldmans; or they can register for the 5K kick-off to the *Thanks and Giving* campaign, *St. Jude Give thanks. Walk.™* (See sidebar at right.)

As it raises necessary funds for St. Jude, the *Thanks and Giving* campaign also raises awareness about the hospital's groundbreaking research and treatment through print, broadcast, outdoor and Internet ads.

Celebrity friends Jennifer Aniston, Robin Williams, Morgan Freeman, George Lopez, Olympic gold medalist Shaun White, and NBA player Dwyane Wade will join Marlo Thomas and the true stars of the campaign—St. Jude patients—in television spots and a movie trailer to share the St. Jude story. Theater partners, including Regal Entertainment Group, Cinemark, Carmike

Cinemas and many more, share the St. Jude message of hope with movie patrons across the country.

The *Thanks and Giving* campaign continues to reach out to the Hispanic community, with the help of popular Puerto Rican musician and actor Luis Fonsi,

who will again share the St. Jude mission through the Spanish-language media.

The work of the hospital will also be prominently featured on NBC's *TODAY* show, where Marlo Thomas will appear for five consecutive days during Thanksgiving week.

"We are incredibly grateful to everyone who joins our *Thanks and Giving* campaign each year and gives so generously to support the lifesaving research and treatment being done at St. Jude," Thomas says. ●

St. Jude Give thanks. Walk. kicks off holiday campaign

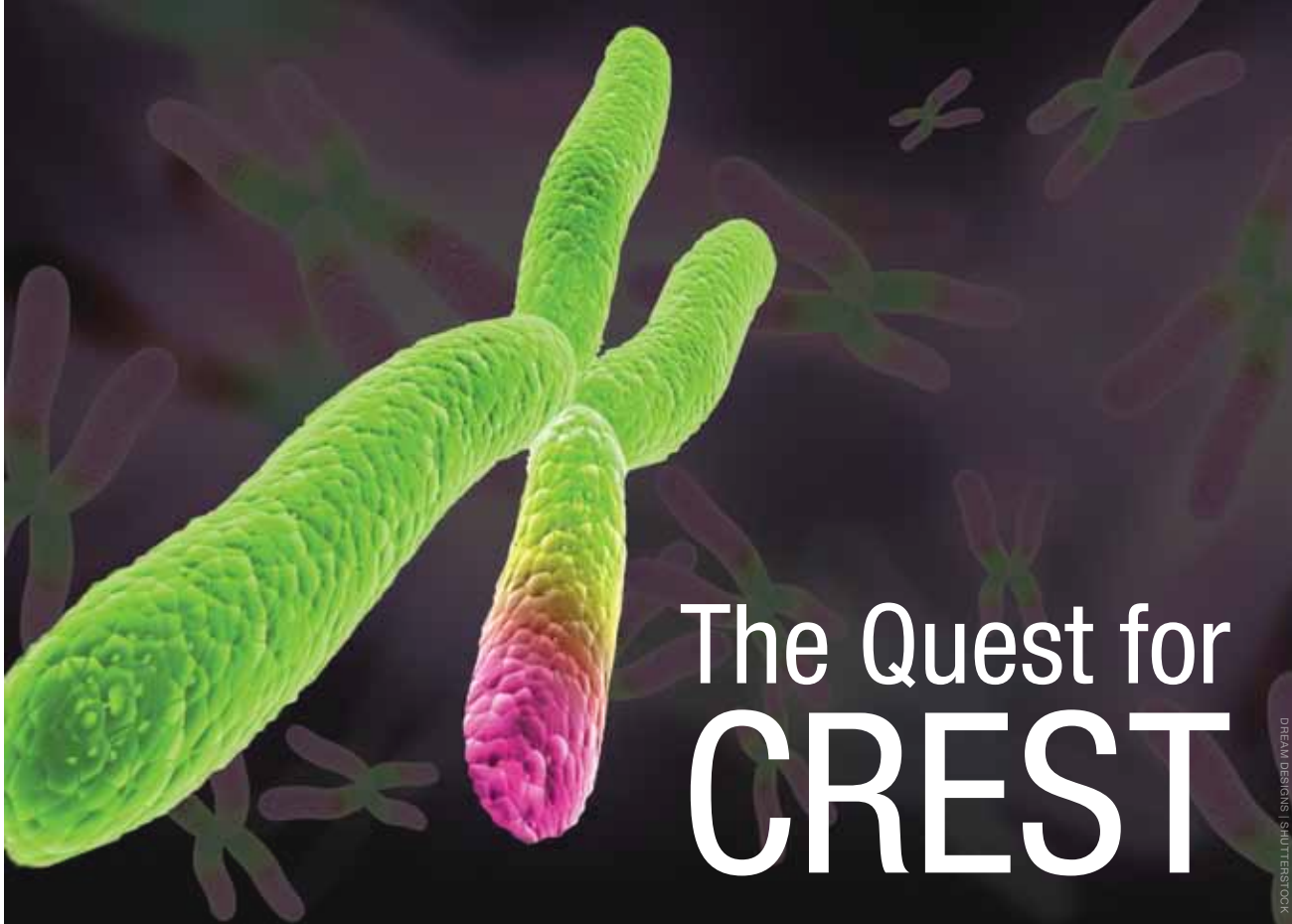
Thousands of people will step out in November to participate in *St. Jude Give thanks. Walk.™* The event will kick off the eighth annual *Thanks and Giving* campaign. This is the fourth year for the walk, which raised \$2.3 million for St. Jude in 2010.

Eighty communities across the country will take part in the November 19 event, a family-friendly 5K walk in parks, malls and zoos to help raise funds and awareness for the mission of St. Jude. The event has grown dramatically from the first walk, which drew supporters to shopping malls in 15 cities across the country in 2008.

To register for the walk, visit www.givethanks.walk.org. Registration is free, and participants are encouraged to ask friends and family to sponsor them with a donation to St. Jude. Walkers can also form teams with family, friends and colleagues to increase the fun and the fundraising. This year, New York & Company, Brooks Brothers and AutoTrader.com return as National Platinum Sponsors of the walk. Kmart will be the local presenting sponsor of the Chicago walk, Hilton HHonors will sponsor the DC Metro walk, GNC will sponsor the Pittsburgh walk and Target/P&G will once again sponsor the Minneapolis walk.

How can you help?

To support the children of St. Jude, look for the *Thanks and Giving* magnifying glass logo wherever you shop this holiday season. Learn more about the campaign by visiting www.tg.stjude.org. There you will find a complete list of *Thanks and Giving* partners. You can also donate now by calling 1-800-4STJUDE.



The Quest for CREST

Scientists working on the Pediatric Cancer Genome Project develop a powerful new tool to pinpoint the structural variations that give rise to childhood cancers.

BY ELIZABETH JANE WALKER

Jinghui Zhang, PhD, began her journey to St. Jude Children's Research Hospital as a preschooler perched high atop a stool in her mother's immunology laboratory.

"My mom developed vaccines for children in China. As a kid, I would watch her doing experiments," Zhang recalls. "I saw that by being a researcher you can save many lives."

Today, Zhang uses her expertise in the computational aspects of genomics, systems biology and related computational sciences to help her colleagues identify the genetic changes that lead to childhood cancers. She and her team recently created a new tool that helps scientists accurately pinpoint cancer-causing mutations that occur within

the 3 billion base pairs of DNA in the human genome.

The tool, dubbed Clipping Reveals Structure or CREST, was developed as part of the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project, which began early last year.

The search for variations

Scientists in the Pediatric Cancer Genome Project are sequencing normal and cancer cells from more than 600 childhood cancer patients. Investigators hope the three-year initiative will help them better understand the origins of childhood cancers and devise more effective ways to treat these diseases.

Soon after the project launched,

scientists began sifting through data in search of structural variations—the chromosomal rearrangements and loss or amplification of DNA that lead to cancer. To find those structural variations, the team initially relied on several existing strategies, each of which had its shortcomings. Some methods yielded numerous false positives; others only indicated the general location of a structural variation, not the exact breakpoint, and missed key genetic lesions. At first, the researchers responded to these challenges by writing "filter" programs to remove the false positives.

"We thought those programs would be sufficient," Zhang says.

Then, by accident, they discovered a gleaming needle in

the genomic haystack. “When we were analyzing one of the leukemia samples, we stumbled upon an important cancer gene that existing tools had not detected,” Zhang recalls. “I realized that we needed to develop our own algorithm to make sure we don’t miss a lot of important hits in the cancer genome.”

The novel computational method the researchers developed identifies exactly when one copy of a normal gene moves to another chromosome. CREST has higher accuracy, precision and sensitivity than other strategies for finding structural variations.

“Other tools miss up to 60 to 70 percent of structural rearrangements in tumors,” Zhang says.

Soft clips, hard data

CREST uses pieces of DNA called soft clips to find structural variations.

Using a technique called next-generation sequencing, scientists break DNA molecules into small fragments, which are then copied and reassembled, using the normal genome as a comparison. Soft clips are segments of DNA that fail to align during that reassembly. Other scientists ignored the soft clips during the rearrangement process, but Zhang and her team used them to find insertions, deletions and inversions in the genomes.

The team tested their technique on a subtype of acute lymphoblastic leukemia (ALL) known as T-lineage ALL. In comparing the normal and cancer genomes of five St. Jude patients, the researchers discovered 89 new structural differences that they validated using other laboratory methods. To determine whether CREST also worked on adult cancers, the researchers applied the technique to a melanoma cell line that had



Jinghui Zhang, PhD, of St. Jude Computational Biology and her colleagues developed a novel tool, called CREST, that helps scientists pinpoint the genetic mistakes that lead to pediatric cancer.

already been sequenced and analyzed. In addition to finding 26 known structural variations, CREST uncovered 50 that had never before been identified.

“It has been really exciting to work on this,” Zhang says. “Through CREST, we were able to see that the rearrangements in the cancer genome can be very complex, involving many chromosomes and causing all sorts of disruptions that we never anticipated could happen. So this actually will provide a better understanding of how cancer initiates, evolves and progresses, and also how it leads to relapse.

“We’ve also found that the structural variation profiles appear to be quite different for different subtypes,” Zhang continues. “This will help with designing specific therapies that treat specific targets identifying these subtypes.”

Spreading the word

When the Pediatric Cancer Genome Project began in 2010, Dr. William E. Evans, St. Jude director and CEO, promised that

the team would publicize its discoveries as they emerged.

“By doing that, we will be fulfilling the mission of St. Jude as well as our responsibility to lead,” he said. “And we will do so by sharing freely with the world what we discover.”

In keeping with that vow, Zhang and her colleagues recently published their results in the journal *Nature Methods* and placed the CREST instructions, user manual and test data online at www.stjude-research.org/site/lab/zhang.

The little girl who began her career in an immunology lab thousands of miles away is now an integral part of a project that may eventually save the lives of children worldwide.

“I think the great thing about working at St. Jude is the close connection between the basic and clinical research,” Zhang says. “Working at St. Jude provides me with the opportunity to see that findings in basic research can turn into therapy. That’s extremely rewarding.” ●

Hitting out of the Rough

BY MIKE O'KELLY

St. Jude helps budding golfer Brennan Simkins through his battle with a rare form of acute myeloid leukemia, which required four bone marrow transplants.

To win a tournament, a professional golfer battles an unrelenting course with such obstacles as deep roughs and sand traps. Adapting to changing winds or extreme temperatures, he stays mentally focused in order to fend off challengers for four rounds and enter the clubhouse as a champion. At age 6, budding golfer Brennan Simkins was beginning to display that kind of focus and tenacity.

But Brennan's world would soon head in a different direction. Although he was dreaming of a future with four rounds of 18 holes each, his reality would consist of four bone marrow transplants in 18 months—and a life-threatening battle with a severe form of acute myeloid leukemia (AML) that would require the world-class treatment available at St. Jude Children's Research Hospital.

An unrelenting course

Brennan loves golf. Several times, he and his brothers have attended the world's most prestigious golf tournament, the Masters, with their parents, Turner and Tara. Known as the Band of Brothers, Brennan and his siblings,

Nat, 11, and Christopher, 7, enjoy golfing with their dad, who jokes that his golf foursome was genetically created, since all three boys are golfers.

Brennan gravitated to the game early with an unusual focus on the short-game skills of pitching, chipping and putting. While other toddlers whacked golf balls as hard as possible, 3-year-old Brennan practiced for hours on the putting green. Soon people began to comment that his swing was one of the most natural they had ever seen. Today, unsure how he acquired his skill or determination, 9-year-old Brennan modestly explains, "I believe I can do something on the golf course, and I just do it."

Usually energetic and full of life, Brennan began feeling lethargic and experiencing leg pain in November 2008. When X-rays revealed no problems with Brennan's legs, a physician advised that Brennan have a blood check-up. During a subsequent family outing to the North Carolina mountains, Brennan did not feel well enough to play in the snow with his cousins.

"I remember going on a hike with Tara and her sister. All three of

us had this gnawing feeling inside that something was wrong," Turner recalls.

Tara took Brennan to the pediatrician for blood work when they arrived home. Later that day, the doctor called to say that additional tests were necessary. Turner and Tara explained to Nat and Christopher that they were taking Brennan to the hospital for more tests. They assumed they would return later that evening.

It would be more than a month before Brennan would return home.

Fore!

At the local hospital, clinicians slipped warming gloves onto Brennan's frigid hands to increase his blood circulation. A transfusion of four units of blood boosted his red blood cell count and restored his energy. The next day, Brennan celebrated his seventh birthday in an oncology unit while doctors sought the cause of his hospitalization.

After changing their diagnosis from acute lymphoblastic leukemia to aplastic anemia, doctors finally determined that Brennan had a rare form of AML marked by a 7q deletion. Most cases of AML are the



result of genetic mutations. The 7q deletion occurs when chromosome 7 loses genetic material. Children with this mutation have an extremely poor prognosis.

Brennan underwent four rounds of chemotherapy before undergoing a bone marrow transplant. In May 2009, Brennan received stem cells from his older brother, Nat, who was a perfect match.

“Brennan and his brothers are best friends,” Tara says. “While Nat might have showed some signs of apprehension about what he was going to endure, he would always let go and focus when we got to the part about helping Brennan.”

Although the transplant was initially successful, a scheduled clinic visit in October revealed low platelet counts. A follow-up bone marrow aspirate confirmed the Simkins’ fears: the 7q deletion was present in 20 percent of Brennan’s cells. Brennan’s only hope was a second bone marrow transplant with an unrelated donor.

A second wind

Because of the risks associated with a second transplant, only a small number of institutions perform them. With limited options available, Brennan was referred to St. Jude in November 2009, where he resumed chemotherapy treatments in an attempt to achieve remission before the transplant.

“When Brennan arrived at St. Jude, a bone marrow aspirate revealed that he had 50 percent immature leukemic cells, or blasts, in his blood,” says Jeffrey Rubnitz, MD, PhD, St. Jude Oncology.

“We first treated him with conventional chemotherapy. He tolerated the therapy well, but had no response. A bone marrow aspirate performed a month later showed he still had about 50 percent leukemic blasts.”

Since Brennan showed little response to conventional therapy, he was enrolled in an experimental protocol and received a more aggressive form of chemotherapy. At the conclusion of that treatment,

Brennan still had 35 percent leukemic blast cells in his blood.

When he received results of the bone marrow aspirate, Turner assumed that a second transplant was now impossible. That evening, he took his son to the grocery store.

“I couldn’t focus on anything,” Turner says. “I was thinking, ‘This is the last time we are going to be coming to this grocery store. We are heading home and are going to be calling hospice.’”

That same night, Rubnitz called the family to deliver surprising news:

St. Jude wanted to proceed with the transplant. Brennan would be the first patient to try a new transplant treatment developed by Wing Leung, MD, PhD, Bone Marrow Transplantation and Cellular Therapy chair.

The protocol involved total-body irradiation twice each day and administration of the drug plerixafor.

“Plerixafor is designed to collect patients’ stem cells for future autologous transplants,” Leung says. “Since it has the property of moving stem cells from bone marrow to blood, we predicted that it could also move leukemia from bone marrow to blood.”

Once in the bloodstream, the leukemia cells may become much more sensitive to the effects of radiation and chemotherapy.

In late January 2010, Brennan underwent his second transplant, receiving the stem cells of a donor whose identity is unknown to the family, but whose cooperation with an ever-changing situation was greatly appreciated.

Mental toughness

A month after his second transplant, Brennan’s disease was again in remission. In June, he returned home to enjoy the summer months with his brothers. He donned a floppy hat, a mask and plenty of sunscreen to participate in a July golf tournament with his brothers, but could only muster a few holes before he felt the aches from osteopenia, a side effect of chemotherapy.

As autumn approached, Brennan slowly resumed the life of an 8-year-old boy—climbing trees and fences, tossing the football and looking forward to attending college football games. In late September, however, a bone marrow aspirate at St. Jude revealed leukemic cells.



Brennan returns to the hospital for monthly checkups that include examinations by Susan Shelton, PA, and other members of the transplant team. “Brennan’s determination and will to press on in the midst of difficult circumstances was an inspiration to all who took part in his care,” Shelton says.

The Simkins family met with Leung, who presented them with two options. The first choice was to do nothing; Brennan had already received more treatment than most children would ever receive. But Brennan and his parents decided to pursue the alternate option—a third bone marrow transplant using stem cells from Turner or Tara. This procedure, Brennan’s only hope, was extremely risky.

“We knew that the risks were greater, but Tara and I both wanted to be picked for the third transplant,” Turner says.

Turner’s cells were harvested for the third transplant, which occurred in early October 2010. Since only half of his cells were matched, there was a significant chance of Brennan acquiring graft-versus-host disease, a condition where the donor’s T cells attack the recipient’s tissues. However, a mild form of graft-versus-host disease is seen as beneficial in attacking the leukemic cells. Once again, plerixafor was used to push the blasts into the bloodstream, where they could be attacked by Turner’s cells.

Weeks after the transplant, Brennan developed a life-threatening viral infection, which led to inflammation in his brain and liver and the build-up of fluid in his lungs. He was placed on a ventilator in the hospital’s intensive care unit, where Nat and Christopher visited their brother for what they feared would be the last time.

But Brennan persevered. He slowly recovered and left the ICU, only to develop aplastic anemia, a condition in which the bone marrow does not produce a sufficient amount of cells to replenish the blood cells. The graft from the third transplant was lost. Brennan began receiving two platelet transfusions daily and

complete blood transfusions every two or three days, which put him at a high risk for infection.

“We knew that without another transplant, he probably didn’t have much time,” Tara says. “We had to move forward with another transplant right away.”

Fending off the field

Leung consulted with Turner and Tara about the risks and complications associated with a potential fourth transplant. This one would be different—it would recover the bone marrow rather than attack the leukemia.

In January 2011, Brennan underwent an extremely rare fourth bone marrow transplant, with his mom serving as the stem cell donor. Less than a week after that procedure, Brennan developed fever, nausea and a build-up of fluid in his lungs. He returned to the ICU. Before being intubated, Brennan gasped for air and uttered, “This is the hardest day of my life.”

Although Brennan underwent multiple organ failure and swelling throughout his body, he slowly improved and returned to the hospital’s Bone Marrow Transplant unit.

Brennan’s condition continued to improve, and he achieved remission in May.

Not long afterward, pro golfer Loren Roberts visited St. Jude and presented Brennan with a flag from the Senior British Open golf tournament. The seasoned veteran was amazed at the boy’s tenacity.

“Brennan told us that when he was in ICU, he felt that his light was going out, but that he had to somehow focus through it,” Turner recalls. “When Roberts heard that, he said, ‘Anybody who can say that can do anything.’”



After four bone marrow transplants, Brennan (at left) is happy to be home, where he enjoys playing with his brothers Christopher (pictured) and Nat, and their dog, Lucky.

In the clubhouse

Brennan was cleared to return home by doctors in June, but not before serving as an honorary caddy during the FedEx St. Jude Classic golf tournament in Memphis. He even wowed spectators and golf professionals with a few swings at the tournament, which benefits the hospital.

Before tournament champion Harrison Frazar walked the victory trail to the clubhouse, he joined several patients. Brennan smiled as he sat on Frazar’s knee for a photo—a true image of persistence. It was Harrison’s first win in 355 tries.

Just days after that snapshot, Brennan returned home. With a grin on his face, he entered the house that has been scarcely occupied the last 2 ½ years.

“This is like a dream come true,” he said.

Brennan now returns to St. Jude for monthly check-ups. He looks forward to returning to the golf course, but for now, he is enjoying his time with his family and his dog, Lucky. Brennan’s parents attribute St. Jude and positive thoughts to keeping their hopes strong through transplants and relapses.

“St. Jude has been a tremendous gift to our family,” Tara says. “It has allowed us to live as a family, and now, when we come back to St. Jude, it’s like a homecoming, a second home.” ●

Perspective

BY LAURA HACKELTON BROWN

Unwrapping the Gift

As we enter the season of giving, one former St. Jude patient explains her attitude of gratitude.



SETH DIXON

It was the spring of 1984, and even though I was 8 years old, I vividly remember the sights and smells of St. Jude Children's Research Hospital: the nausea-inducing chemotherapy, the radiation sessions, the metallic smell of drugs in the Medicine Room.

I had high-risk acute lymphoblastic leukemia, and the doctors at St. Jude said they couldn't make any promises about the outcome.

I recall brushing the long hair of my Barbie™ and crying because I missed my hair.

"Mom, why can't I just be normal?" I asked.

"Baby, God created you for a special reason," my mom replied. "There are other children here who are worse off than you are."

There I was, nearly bald and throwing up all day because of the chemotherapy, and my mom was finding the good in everything.

About that time, a family friend sent me a basket of gifts. I got to open one present every day.

"Each day is like one of those gifts," my mom explained. "It's a neatly wrapped little box with a beautiful little bow.

When you open it up, it's yours, and it's up to you how you're going to receive it."

Gradually, my health improved, and I returned to St. Jude for annual checkups. Doctors cautioned that the treatments I had received might affect my ability to have children. Yet my husband and I were able to have three healthy boys. They are our three little miracles.

Today my life is extremely busy. While my husband flies Black Hawk helicopters in Iraq, I spend my days teaching special education and my afternoons running our sons to their activities. My candle burns at both ends, and my elasticity is about stretched until it's gone, but I have much to be happy about. My life is great, and I couldn't be

more blessed.

I returned to St. Jude recently to participate in the St. Jude LIFE study for long-term cancer survivors. Talking with Dr. Tim Folse, I learned that my chronic fatigue and memory problems are due to the chemotherapy and radiation I received during treatment. Because of St. Jude LIFE, I better understand the effects of my treatment, and I've gotten ideas on how I can cope with my medical challenges. But I'm also helping future survivors. I hope that by participating in the St. Jude LIFE research that I'll help at least one child not have to deal with those same issues.

Every year on April 13, I find the nearest ice cream shop and have my own private celebration. You see, on that day in 1984, a doctor walked into the Medicine Room at St. Jude and said, "Laura, we have good news. You are in remission."

My mom and I rejoiced when we received that gift, celebrating the milestone with an ice cream sundae. My mother is no longer with me, but every year I make sure to observe that anniversary. It reminds me that every day is a gift. It's up to us to decide how to receive it and what we are going to do with it. ●

DONATE TO **ST. JUDE** NOW & SHOP WHERE YOU SEE OUR LOGO.

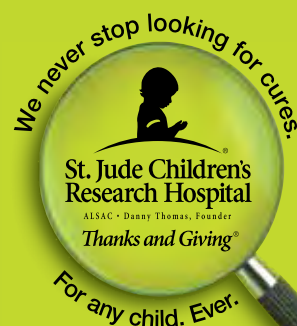
HELP HER LIVE

Hayli, Age 2

Those magical first steps. Hayli's parents were crushed when she limped and winced through hers. She was treated first for a bone infection, but the pain just worsened. The devastating diagnosis—acute myeloid leukemia. Thankfully, she was sent to St. Jude Children's Research Hospital®. Today, she is in remission and thriving. But too many children still die in the dawn of life. Help us change that.

THIS HOLIDAY, GIVE THANKS FOR THE HEALTHY KIDS IN YOUR LIFE, AND GIVE TO THOSE WHO ARE NOT.

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CHANGE SERVICE REQUESTED

GRAMMY® award-winning artist Sheryl Crow visits with St. Jude patient Kennedy Harris during the recent launch of a new music campaign called Music Gives to St. Jude Kids. This program mobilizes the music industry to raise funds for the hospital. Moved by her visits to St. Jude, her own battle with cancer and her role as a mom, Crow is helping Music Gives to St. Jude Kids rise to the top of the charts. The program unites artists and their fans to get involved and support St. Jude through a variety of opportunities including concert promotions, text to donate messages, social media and a range of other fundraising opportunities. Visit www.stjude.org/musicgives to learn more.



Finding cures. Saving children.