

# St. Jude promise

[stjude.org/promise](http://stjude.org/promise) winter 2018

**Help for kids with  
sickle cell disease** *page 14*

Why do some cancers  
**run in families?** *page 4*

**St. Jude LIFE** celebrates  
10 years *page 19*





## Cover Story

### 14 When More Is Better

Researchers prove that increasing the dose of hydroxyurea helps patients with sickle cell disease thrive.



## Features

### 03 Heavy Mettle

A St. Jude Hero goes the distance—and then some.

### 04 Shaking the Family Tree

Why do some cancers run in families?

### 08 Eight is Great

Children in Oklahoma can receive care close to home.

### 10 Lessons from the Heart

Bereaved parents help educate medical staff.

### 13 Partners in Life

Couple begins a new chapter.

### 18 Home Run: St. Jude

St. Jude LIFE helps survivor hit one out of the ballpark.

### 20 Still Rare, No Longer Obscure

Experts advance research and care for histiocytosis.

### 28 An Expression of Grace

Savor a cup of tea with the St. Jude chaplains.

## Research Highlights

### 25 Science News Briefs

Learn about the latest news at St. Jude.

---

The mission of St. Jude Children's Research Hospital is to advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment.

St. Jude Children's Research Hospital, American Lebanese Syrian Associated Charities, ALSAC and *Thanks and Giving* are registered trademarks.

St. Jude is an Equal Opportunity Employer. Articles may be reprinted with written permission. ©2018





**St. Jude President and  
Chief Executive Officer**  
James R. Downing, MD

**ALSAC President and  
Chief Executive Officer**  
Richard C. Shadyac Jr.

**St. Jude Communications  
and Public Relations**  
Echelle Rutschman

**Editor**  
Elizabeth Jane Walker

**Graphic Design**  
Jessica W. Anderson  
Ashley Durand  
Timothy Hammond  
Jennifer Hardin  
Jerry Harris

**Contributing Writers**  
Richard Alley  
Keith Crabtree, PhD  
Kerry Healy  
Chris Lewis  
Mike O’Kelly  
Maureen Salamon

**Photographers**  
Peter Barta  
Seth Dixon  
Ann-Margaret Hedges  
Justin Veneman

**Editorial Advisory Board**  
Justin Baker, MD  
Leah Brooks  
Christine Broughton  
Debbie Crom, RN, PhD  
Aditya Gaur, MD  
Hiroto Inaba, MD, PhD  
Joseph Opferman, PhD  
Amy Scott  
Barry Shulkin, MD  
Carrie L. Strehlau  
Regina Watson  
Carole Weaver, PhD  
John Zacher

*On the cover:*  
Courtney Davis  
Photo by Peter Barta

**Discrimination is Against the Law**

St. Jude Children’s Research Hospital complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. St. Jude does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

- St. Jude Children’s Research Hospital:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
    - Qualified sign language interpreters
    - Written information in other formats (large print, audio, accessible electronic formats, other formats)
  - Provides free language services to people whose primary language is not English, such as:
    - Qualified interpreters
    - Information written in other languages

If you need these services, contact the Patient Relations Coordinator at 901-585-8383 or the operator at 901-595-3300.

If you believe St. Jude Children’s Research Hospital has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: St. Jude Patient Relations Coordinator, 1-901-595-8383; 1-866-278-5833, 1-901-595-1040, Fax # 1-901-595-8600 or at *PatientRelationsCoordinator@stjude.org*. You can file a grievance in person or by mail, email or fax. If you need help filing a grievance, Jim Mobley, patient relations coordinator, is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 1-800-368-1019, 800-537-7697 (TDD) Complaint forms are available at <http://www.hhs.gov/ocr/filing-with-ocr/index.html>.

ATTENTION: If you speak another language, assistance services, free of charge, are available to you. Call 1-866-278-5833 (TTY: 1-901-595-1040).

**Amharic:**  
ማስታወሻ: የሚናገሩት ቋንቋ እማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጅተዋል።ወደ ሚከተለው ቁጥር ይደውሉ 1-866-278-5833 (መስማትለተሳናቸው: 1-901-595-1040).

**Arabic:**

تنبيه: إذا كنت تتحدث باللغة العربية. فيمكنك الاستعانة بخدمات المساعدة اللغوية المتوفرة لك مجاناًيرجى الاتصال بالرقم 1-866-278-5833 . (الهاتف النصي: 1-901-595-1040)

**Chinese:**  
注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1-866-278-5833 (TTY：1-901-595-1040)

**French:**  
ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-866-278-5833 (ATS : 1-901-595-1040).

**German:**  
ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-866-278-5833 (TTY: 1-901-595-1040).

**Gujarati:**  
સૂચના: તમે ગુજરાતી બોલતા હો તો બિ:શુલ્ક ભાષા સહાય સેવા તમારા માટે ઉપલબ્ધ છે. ફોન કરો: 1-866-278-5833 (TTY: 1-901-595-1040).

**Hindi:**  
ध्यान दें: यदि आप हिंदी बोलते हैं, तो आपके लिए मुफ्त में भाषा सहायता सेवाएं उपलब्ध हैं। 1-866-278-5833 (TTY: 1-901-595-1040) पर कॉल करें।

**Japanese:**  
注意事項：日本語を話される場合、無料の言語支援をご利用いただけます。1-866-278-5833 (TTY: 1-901-595-1040) まで、お電話にてご連絡ください。

**Korean:**  
주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1-866-278-5833 (TTY: 1-901-595-1040)번으로 전화해 주십시오.

**Laotian:**  
ໂປດຄຳບ: ຖ້າທ່ານເວົ້າພາສາອື່ນ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາໂດຍບໍ່ເສຍຄ່າແມ່ນມີໃຫ້ແກ່ທ່ານ. ໂທ 1-866-278-5833 (TTY: 1-901-595-1040).

**Persian:**  
اگر به فارسی گفتگو می‌کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می‌باشد. با (۴۰ - ۱۰۵ - ۹۰۱ - ۱ - ۸۵۸۳۳) (TTY: ۱ - ۹۰۱ - ۵۹۵۶۲۷ تماس بگیرید.

**Russian:**  
ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-866-278-5833 (телетайп: 1-901-595-1040).

**Spanish:**  
ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-866-278-5833 (TTY: 1-901-595-1040).

**Tagalog:**  
PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-866-278-5833 (TTY: 1-901-595-1040).

**Vietnamese:**  
CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-866-278-5833 (TTY: 1-901-595-1040).



# Heavy Mettle

A St. Jude Hero goes the distance—and then some—in the fight against childhood cancer.

By Richard J. Alley

Running the 13.1 miles of a half-marathon requires strong legs, lungs and will. To run as a St. Jude Hero takes enormous heart, as well.

“I’ve always had a heart for children’s hospital charities,” says Elizabeth Newton of North Carolina, who ran 10 half-marathons in 2017—five as a St. Jude Hero.

Newton has a habit of giving 10 percent of her income to charity. That tradition, along with the Rock ‘n’ Roll Marathon Series last year, has helped her raise about \$20,000 to help support the mission of St. Jude Children’s Research Hospital.

She first toured St. Jude as a college student.

“Obviously, the kids know that they’re fighting, and the parents know that they’re fighting, but I feel like St. Jude does so much to try to distract from

---

**“St. Jude does so much more than just treat the illness. They treat the whole child and the whole family, and that is huge.”**

---

that,” she says, “from the way the hallways are painted to the fact that the parents don’t have to worry about paying for food or housing. A lot of the stressors are taken off of them.”

In addition to the halves, Newton ran the full Boston Marathon in April. Her heart—and her personal experience with cancer—keep her going.

“I’m a two-time cancer survivor,” she says. “It happened my senior year of college, so I was much older. It was melanoma, and I didn’t have to do chemo or radiation. But, I understand how stressful it can be as a 22-year-old dealing with cancer and watching my mom have to be strong while her adult child is going through something like that. I can’t imagine what it’s like for a parent who has a child going through it.

“St. Jude does so much more than just treat the illness,” she continues. “They treat the whole child and the whole family, and that is huge. It’s not just going to the hospital, getting your treatment and leaving.” ■

For more information on running as a St. Jude Hero, visit [stjude.org/heroes](http://stjude.org/heroes).







# Shaking the Family Tree



St. Jude investigators explore why some cancers run in families and why certain people get more than one cancer.

## Medical mystery

Madeleine Martin and her mom, Katie, both developed kidney cancer as children. Yet, no mutations have been found to account for the disease. “There has to be a genetic link, with both of them getting cancer at the exact same age,” Madeleine’s dad says. “We just haven’t found it yet.”





### In search of answers

Chimene Kesserwan, MD (at right), is leading an effort to find out why some cancers run in families and why certain people get more than one cancer. As part of that project, she consults with Jason Quave, Amanda Seymour and their children.

Madeleine Martin has her mom's rich, brown eyes and her dad's broad, engaging smile. She has her mother's hair and her daddy's hands. But one similarity has befuddled both her family and the medical community: Like her mom, Madeleine developed a cancer of the kidney called Wilms tumor.

The odds of a parent and child having this rare cancer are miniscule.

In 1979, Madeleine's mom, Katie, then 18 months old, received Wilms tumor treatment at St. Jude Children's Research Hospital. When Katie grew up and became a nurse practitioner, she learned her baby would have only a 1 to 3 percent chance of having that cancer. Nevertheless, soon after Madeleine's birth, Katie requested an ultrasound—not because her baby had exhibited symptoms, but because of a small, nagging concern.

Sure enough, the scan showed Madeleine had Wilms tumor.

Genetic testing revealed no mutation that would account for the disease in both mother and daughter. The Martins enrolled in a Wilms tumor study at

another medical center. Again, no common mutation was found.

"There has to be a genetic link, with both of them getting cancer at the exact same age," says Katie's husband, Justin. "We just haven't found it yet."

### In search of medical mysteries

St. Jude recently opened a new study aimed at uncovering answers to this and other unexplained familial cancers. It is the largest effort to date at St. Jude to discover additional cancer predisposition genes.

The SJFAMILY clinical trial is designed to find out why some cancers run in families and why certain individuals get more than one cancer. The study is open not only to St. Jude patients, but also to families worldwide who have possible hereditary cancers.

"We want to talk with families like the Martins, who have gone through testing already to figure out the link and have come up negative," says Chimene Kesserwan, MD, of St. Jude Oncology.

She and her colleagues are seeking

individuals who developed one or more cancers, with the first cancer before age 26, and who also have close relatives (such as children, parents, siblings, aunts, uncles or grandparents) diagnosed with cancer before age 50. The researchers would like to enroll members of these families into the research study, both those with and those without cancer. The researchers are also looking for people who have known genetic conditions that increase the risk of cancer.

The ambitious project aims to enroll about 3,000 participants over the next 10 years. Kesserwan, the study's principal investigator, has already received inquiries from physicians as far away as Argentina, Australia, Ireland and Lebanon.

"The word is out," she says.

### Birth of a registry

Kim Nichols, MD, director of the St. Jude Cancer Predisposition Division, envisions the study will result in a rich registry of clinical data and biological samples. Researchers will

**SJFAMILY is open not only to St. Jude patients, but also to families worldwide who have possible hereditary cancers.**



Kim Nichols, MD and  
Janilef Barranco Vazquez

delve into that resource to identify new cancer predisposition genes and syndromes.

"We know the causes for some familial cancers," Nichols says. "But some families—like the Martins—have members with cancer and we don't know why. Sometimes, people in the same family may develop more than one cancer. Why does that happen? The answer may lie in the genes. But the genes that cause those particular cancers have not yet been identified. That's what we hope to do through the SJFAMILY study."

Participation is easy, and can occur without traveling to St. Jude. Individuals in the study simply provide blood samples and health information that will be used for current and future research. When possible, scientists will also collect and store other biological specimens such as leftover tumor or bone marrow samples.

Thus far, St. Jude has enrolled about 60 families, including the Martins.

### Researching genetic inheritance

Changes in DNA can lead to cancer and other diseases. Through SJFAMILY, scientists will use DNA sequencing to look for genetic

changes in the donated samples. This technology "reads" each letter of DNA to find mutations that may contribute to cancer development. Nichols and Kesslerwan emphasize the research study does not take the place of clinical genetic testing or counseling.

The samples and information submitted for SJFAMILY will be used as part of a larger ongoing research project. Scientists in the St. Jude Computational Biology Department will use innovative approaches and visualization tools to analyze the massive amounts of data that will be accumulated through the project.

Because this long-term study is designed to find connections among samples, every family may not necessarily receive details about their specific situation. Families who are interested in learning such information should pursue clinical genetic counseling and testing.

### Mark the markers

In addition to identifying new genes, researchers hope to find genetic markers that might influence how a known genetic syndrome presents within a particular family. For instance, in some families, cancers occur in

younger individuals. In other families, the cancers may only affect a given organ. What influences whether a person gets cancer?

"There are some people who have increased risk to have a certain disease but they don't get that disease," Nichols explains. "One reason may be that certain people have a genetic modifier. For example, there are people who harbor changes in a cancer predisposition gene who never develop cancer despite having an increased risk. Sometimes in the same family we even see two people with the same mutation where one person develops cancer and the other does not."

"So, the second aim of the study is to try to identify genetic markers that might influence how a disease manifests in a family with a known genetic condition."

### The big picture

St. Jude researchers predict the project's findings may also extend far beyond childhood cancer.

Studying rare familial syndromes can have broad implications to our understanding of cancer biology. For instance, *RB1* was the first gene identified that was linked to a



familial form of cancer: the eye cancer retinoblastoma. Only 250 to 300 children in the United States are found to have retinoblastoma each year. About 40 percent of those have a hereditary form of the disease.

So why study a familial link that affects so few people?

"It turns out the genes altered in the healthy cells of people with familial cancers are often the same genes altered more broadly in cancer cells in general," Nichols explains. "The *RB1* gene and genetic pathway is one of the mostly commonly altered genes in all of human cancers."

For example, in addition to retinoblastoma, *RB1* mutations are also implicated in the development of bladder cancer as well as some cancers of the lung, breast, bone and skin.

### Today's research, tomorrow's cures

Many families who take part in SJFAMILY simply want to help St. Jude make discoveries that will help future generations.

For the Martins, participation is a way to give back to the hospital that saved the lives of both Katie and Madeleine. But the family also understands the intrinsic value of research.

"Scientific advancement is the reason Madeleine's alive," Justin says. "And it's got to keep going. Cancer happens when genes have an error. If scientists can figure out how to

stop that error from happening so others won't have to go through significant treatment, it would be a fantastic objective and worth achieving." ■

Learn more: [stjude.org/SJFAMILY](http://stjude.org/SJFAMILY)

## How does St. Jude find the connections?

The SJFAMILY study will use whole-genome and whole-exome sequencing to discover new cancer predisposing genes.

### Whole-Exome Sequencing

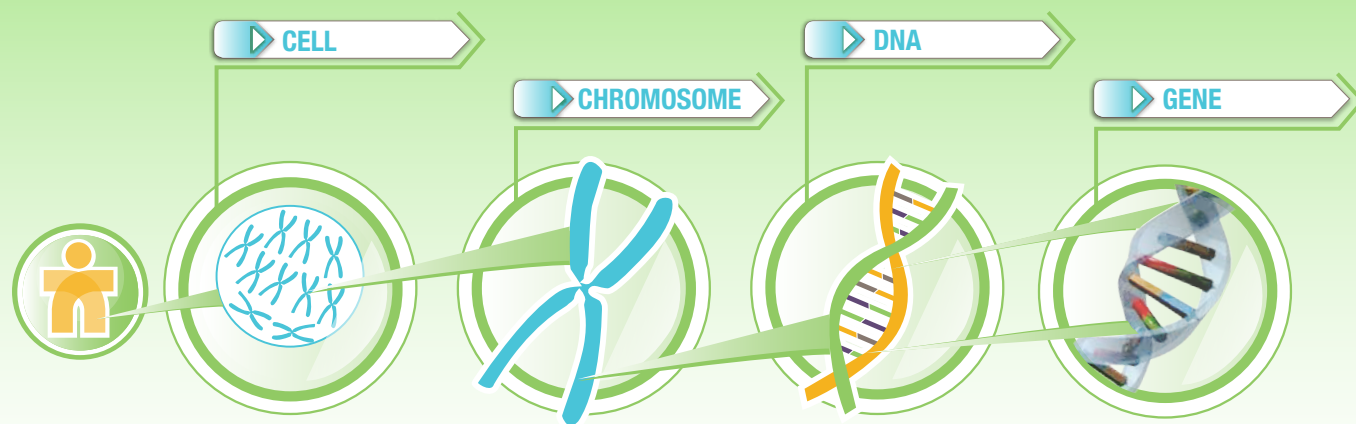
looks at a slice of the human genome—about 1–2%

### Whole-Genome Sequencing

determines the exact order of the 3 billion nucleotides in our DNA

These processes enable researchers to find as many genetic abnormalities as possible. The findings may lead to new and better ways to diagnose and care for people with familial cancer.

## GENES AND DNA: DID YOU KNOW?




Our bodies are made up of very tiny building blocks known as cells.

Our cells contain chromosomes, which are made up of DNA.

DNA is organized into smaller units called genes.

Genes are instructions that tell our cells how to function. The complete set of human genes is called our "genome."

St. Jude will use technology called genome sequencing to examine every one of the 3 billion letters of the genetic code.



By opening its eighth affiliate clinic, St. Jude enables Oklahoma-based children to receive care close to home.

# eight is great

By Chris Lewis

**S**ince its founding in 1972, the St. Jude Affiliate Program has extended the mission of St. Jude Children's Research Hospital far beyond the walls of the hospital in Memphis, Tennessee.

To enable more children to benefit from the hospital's research and treatment, the program has opened eight affiliate clinics in locations from Louisiana to Illinois.

The newest clinic, known as the St. Jude Affiliate Clinic at The Children's Hospital at Saint Francis, opened in Tulsa, Oklahoma, last year. Considered a game changer for Tulsa's pediatric care, the affiliation offers St. Jude experience and expertise to the children and families of Oklahoma.

By allowing pediatric hematologists and oncologists at the affiliate to enroll patients in St. Jude clinical trials, the clinic offers children more access to clinical trials in the region. In doing so, children can acquire medical care closer to home so that they may rarely, if ever, need to leave the state.

"Children in Oklahoma can acquire the same care that St. Jude offers—in a way that's convenient for their families," says Carolyn Russo, MD, medical director of the St. Jude Affiliate Program. "Without that option, patients and family members would have had to travel to Memphis for the majority of their medical care."

## Familiar faces, supportive caregivers

When 5-year-old Caroline McKinney was diagnosed with leukemia, her oncologist reassured her parents that she could

receive the same type of treatment in Tulsa as she would in Memphis. Caroline's parents say they were excited to learn that their daughter would be able to

## Home, sweet home

Caroline McKinney was able to remain in Tulsa with her four siblings during therapy. "Having a developed relationship with her hometown doctors and nurses, while also not having to travel back and forth, has given Caroline stability, as well as peace for our family," her mom says.

remain with her four siblings during therapy.

"Having a developed relationship with her hometown doctors and nurses, while also not having to travel back and forth, has given Caroline stability, as well as peace for our family," says Caroline's mom, Megan. "The support and love she received was a big deal for our family. We really got closer because of this journey, rather than being torn apart."

During Caroline's treatment in Tulsa, she has rarely been hospitalized.

"She's surrounded by such a positive environment by being home with her older siblings, friends and the people who love her," Megan adds. "There's



definitely a role to play in the stability of the environment around you.”

### Ensuring high-quality care

In addition to offering patients and families medical treatment close to home, the affiliate is also participating with St. Jude in quality projects that aim to reduce the number of central-line infections that occur in pediatric cancer patients. Children with lowered immune systems are at high risk for infections.

The affiliate is also participating in a project to prevent low blood sugar levels in patients. Oftentimes, children with leukemia have procedures that require anesthesia. Prior to the procedures, they can't have anything to eat or drink, which can make them cranky and cause dizziness and other problems.

“These are little toddlers who eat more frequently than grown-ups sometimes,” Russo says. “When they have to fast before procedures, their blood sugars can go down. This project is designed to eliminate that issue and ensure the children receive the best possible care.”

### A successful transition

To prepare for the transition of becoming a St. Jude affiliate, the pediatric oncology clinic at The Children's Hospital at Saint Francis upgraded its services and facilities to improve patients' experiences and align its environment to St. Jude models. The clinic's new layout encourages patients and families to interact and get to know each other.

“It allows children to see that they're not the only ones going through these hard times,” says Megan, who notes that the affiliate also covers medical costs that Caroline's insurance doesn't cover. “And they also have fun together and build relationships with one another.”

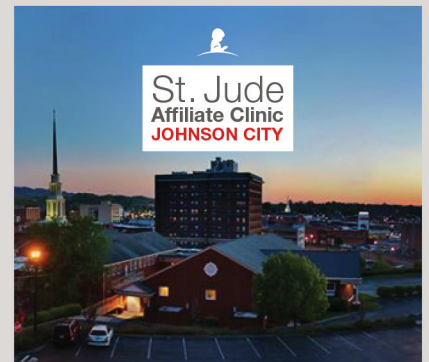
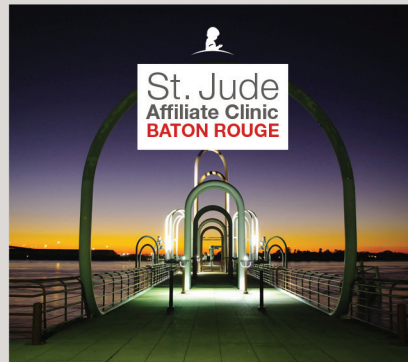
The affiliate has given the hospital's nurses access to additional education and training.

“Excellent nursing care is the central hub of what we do,” says Greg Kirkpatrick, MD, pediatric hematologist and oncologist at the affiliate. “Our staff can now go to St. Jude to take advantage of seminars and other educational opportunities.”

As Megan reflects on the transition process, she is thankful for the changes, along with the progress that has occurred because of the affiliation.

“We are pretty enamored with the clinic,” she explains. “The staff has saved our daughter's life, and they continue to love on her every day.” ■

## The St. Jude Affiliate Program cares for children in:







# *Lessons from the* **HEART**

By Elizabeth Jane Walker

## **Healing hugs**

Bereaved parent mentors Dean and Tasha Ives embrace Justin Baker, MD, during the hospital's annual Day of Remembrance. "We can make a difference if we can help you and love on people like you who have loved us," Tasha says.





*In the only  
program of its  
kind, bereaved  
parents guide  
staff in mastering  
compassionate  
communication.*

**D**uring the final hours of her life, 7-year-old Catie O'Brien issued a poignant, yet powerful, mandate to her grief-stricken parents.

"Do everything you can for St. Jude," said the little girl, "so that no other family has to go through what we went through."

During the past eight years, Christine and Kevin O'Brien have taken that command to heart. They now serve as educators in an innovative program at St. Jude Children's Research Hospital. The O'Briens help nurses, doctors and other clinicians master palliative care concepts and skills. It is the first such program to use highly trained bereaved parents as educators.

"We could spend the rest of our lives holding Catie's picture or her favorite stuffed animal and just being sad," Christine says, "or we could make a difference. And hopefully that difference will someday lead to a cure."

### **Parents as faculty**

During medical and nursing school, students learn about physical ailments and medical procedures. But scant attention may be paid to the art and practice of compassion. St. Jude addresses that component of care by offering palliative and end-of-life programs that enlist bereaved parents as faculty members.

Every clinical nurse at the hospital completes 25 credit hours of training in palliative and end-of-life care. All clinical fellows also undergo training to enhance their communication skills. Both programs use role-playing sessions and honest conversations with bereaved parent educators.

The 24 parents who take part in these efforts go through rigorous training so that they can understand and communicate the objectives of each educational session.

These volunteers may also help with strategic planning and mentor other St. Jude families. The parents lead sessions as part of the hospital's annual Day of Remembrance, a workshop to give bereaved families tools for the healing journey.

Many of the parents also took part in the hospital's 2017 Pediatric Palliative Oncology Symposium, which focused on the care of children with cancer and their families. The conference attracted health care experts from around the world.

"Our parent educators are making a difference for staff as well as for families who are experiencing something that nobody would wish on anybody," explains Justin Baker, MD, chief of the Division of Quality of Life and Palliative Care.





### Lasting legacy

“Do everything you can for St. Jude,” Catie O’Brien told her mom and dad, “so that no other family has to go through what we went through.” The O’Briens and other bereaved parents now help nurses, doctors and other clinicians learn palliative care concepts and skills.

### Experts offer guidance

Christine O’Brien adds her perspective to an employee discussion.



**“If you make an impact on the life of one person, is your life worth it? Is your effort worth it?”**

– Christine O’Brien

### ‘Leaning in’ to difficult conversations

During a recent training session, Mary Lorino, RN, who works in the hospital’s Intensive Care Unit, says she gleaned tips she can use in her practice every day. Lorino says she appreciated the ability to discuss delicate topics.

“We could ask the questions we’ve always wanted to know,” she says. “Like, ‘Are we doing enough? Are we where we need to be? Are we asking the right questions? Are we addressing you in the right way? Is hugging appropriate?’ Having that open and honest communication about how we can better serve families was huge.”

Jonathan Miller, MD, PhD, a clinical fellow in Oncology, says he is humbled, inspired, encouraged and challenged by the perspective provided by parent educators.

“The sessions challenge us to ‘lean in’ to the difficult conversations that are pivotal in providing holistic care to patients,” he says. “The programs also emphasize the importance of a multidisciplinary approach that involves not only the family but nurses, social workers, Quality of Life staff and others.”

### Giving back, finding meaning

Baker says many of the parent educators regard their participation as a legacy-building activity.

“It’s a way of giving back and a way of finding meaning in their child’s death,” he says.

During a recent panel discussion, Tasha and Dean Ives said their daughter Sydney set the bar high in helping them handle grief and other tough issues.

“We feel like we are sharing her light,” Tasha explained to the nurses in attendance. “We can make a difference if we can help you and love on people like you who have loved us.”

As the busy mother of five other children, Christine O’Brien often travels to Memphis to share her wisdom and experiences with St. Jude staff. It’s not easy, but it’s one way she and her husband can fulfill the wishes of their daughter and honor her memory.

“If you make an impact on the life of one person, is your life worth it?” Christine asks. “Is your effort worth it? I think so.” ■



# Partners in Life

**"We hope these studies will help researchers learn more and will lead to greater understanding of these diseases so the mission can continue."**



**After 17 moves, four children and 55 years of marriage, one couple begins a new chapter, supporting two exciting programs at St. Jude.**

By Kerry Healy

Tom and Judy Sheehan have been partners in life for more than 55 years, equally sharing the joys and burdens of marriage and raising four children.

"It wasn't *my* career, it was *our* career," says Tom, a retired automotive electronics executive. "We moved 17 times for my job. It takes a special family to do what we did."

Recently, the couple extended their partnership to helping save the lives of children battling cancer and other life-threatening diseases at St. Jude Children's Research Hospital. The Sheehans made gifts to support the hospital's Genomes for Kids study and gene therapy.

"Danny Thomas started St. Jude in 1962, the same year we were married," Judy says. "We've grown up with St. Jude. We hope these studies will help researchers learn more and will lead to greater understanding of these diseases so the mission can continue."

The couple's personal ALSAC/St. Jude representative, Erika Rudd, says the Sheehans have a deep desire to understand and support the hospital's research and treatment.

"Supporters like Tom and Judy want to dream big with

St. Jude," Rudd says. "They told me, 'Let's think big. We want to know what the latest promising research is; what the doctors and researchers at St. Jude are dreaming about that could be the next big breakthrough.'"

The Sheehans' latest gift, made in the form of a stock transfer, was fortuitous for them and for St. Jude.

"The stock market had great gains in the first half of 2017," Tom says. "By moving some of our appreciated stock to charity, we were able to avoid capital gains and give St. Jude a larger gift."

Reflecting on their support, Tom says, "St. Jude is absolutely a great investment. The mission is right, and the concept of thinking big and doing whatever they can to find cures is what they are all about."

Adds Judy: "St. Jude doesn't have an institutional feel. There are some very sick children there, but everyone always seems to be smiling. It's a happy place, and we are proud to be a part of it."

*For more information about donating stock to St. Jude or other ways you can support the hospital's lifesaving mission, call 1-800-910-3188 or email [giftplanning@stjude.org](mailto:giftplanning@stjude.org).* ■



# WHEN more is BETTER

By Keith Crabtree, PhD

Sixteen-year-old Courtney Davis remembers to take her daily medication for sickle cell disease, an inherited blood disorder, in an unusual way.

Broadway, her Maltese-Yorkshire dog, barks for attention at a certain time each evening.

“I always take my medicine before I take out my dog,” Courtney says, explaining her bedtime ritual.

A high school junior, Courtney enjoys cheer, dance, musical theater and history class. She wants to be an attorney one day, and she’s doing her part to succeed. She enrolls in Advanced Placement classes and takes part in extracurricular activities.

Most importantly, she faithfully takes a drug called hydroxyurea to manage her sickle cell disease.



"If a physician can induce the patient's fetal hemoglobin to above 20 percent, you effectively reduce the number of times the patient is admitted to the hospital."

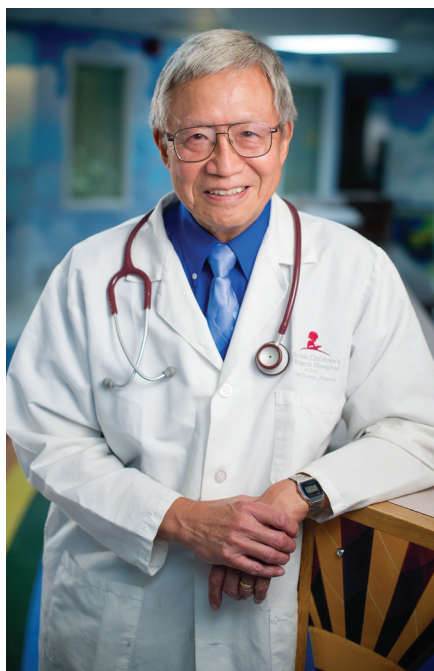
– Jeremie Estepp, MD



#### Hydroxyurea and health

Jeremie Estepp, MD, chats with Courtney Davis during a recent visit to St. Jude. As Courtney's fetal hemoglobin level has increased, her health has improved.





## New Research: Hydroxyurea and IQ Levels

Winfred Wang, MD, of St. Jude Hematology, recently discovered that hydroxyurea may have another benefit for school-aged children with sickle cell disease. Research shows the drug protects and possibly improves the children's ability to learn, think and understand.

After a year of hydroxyurea treatment, IQ scores of children in the study increased by about three points.

IQ scores tended to drop in patients whose parents declined hydroxyurea therapy.

The study is among the first to demonstrate such benefits from hydroxyurea.

## Sickled cells and traffic jams

Sickle cell disease can cause pain crises, pneumonia and organ damage. The disorder occurs because of problems with hemoglobin. This molecule in red blood cells ferries oxygen throughout the body.

Babies born with sickle cell disease are protected early in life by fetal hemoglobin. However, when the fetal hemoglobin level begins to drop off as children age, the flexible, round red blood cells become rigid and rod-shaped. That sickle shape makes it difficult for the blood cells to squeeze through tiny blood vessels.

The resulting traffic jam can cause life-threatening problems. Hydroxyurea can keep hemoglobin levels high, reversing the effects of sickle cell disease.

Jeremie Estepp, MD, a hematologist at St. Jude Children's Research Hospital, and his colleagues recently published a paper in the *American Journal of Hematology*. The findings may resolve a debate about the best dose of hydroxyurea. This issue is crucial for Courtney and others with the disease.

## The Goldilocks effect

Courtney started taking hydroxyurea when she was 3 years old. Now, doctors recommend children with the disease begin taking it at 9 months. Estepp says about 400 to 450 patients in the St. Jude Hematology Clinic take the medication.

When taken daily, hydroxyurea helps prevent abnormal sickle-shaped red blood cells from forming. The drug also reduces other problems related to the disease.

Hydroxyurea improves the efficiency of oxygen-carrying proteins in red blood cells.

Like the bowl of porridge in "Goldilocks and the Three Bears," the dose of hydroxyurea needs to be just right—not too low and not too high. A dose that's too low is not as effective as it could be. A dose that's too high can cause a drop in the number of white blood cells, which fight off infection.

So what's the best dose?

Some doctors use a minimal effective dose, increasing the dose until improvement occurs. Others use a

maximum-tolerated dose (MTD). They find the highest possible dose that avoids unacceptable side effects. Still other doctors combine the two regimens, using elements of both approaches.

## Do the HUSTLE

As part of the federally funded HUSTLE study, Estepp and other researchers followed 230 patients with sickle cell disease for four years.

For new patients, physicians started with a dose that was low, safe and well tolerated. Then doctors gradually increased that dose to achieve MTD. The goal was to minimize the risk of complications by giving the highest dose of hydroxyurea possible to provide the best response in patients' white blood cells, hemoglobin and fetal hemoglobin levels.

More than three-quarters of participants reached the MTD level. During four years of follow-up, their average level of fetal hemoglobin at MTD was above 20 percent. By keeping the fetal hemoglobin at that level, doctors found success.

When fetal hemoglobin fell to 20 percent or less, children were twice as likely to be hospitalized for any reason, and more than four times as likely to be admitted for fever.

"If a physician can induce the patient's fetal hemoglobin to above 20 percent, you effectively reduce the number of times the patient is admitted to the hospital for pain, acute chest syndrome or for any reason at all," Estepp explains.

## Avoiding pain and suffering

Courtney's mother, Audrey, vividly remembers her daughter's first pain crisis.

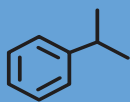
"She screamed at the top of her lungs," Audrey recalls, remembering the toddler's attempt to walk a few steps. "I'm holding my child when I look down and see her toes are double the size they should be."

Audrey's nephew died of sickle cell anemia complications when he was 2 years old, a tragic reminder of what's at stake.

Audrey understands the importance of reducing the complications and hospitalizations associated with sickle cell disease. Courtney was hospitalized



# How Does Hydroxyurea Work?



Sickle cell disease occurs because of problems with hemoglobin. This **molecule** in red blood cells ferries oxygen throughout the body.



**Babies** born with sickle cell disease are protected early in life by fetal hemoglobin.



When the fetal hemoglobin level begins to drop off as children age, the flexible, round red **blood cells** become rigid and **rod-shaped**.



That sickle shape makes it difficult for the blood cells to squeeze through tiny **blood vessels**.



The resulting **traffic jam** can cause life-threatening problems.



Hydroxyurea can keep hemoglobin **levels high**, reversing the effects of sickle cell disease.

more than 20 times in 16 years, most recently with acute chest syndrome, a life-threatening complication.

## Worth the effort

More than 90 percent of sickle cell patients at St. Jude regularly take their medications, a rate much higher than that of many other institutions.

"We expend a lot of effort to keep patients engaged in clinic," Estep says.

After beginning hydroxyurea, patients must wait up to six weeks to notice improvement. Then they must wait an additional eight to 10 months to achieve MTD. As a result, progress seems to occur in slow motion, as patients experience fewer and fewer complications. Because of

that lag time, medication adherence can be difficult to maintain.

Estep attributes the hospital's high adherence rate to the resources St. Jude provides. A large team of doctors, nurse case managers, social workers and other staff provides ongoing support.

"We'll even send a car to get them," Estep says, referring to patients who miss appointments for lab checks. Patients can also fill their prescriptions at St. Jude, a convenient and time-saving benefit.

## The bottom line

For Estep, the implications of his study are clear.

"The findings mean that if you're treating somebody with hydroxyurea and they are

not at maximum tolerated dose and have a hemoglobin of less than 20, you should increase their dose," he says. "You could potentially reduce the risk of hospitalization by 50 percent."

Unfortunately, not every patient can achieve a 20 percent fetal hemoglobin level. Doctors cannot predict how well a patient will respond to hydroxyurea. Also, researchers do not fully understand why some patients respond better to the medication than others.

"I don't think Courtney's at 20 percent yet," says Audrey, referring to her daughter's fetal hemoglobin level. But Audrey says the level has increased with treatment. As a result, Courtney's health has improved, reducing the number of complications and hospital admissions.

"I just feel better," Courtney says. "I have so many fewer pain crises than I did when I was younger."

## A promising future

Estep and his colleagues continue to flesh out the best dosing strategy for hydroxyurea. A pilot study is underway for a multicenter trial to evaluate a low fixed-dose of hydroxyurea versus escalation to MTD. That study should help investigators better understand the benefits of elevating fetal hemoglobin in young children.

Estep is also interested in expanding access to hydroxyurea worldwide and opening combination therapy studies.

Courtney will likely be one of the first to enroll in an upcoming combination therapy clinical trial. She is excited about combining another medication with hydroxyurea to possibly achieve even greater benefit.

For Courtney, excellent clinical care has offered her the chance to live a normal teenage life: walking her dog, preparing for college and hanging out with friends.

"St. Jude is such a loving and amazing place," Courtney says, reflecting on her years as a patient. "I know that there are people who are working so very hard for me to improve." ■



# Home Run

## St. Jude

On the 10th anniversary of the **St. Jude LIFE long-term follow-up study**, one of the hospital's earliest patients reflects on the hospital and his legacy.

By Dwight Tosh



As a 13-year-old boy in 1962, my life revolved around baseball and basketball. I dreamed my legacy would be to hit a game-winning home run in the World Series or a buzzer-beater in the championship game. So when I started to feel weak and run a fever, my parents and I were shocked to learn I had cancer. Suddenly, I was staring death in the face.

At our local hospital, they advised my family to prepare for the worst. Then my parents found out about a new hospital in Memphis, Tennessee.

Ultimately, my legacy was not to be a sports hero. My legacy was to be patient No. 17 at St. Jude Children's Research Hospital.

There, we found something we didn't have before: *hope*. St. Jude wrapped its arms around me, and they never let go. The day I arrived, they literally carried me through the front doors. When I left, I walked out on my own.

In 2007, I was the first survivor to enroll in a long-term follow-up study called St. Jude LIFE. I had often wondered if my health issues were related to my cancer treatment. I thought this study might help me answer that question. But my involvement might also help other children. If there's anything I could do to prevent some mom or dad from having to say goodbye to their child, I stood ready to do it.

Ten years later, St. Jude LIFE has brought thousands of childhood cancer survivors to campus for regular health screenings. As a result, scientists are making exciting discoveries about the long-term effects of cancer and its treatment.

I've lived a full and productive life. I married my high school sweetheart, and we've got two wonderful kids and four outstanding grandchildren. My hope and prayer would be that every child at St. Jude would someday be able to do what I've been able to do—to explain, more than 55 years later, how St. Jude helped them when it seemed there was no hope at all. ■

*After a 37-year career with the Arkansas State Police, Dwight Tosh was elected to the Arkansas House of Representatives, where he serves today.*



# Celebrating 10 years of St. Jude LIFE

## What is St. Jude LIFE?

Since 2007, the St. Jude LIFE long-term follow-up study has invited St. Jude childhood cancer survivors back to campus for medical testing. The goal is to find out if they have side effects related to their cancer or its treatment.

St. Jude LIFE has become one of the nation's most significant survivorship research efforts.

## Who enrolls in St. Jude LIFE?

The study follows cancer survivors throughout their lifetimes. St. Jude cancer patients who are five years past treatment are eligible to take part.

More than 5,000 St. Jude patients have enrolled, with the numbers steadily increasing.

## Why do childhood cancer survivors agree to take part?

Through the study, survivors:

- Learn how childhood cancer treatment has affected their health
- Find out what they can do to lead healthful lives
- Help researchers better understand the long-term effects of cancer therapy
- Help scientists learn more about how genetics contribute to lifetime cancer risk

The study's findings will help researchers save more lives while reducing the side effects of treatment.

## What happens during a St. Jude LIFE visit?

The typical survivor visits the hospital for two or three days.

The visit usually includes:

- Physical exam
- Tests of walking, flexibility, muscle strength, heart rhythm, hearing, lung capacity, balance and overall physical performance
- Blood tests, X-rays and other medical tests, depending on the type of treatment the survivor received as a child
- Consultation with a clinical social worker

## What are we learning from the study?

About 85 scientific papers reporting on St. Jude LIFE findings have been published or are in press.

Many of the results will be used to design future cancer treatments.

St. Jude LIFE has shown that most childhood cancer survivors have at least one chronic health condition.

The overall frequency of these complications has decreased as cancer therapies have become more individualized.



### Ten for 10

A decade after enrolling in the St. Jude LIFE long-term follow-up study, Dwight Tosh returns for a checkup. Jeremy Crowe of Epidemiology and Cancer Control administers Tosh's fitness tests in the Human Performance lab.

"I had often wondered if my health issues were related to my cancer treatment. I thought this study might help me answer that question. But my involvement might also help other children."

— Dwight Tosh



A dedicated team of experts advances research and care for **histiocytosis**.

Still  
**RARE,**  
No Longer  
**OBSCURE**

By Maureen Salamon





**For six long months,** tiny Jamie Jones lay in a hospital, hooked to a feeding tube. Clinicians puzzled over the mysterious illness that wracked her little body. Her gut could not absorb nutrients, causing severe weight loss. Her liver had grown to fill her belly, which made breathing difficult. Finally, a biopsy revealed that an apparent diaper rash was actually a sign of a rare and dangerous disorder.

Doctors rushed Jamie to St. Jude Children's Research Hospital. There, she had an incredible turnaround, thanks to her oncologist and the Histiocytosis Treatment Team.

Patrick Campbell, MD, PhD,  
and Jamie Jones





JUSTIN VENNEMAN

## Collaborating for cures

The Histiocytosis Treatment Team includes (from left) oncologist Patrick Campbell, MD, PhD; Melissa Hines, MD, of Critical Care; Kim Nichols, MD, of Cancer Predisposition; and Gabriela Marón, MD, of Infectious Diseases.

The name of Jamie's diagnosis is a mouthful: Langerhans cell histiocytosis, or LCH. This disease occurs when abnormal immune cells known as histiocytes grow and divide nonstop, often killing healthy cells nearby.

St. Jude is leading international efforts to ensure Jamie and others with histiocytosis benefit from treatment advances.

Now age 4, Jamie continues to receive care at St. Jude, including physical therapy to offset lingering weakness. She loves to sing and dance and play school with her two older sisters.

"I don't have the words to explain how it feels to be a parent who watched her child lying there lifeless—and now she's walking around, smiling and jumping," says Jamie's mom, Teairra Ramsey. "Just to see her now is a blessing."

## A dedicated team of experts

The team that took care of Jamie includes experts in cancer, genetics, critical care, infectious diseases, cancer predisposition and bone marrow transplant.

"I believe the knowledge and expertise of our Histiocytosis Treatment Team rival that of any place in the country or the world," says Jamie's oncologist, Patrick Campbell, MD, PhD, St. Jude associate chief medical information officer.

The two main types of histiocytosis

are LCH and hemophagocytic lymphohistiocytosis, or HLH. The rarity of these diseases makes them difficult to study and understand.

"All we knew for a long time was that special immune cells called histiocytes were found in the tissue of patients who were sick," says Melissa Hines, MD, of St. Jude Critical Care. "But what we've come to understand is that the way LCH and HLH come about and the illness caused by them are completely different.

"HLH is a defect in the immune system where your body cannot turn off inflammation," she continues. "Typically, if you get

really sick, your body has an automatic stop button to dampen the immune response, but in HLH that emergency stop button doesn't exist. LCH is quite different. We think LCH is more like cancer than an inflammatory disorder, but it has components of both."

As many as two dozen children with histiocytic disorders are treated at St. Jude annually. The hospital's experts also consult on many additional cases.

## A spectrum of symptoms

Early recognition and treatment are critical to ensure the best outcomes for LCH and HLH. But identifying and treating these disorders has long been a challenge. Symptoms range from mild, such as a skin

## What are histiocytic disorders?

These conditions affect the **immune system**. Children with histiocytic disorders have abnormal cells that no longer protect the body against infection. Instead, the cells become overactive, damaging tissues and organs such as the **liver, bone marrow, spleen** and **central nervous system**.

### Hemophagocytic Lymphohistiocytosis (HLH)

- In HLH, normal immune cells divide nonstop and release large amounts of certain **chemicals** into the blood. These chemicals cause the HLH symptoms.
- About **1** out of every **50,000–100,000** children has HLH.
- There are **2** major types of HLH:
  - **Familial HLH** can be passed down through families.
  - **Acquired HLH** is thought to result from certain infections, cancers and autoimmune disorders.
- HLH survival rate: about **50%**.

### Langerhans Cell Histiocytosis (LCH)

- In LCH, **abnormal Langerhans cells**, a type of histiocyte, multiply in different tissues. The abnormal cells form tumors and activate other immune cells, causing LCH symptoms.
- About **2 to 3** out of every **1 million** children have LCH.
- LCH shares similarities to some cancers. LCH often requires treatment with **steroids** to calm inflammation and **chemotherapy** to kill amped-up immune cells.
- Low-risk LCH survival rate: **99%**; high-risk: about **80%**.



rash, to dire, such as multi-organ failure.

Scientists have learned that in some HLH patients, the disorder is caused by inherited changes in certain genes. In other HLH patients, those genes contain no obvious changes; however, the patients may be more apt to develop the disorder after an infection or as a result of a cancer or autoimmune disease.

In LCH, there's no such risk factor, Campbell explains. While LCH and HLH are quite different, what unites them, he says, is how tough they are to diagnose. The array of symptoms—like Jamie's—often resembles something else entirely.

### The need for research

Five-year survival rates for children with HLH hover at about 50 percent, reinforcing the need for more research.

Kim Nichols, MD, St. Jude Cancer Predisposition Division director, and her colleagues are working to better understand the cellular processes that cause HLH. In the lab, her team recently discovered a promising new HLH drug. This medication blocks specific signaling pathways to dampen inflammatory responses. The researchers found that the medication significantly lessens disease signs and symptoms. The drug will soon be tested in patients with HLH.

"It's fantastic to have a Histiocytosis Treatment Team where we can discuss patients and bounce research ideas off each other," Hines says. "St. Jude can give information back to the scientific communities about what to do with these disorders in the future. The group has allowed us to better solidify research ideas and decide where we're going to go next as far as testing therapeutics for both LCH and HLH and starting clinical trials."

### New treatments on the horizon

At St. Jude, histiocytosis treatment is tailored to each patient. Children with mild disease may require only a watch-and-wait approach. Others may become critically ill and need bone marrow transplants to survive. Therapies often include steroids to calm inflammation and chemotherapy

to kill amped-up immune cells.

Scientists recently made an important discovery about LCH, the disorder Jamie battled.

Researchers found a mutation in the *BRAF* gene in LCH tumors. Unlike the gene changes in HLH, the mutations in LCH tumors are not inherited. The *BRAF* mutation is found in about half of LCH tumors. About 35 percent of additional LCH tumors have mutations in related genes, Campbell says. The presence of these mutations convinced scientists that LCH is a cancer-like disease.

The altered genes also pointed the way toward using targeted therapy. This

treatment attacks overactive immune cells without harming other cells. Oral drugs known as *BRAF* inhibitors are now being used to treat children with LCH who have failed other treatments and whose disease contains the *BRAF* mutation. More targeted treatments are on the horizon.

That's progress Jamie and her family appreciate every day.

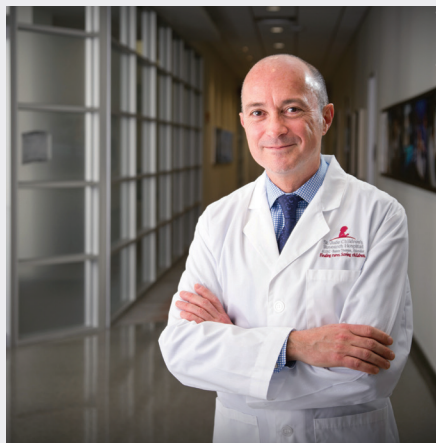
"She's had an unbelievably good response," Campbell says. "Her progress shows the kinds of advances and benefits of these newer therapies." ■

### Learn more:

[stjude.org/histiocytosis-treatment](http://stjude.org/histiocytosis-treatment)

## St. Jude-based NACHO chomps down on research

Carlos Rodriguez-Galindo, MD, has long had a soft spot for so-called orphan diseases. These conditions are so rare that little interest or funding is generated for extensive scientific research. So it seems natural that histiocytosis—a life-threatening group of disorders affecting the immune system—would hit his radar.



Rodriguez-Galindo is executive vice president and chair of Global Pediatric Medicine at St. Jude. He is also a founding member and co-leader of the North American Consortium for Histiocytosis, better known as NACHO.

The consortium consists of nearly three dozen institutions. NACHO's members work closely to develop new and better treatments for histiocytic disorders and test them in clinical trials.

The clinical trials organized through NACHO are available to children treated at St. Jude, which is the consortium's center of operations. With so few patients worldwide—perhaps three children in a million—collaborating with others is crucial to finding ways to improve outcomes.

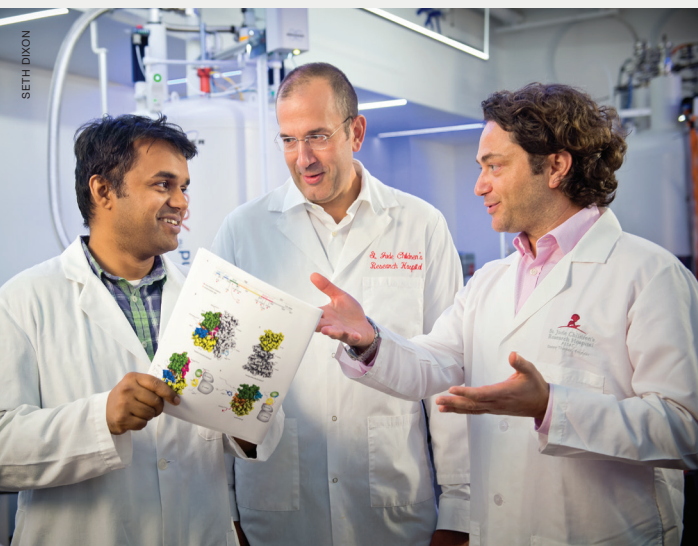
The discovery that Langerhans cell histiocytosis is often driven by a gene mutation implicated in other cancers paved the way for NACHO to sponsor three clinical trials and two basic-science studies.

"Pediatric cancer is already a rare disease, but the rarest of the rare actually may fall through the cracks in terms of benefiting from knowledge, resources and clinical trials," Rodriguez-Galindo says. "We need to really understand histiocytosis better. We need to find better ways to treat these kids."



## SCIENCE comes to life

St. Jude patients and siblings recently teamed up with the hospital's research staff for a Hands-on Science Fair. Ceylin Kubali looks through a microscope at one of the science fair stations under the guidance of Sajjan Koirala, PhD, Cell and Molecular Biology.



From left: Tamjeed Saleh, PhD, Paolo Rossi and Charalampos Kalodimos, PhD

## SHAPE-SHIFTER'S STRUCTURE regulates activity

St. Jude structural biologists have figured out how the structure of an enzyme called Abl regulates its activity.

Abl switches itself on and off by altering its shape. Knowing how that works is important because a mutant form of the enzyme (Bcr-Abl) is over-activated in chronic myeloid leukemia (CML) and other cancers.

Abl controls growth in white blood cells. The enzyme's over-activation spurs mutated cells to multiply, causing leukemia.

Although clinicians have successfully treated CML with drugs that switch off the enzyme, Abl often mutates to become drug resistant. The St. Jude study reveals new details about such drug-resistant mutations. The findings also offer a path to possible treatments to overcome that resistance.

The research, led by Charalampos Kalodimos, PhD, St. Jude Structural Biology chair, appeared in *Nature Structural & Molecular Biology*.



## ANTIBIOTIC reduces infection risk in leukemia patients

St. Jude researchers recently identified that an antibiotic could greatly reduce the risk of infections in children who were beginning treatment for acute lymphoblastic leukemia (ALL). There was no sign that the drug increased antibiotic resistance.

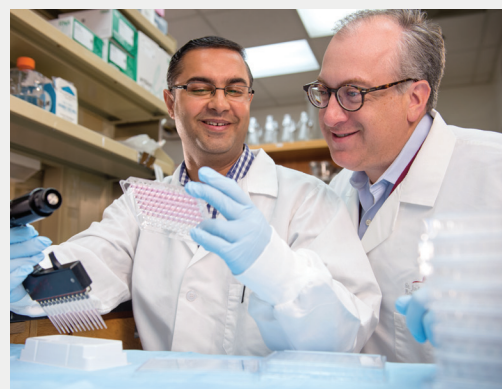
The early weeks of chemotherapy often lead to a drop in white blood cells. This problem leaves patients at risk for life-threatening infections. The St. Jude study was the largest yet to gauge the safety and effectiveness of preventive antibiotic therapy in these children.

Joshua Wolf, MD, and his colleagues found that preventive therapy with levofloxacin or other antibiotics reduced the odds of infection by 70 percent or more. Levofloxacin also reduced patients' odds of infection with *Clostridium difficile* by at least 95 percent. This is important, because children with hospital-acquired *C. difficile* infections have a nearly seven-fold increased risk of death.

The findings were used to help design the infection prevention component of a new St. Jude clinical trial for children and adolescents with ALL.

A report on this research appeared in the journal *Clinical Infectious Diseases*.

From left: Dakota Cunningham, Sima Jeha, MD, and Joshua Wolf, MD



From left: Amit Budhraj, PhD, and Joseph Opferman, PhD

## ANTI-MALARIA DRUG paves way for targeted therapy

St. Jude scientists have shown that an anti-malaria drug sensitizes a high-risk subtype of acute lymphoblastic leukemia (ALL) to treatment. The discovery raises hopes for more effective therapy.

The study focused on BCR-ABL–positive ALL, also known as Philadelphia chromosome–positive ALL. This subtype accounts for about 5 percent of childhood ALL cases and about 40 percent of adult cases.

Five-year survival for children with this subtype is about 70 percent and about 50 percent for adults. The path to a cure involves intensive chemotherapy and blood stem cell transplants.

BCR-ABL–positive ALL has resisted targeted therapies that have been successful with other leukemias.

In this study, researchers showed that an anti-malaria drug called DHA made cancer cells sensitive to a drug called ABT-263. The scientists also showed how that happened.

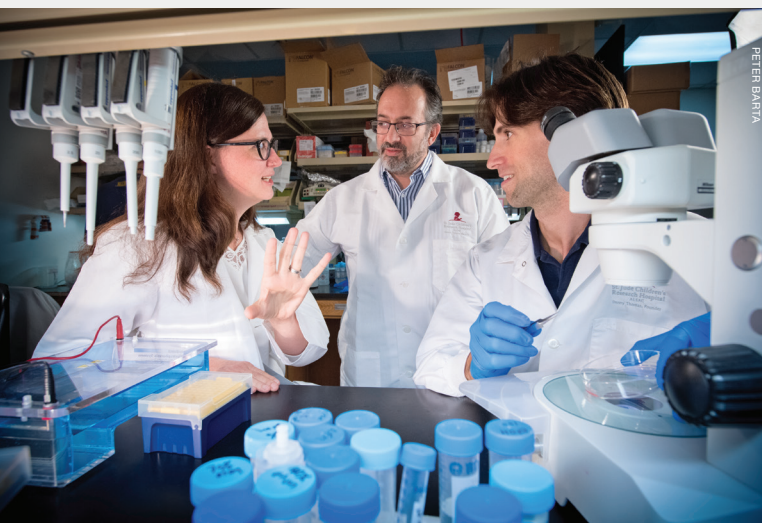
“Our findings suggest that combining DHA with ABT-263 can significantly improve treatment response,” said Joseph Opferman, PhD, of St. Jude Cell and Molecular Biology.

A report on this work appeared in *Clinical Cancer Research*.

PHOTOS BY SETH DIXON



## DISCOVERY offers insight into disease origins



From left: Shannon McKinney-Freeman, PhD, David Finkelstein, PhD, and Miguel Ganuza, PhD

Like genealogists filling gaps in a family tree, St. Jude scientists have found that lifelong blood production relies on hundreds more “ancestor” cells than previously reported.

Blood-forming stem cells have the capacity to make any type of blood cell in the body. These cells form from precursor cells that emerge during prenatal development. The cells specialize to become the heart, kidneys, blood and other organs.

“All previous studies had reported that very few precursor cells are involved in establishing the blood system,” said Shannon McKinney-Freeman, PhD, of St. Jude Hematology. In the lab, she and her colleagues found that blood-forming stem cells arose from about 500 precursor cells rather than fewer than 10, as was previously assumed.

Blood-forming stem cells are used to restore blood production and immunity in bone marrow transplant patients. Understanding how the blood system develops provides insight into the origins of infant leukemia and other blood diseases. The study was published in the journal *Nature Cell Biology*.

## THE PATH to precision

St. Jude scientists have discovered a promising target for precision medicines to block a mechanism that drives several cancers, including the brain tumor medulloblastoma.

In about 30 percent of patients with medulloblastoma, a signaling pathway called Sonic Hedgehog is switched on by mistake. This causes cells to divide uncontrollably.

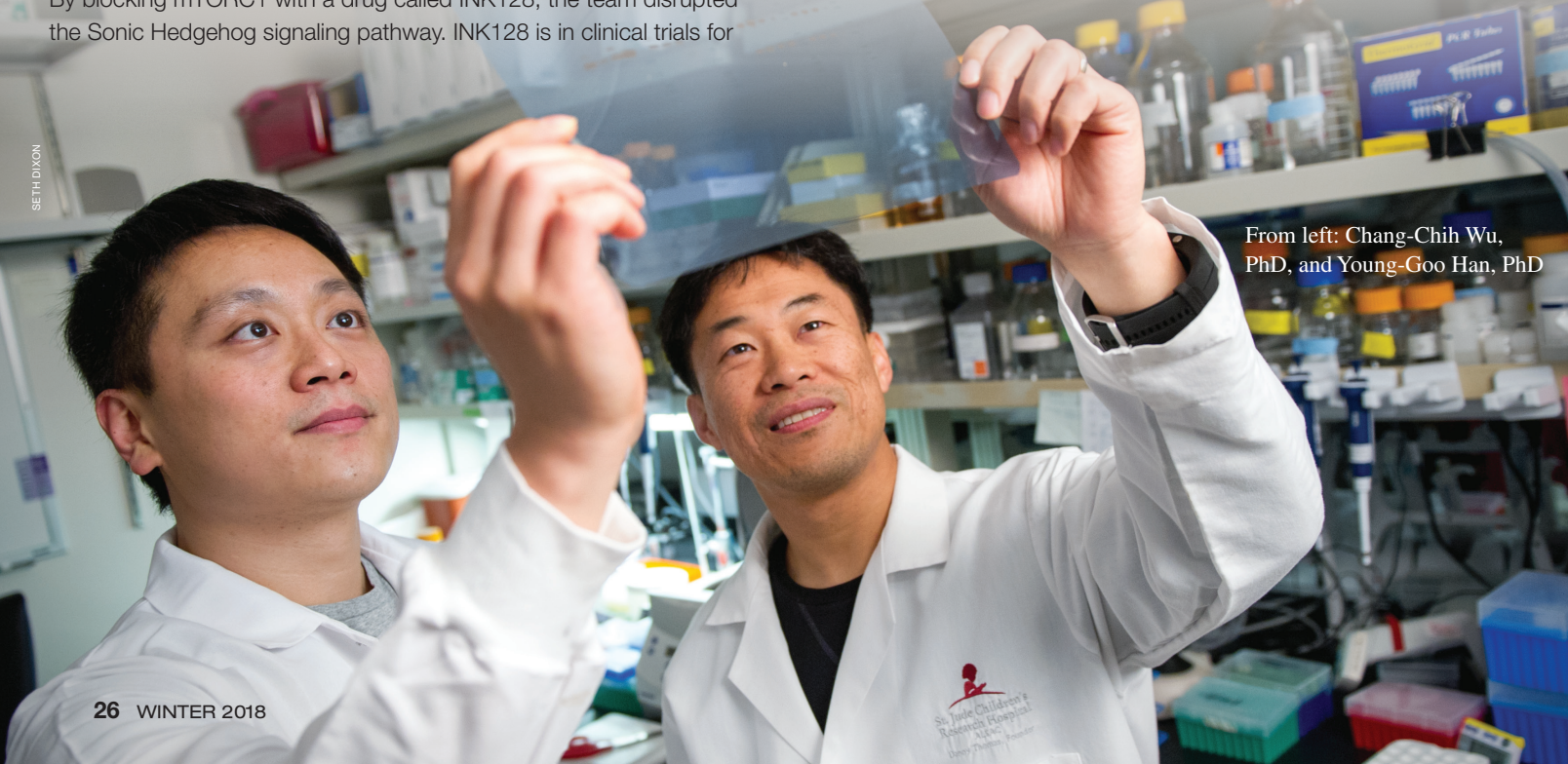
The researchers found that the Sonic Hedgehog pathway depends on another pathway that requires mTORC1 to function.

By blocking mTORC1 with a drug called INK128, the team disrupted the Sonic Hedgehog signaling pathway. INK128 is in clinical trials for

treatment of another brain tumor and other solid tumors.

“The role of mTORC1 in the Hedgehog pathway was unexpected. It highlights the mTORC1 pathway as a potentially important molecular target for developing much-needed precision medicines for patients with the Sonic Hedgehog medulloblastoma subtype,” said Young-Goo Han, PhD, of St. Jude Developmental Neurobiology. “The results also raise hopes for combination targeted therapies to improve outcomes and ease treatment side effects.”

The findings appeared recently in the journal *Developmental Cell*.



From left: Chang-Chih Wu, PhD, and Young-Goo Han, PhD





Elisabeth Adderson, MD

## YOUNG LEUKEMIA patients need extra flu protection

A St. Jude study published in the *Journal of Pediatrics* showed that young leukemia patients who were vaccinated against influenza were just as likely as their unvaccinated peers to develop flu.

The study looked at rates of flu infection during three flu seasons in 498 St. Jude patients being treated for acute leukemia. Researchers found the patients who received flu shots had almost identical rates of flu and flu-like illness as patients who were not vaccinated.

Doctors still recommend the annual flu shot for children with acute leukemia.

"The results highlight the need for additional research in this area and for us to redouble our efforts to protect our patients through other means," said Elisabeth Adderson, MD, of St. Jude Infectious Diseases.

Along with good hand hygiene, Adderson said at-risk patients should avoid crowds during the flu season. Patients may also benefit from "cocooning," a process that focuses on getting family members, health care providers and others in close contact with at-risk patients vaccinated.



## CELEBRATION of survival

Hundreds of survivors and their families returned to the St. Jude campus in September for a celebration filled with reunions, reflections and camaraderie. Tim Folsie, MD (center), was among dozens of faculty and staff who attended the event, which also featured speaker and best-selling author Wendy Harpham, MD.

## TEENS with cancer may benefit from more support



Liza-Marie Johnson, MD

one percent had experienced multiple losses through death. Thirty-seven percent of the patients had lost friends, with two-thirds related to cancer.

Researchers found that about a third of the patients had rarely or never talked to anyone else about their losses.

"This private, often unrecognized grief may make it more difficult for patients to process or make meaning of a death," said Liza-Marie Johnson, MD, of St. Jude Oncology. "It also leaves them at increased risk for depression, anxiety and other problems."

Johnson said the results highlight the need for long-term studies to understand and support adolescents and young adults who are going through bereavement while coping with life-threatening illnesses.

A report on this research appeared in the journal *PLOS One*.

Teens and young adults with cancer have experienced more death, particularly of friends, than their healthy peers. But recent St. Jude research shows that many of these patients rarely, if ever, talk about their losses.

Eighty percent of St. Jude patients surveyed in a recent study had experienced the death of a relative, friend or someone else. Sixty-





**"We arrive in the middle of a busy workday so our staff members are reminded that people are thankful for what they do and that what they do is noticed and recognized."**

**Chaplain Mark Brown**

Chaplains Walter Spears (center) and Mark Brown serve up lively conversation and elegant snacks to staff.

# An Expression of Grace

St. Jude chaplains' Tea Time offers clinicians welcome interruptions to busy workdays.

By Mike O'Kelly

It's a busy Thursday in the Assessment/Triage Clinic at St. Jude Children's Research Hospital. Suddenly, the doors of the bustling unit swing open. Nurses look up from their posts as they hear rolling wheels and light footsteps echo through the clinic.

The smiling faces of chaplains Mark Brown and Walter Spears of St. Jude Spiritual Care Services greet the clinic's staff.

"It's Tea Time," Brown cheerfully exclaims, as the duo guides a refreshment cart to the clinic's break room.

Word of the afternoon visitors spreads quickly. Staff members find their way to the area for refreshment and conversation.

"Y'all have made my whole day," says Samantha Brannon, an Assessment/Triage nurse, who is one of the first in line for the selection of tea, coffee, hot chocolate and three types of scones baked by St. Jude Food Services.

Tea Time with the Chaplains began in 2013 as a surprise respite for clinicians throughout the hospital. Two of the hospital's four chaplains spend an afternoon each month visiting clinical areas to serve refreshments.

Chaplains offer the warm beverages in fine china—cup and saucer included. There are no to-go cups, a touch of elegance that encourages a few minutes of face-to-face interaction. Cart-side discussions range from workday experiences to more personal conversations about life.

"What we are doing is bringing an expression of grace into the workplace," says Brown, who coordinates the program. "We arrive in the middle of a busy workday so our staff members are reminded that people are thankful for what they do and that what they do is noticed and recognized."

Jo Ann Powell, of St. Jude Assessment/Triage, says staff members look forward to the visits, which often are timed perfectly.

"We pretty much work nonstop in the mornings seeing patients," she says. "For our chaplains to do this shows that it's OK to take a break, enjoy a moment and have some social time."

"Tea Time is one of the most joyous things we do as chaplains," Brown says. "It is a moment of hospitality and care." ■



# Her future starts with your legacy.

©2018 ALSAC/St. Jude Children's Research Hospital (31847)



"The extraordinary work St. Jude performs for children, including those who are treated from other countries, cemented my commitment to leave a bequest for St. Jude in my will."

—Sandra Kitt

## Establish a lifesaving legacy that costs you nothing now.

Remembering St. Jude with a gift in your will costs you nothing now, yet gives you the satisfaction of knowing the legacy of your compassion will continue into the future, helping to save the lives of children like Rylee who are battling cancer and other life-threatening diseases.

**Begin your legacy today.**

(800) 910-3188 | [stjude.org/bequests](http://stjude.org/bequests)

St. Jude patient Rylee,  
osteosarcoma



*Finding cures. Saving children.*





501 St. Jude Place  
Memphis, TN 38105

Non-Profit Org.

**U.S. POSTAGE**

**PAID**

St. Jude Children's  
Research Hospital

## Fix 'er up, shave it off

Chip and Joanna Gaines, stars of HGTV's *Fixer Upper*, recently collaborated with Target to renovate the dining room at St. Jude Target House. Chip also promised to cut his hair if the couple's social media followers raised \$25,000 for the hospital.

The public rose to the challenge, raising \$230,000. After unveiling the Target House renovation, Chip fulfilled his part of the bargain by shaving his head—to the delight of fans, as well as patients and families of St. Jude.

MIKE BROWN



*Finding cures. Saving children.*