St. Jude promise

stjude.org/promise spring 2017

St. Jude solves **mysteries** of **high-risk leukemias** *pg. 10*

Clinic ensures **babies, toddlers** continue to grow and **develop** *pg. 16*

St. Jude Children's Research Hospital
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04

Cover story

Features

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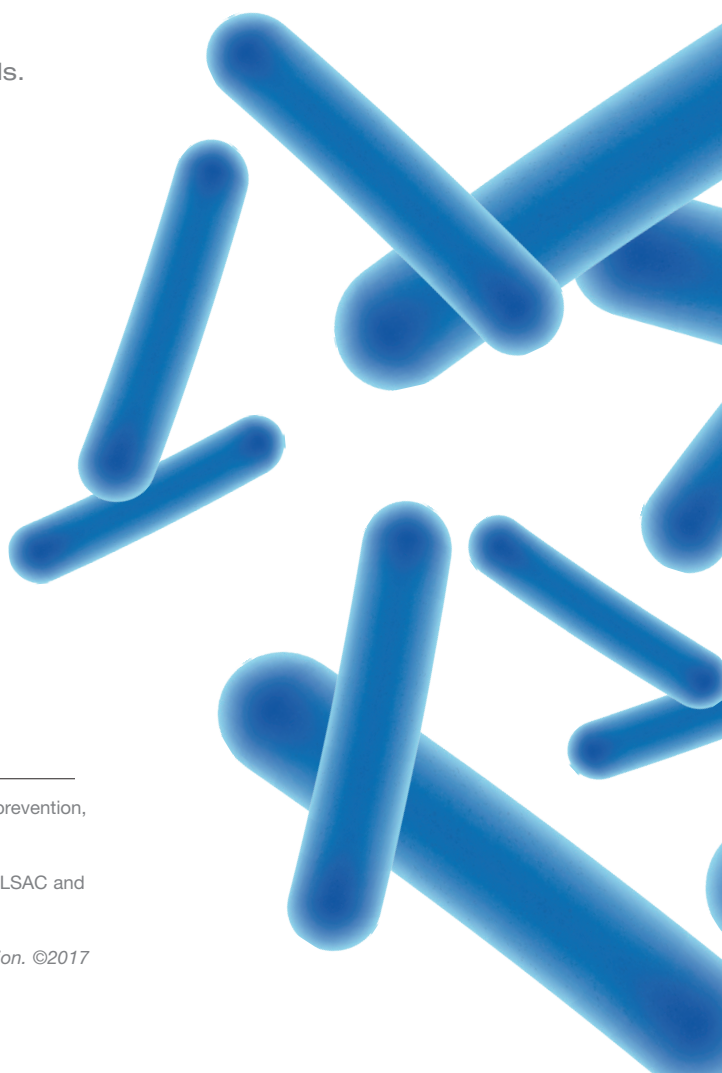
SPRING 2017

Research Highlights

Where Are They Now?



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.

On the cover:
Stella Ellwood
Photo by Peter Barta

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A Different Kind of Donation

By Corey Carmichael

JUSTIN VENEMAN

St. Jude volunteer Chris Clark celebrates his 400th donation to the St. Jude Blood Donor Center.

St. Jude performs about 800 blood product transfusions each month. You can help a child by donating blood or platelets in Memphis.

As a contractor, Chris Clark uses the materials and tools at his disposal to build, create and accomplish his goals. So when he considered helping St. Jude Children's Research Hospital, he turned to the tools at his disposal: donations of time and blood products.

Clark began donating platelets at the St. Jude Blood Donor Center in 1996. Since then, he has returned to St. Jude for donations twice each month. He also volunteers regularly in the hospital's patient care areas.

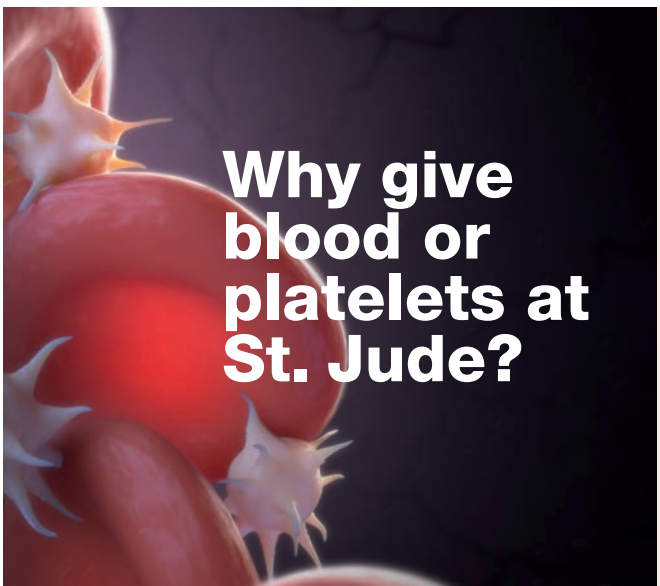
"When you sit with patients, you realize how grateful you are to be in a position to support St. Jude," Clark says.

Throughout the years, he has donated more than 400 units of platelets at the Blood Donor Center.

"It's so easy to give platelets," Clark says, "and there's no doubt that when you donate platelets, a patient will benefit."

Every day St. Jude performs about 15 to 25 platelet transfusions for children undergoing treatment. Through Clark's efforts, the center has saved up to $280,000 by not having to purchase blood products from outside suppliers.

If you live in the Memphis, Tennessee, area or plan to visit the hospital, you can schedule an appointment to donate blood or platelets. Call 901-595-2024 or 1-866-278-5833, ext. 2024. ■



Why give blood or platelets at St. Jude?

- All products collected at the St. Jude Blood Donor Center go directly to St. Jude patients.
- By donating blood products at St. Jude, you help the hospital offset the cost of having to purchase blood products from outside sources.
- Purchasing one unit of platelets from an outside provider costs the hospital between $500 and $700. A whole-blood unit costs about $250.
- About 800 blood product transfusions are performed during a typical month at St. Jude.
- A patient whose treatment involves a bone marrow transplant will typically require 20 units of whole blood and 120 units of platelets during treatment.

On National DNA Day, local students learn about the famous double helix through fun, interactive science "camps" led by St. Jude researchers.

Schooled in Science

St. Jude research comes alive for students and their teachers.

By Carole Weaver, PhD

Kate Ayers vividly remembers a moment when she saw her teaching completely change someone's life.

"One of my middle school students had lived her whole life thinking she would definitely have cancer one day, just because her mom had it when she was pregnant with her," Ayers recalls.

"When we went through the science and she realized that wasn't true, she was so relieved—you could see it immediately on her face. She let out a huge sigh. And the thing is, she hadn't even known to ask the question."

Today, as Ayers coordinates educational activities for St. Jude Children's Research Hospital, she continues to give students—and their teachers—"a-ha" moments about the science of cancer.

"St. Jude is not just helping children with catastrophic diseases," Ayers says. "We are also impacting the lives of children in our local community. And we are helping them learn about science careers they might never have considered."

One of several major outreach initiatives, the St. Jude Cancer Education for Children Program brings Ayers and a volunteer cohort of researchers, called St. Jude Science Ambassadors, to local classrooms and libraries. There, they teach elementary, middle and high school students about the science of cancer and how a healthy lifestyle can help prevent disease. The volunteers also bring science alive by sharing personal stories about their lives as researchers.

PHOTOS BY JUSTIN VENEMAN

Peter Mercredi, PhD, a senior scientist in Therapeutics Production and Quality, brings the joys of science to elementary school students.

In local classrooms and libraries, St. Jude researchers bring science to life for young students.

2,000 balls in motion

Volunteering is a way for scientists to pay it forward, says Science Ambassador Laura Hamel, PhD, of St. Jude Developmental Neurobiology.

"I think back to what set my career in motion. I didn't know which direction to go, because in high school I was just absorbing everything," she says. "I was really good in math. I liked art. I loved playing field hockey. But what could I make a career out of? It was my teachers who said, 'Have you thought about going into the sciences?'"

Hamel now volunteers her personal time—outside of a heavy research workload—to feel the joy of sparking interest in science and scientific careers among a new generation of students.

"My high school experiences set that ball in motion," she says. "So for me, it's really exciting to be a part of something that could do that for someone else."

In 2016 alone, more than 2,000 Memphis-area students and teachers worked with Ayers and the Science Ambassadors. Thousands more explored freely available lesson plans and interactive case studies via the *Cure4Kids for Teachers* website and the *Cancer Education for Children* e-newsletter *(see sidebar, page 7).*

Double helix, double fun

Science Ambassadors also host other local and online educational activities. On National DNA Day, an annual event celebrating the discovery of the famous double helix, researchers bring fun, interactive science "camps" to local schools.

Last year, one of those camps was held steps away from researchers' labs at St. Jude. Patients in the hospital's school program were offered new ways to learn about science.

"It was terrific," says researcher Peter Mercredi, PhD. "We organized a lesson plan about sports drinks, and the kids were so interested."

Thanks to the event's success, more schools and libraries will be included this year, Mercredi says. "We'll be doing a 'monster DNA' project this year," he says. "It's really cool."

But no worries—no Dr. Frankenstein here. The monsters will be spooky, but strictly theoretical. By deciphering DNA code, students will spell out instructions for drawing a unique monster. "Their monster can have one eye, two heads, horns and features like that," Mercredi says. "And they'll get a big piece of paper to draw it on so they can keep the monster they build with their DNA code."

JUSTIN VENEMAN

"St. Jude is not just helping children with catastrophic diseases," **Kate Ayers** says. "We are also impacting the lives of children in our local community. And we are helping them learn about science careers they might never have considered."

Scholars in training

Bringing science to the classroom helps students imagine life as a researcher. But what if they could spend time in real laboratories?

Last year, St. Jude President and Chief Executive Officer James R. Downing, MD, encouraged the hospital's staff to provide such opportunities.

"Dr. Downing wanted to support the development of the next generation of scientists from our local community who could one day have careers at St. Jude," says Melissa Jones, of the hospital's Comprehensive Cancer Center. "He said, 'I want to bring high school students on campus and show them what we do.'"

Jones partnered to build the program with neurobiologist Suzanne Baker, PhD, who took the helm as faculty lead. They worked countless hours with a team that included Ayers; Comprehensive Cancer Center Director Charles Roberts, MD, PhD; other St. Jude faculty and staff; and a group of on-campus volunteers.

The team also had a secret weapon to help ensure the program would be engaging and exciting for students: "We found a core group of teachers who wanted to be involved and expressed a passionate interest in helping us develop the program," Jones says. "We held a focus group, and they asked Dr. Downing questions and had a nice exchange of ideas and concepts."

Since its launch, the annual Science Scholars of Tomorrow Symposium has welcomed hundreds of area high school students and their teachers to St. Jude for an event-filled day. While learning about the latest discoveries from renowned scientists, students experience slices of life at St. Jude. Students and teachers take lab tours, peer into state-of-the-art microscopes and scrub up for visits to the surgery suite.

"Our goal is to show kids first hand what it means to be a scientist, what it means to do cancer research, and how they can become part of that pioneering effort to make discoveries," Jones says. "We're teaching them to feel like this is a future that is available to them."

The model seems to be working. Jones recalls

one student's response to a talk by St. Jude neuropsychologist Heather Conklin, PhD.

"This student became so excited about becoming a pediatric neuropsychologist, and until that day he hadn't even known the profession existed. For him, it was like, 'Boom!'" Jones says.

> **"Our goal is to show kids first hand what it means to be a scientist, what it means to do cancer research, and how they can become part of that pioneering effort to make discoveries."**
> —MELISSA JONES

Teaching the teachers

Students aren't the only ones who have found their time at St. Jude transformative. Their teachers love it, too, according to feedback received after the symposium.

"This was an amazing experience for our students and for me," wrote one teacher.

"My students are still talking about it," wrote another. "They were completely enthralled."

Expanding the program's impact is exactly what organizers sought when they included teachers, Jones says.

"The more teachers we can reach, the more students we can reach," she says. "Those teachers are getting inspired, and they're making connections with professionals that help them enhance their own classrooms, their lessons and their curriculums."

The inspiration goes both ways.

"You never know what's going to light someone's fire," Ayers says. "When you see that light bulb turn on over their head, and see that they're truly engaged. That's what you look for—those moments." ■

St. Jude in Your Classroom

Do you teach science or know a science teacher? St. Jude offers a host of fun, interactive lesson plans and online resources designed to teach K–12 students about the science of cancer, healthy living and careers in research. These free resources are available at the *Cure4Kids for Teachers* website, ***cure4kids.org/teachers***.

Downloadable teaching tools
The website offers free resources for teaching the science of cancer, including videos, books, lesson plans, lab activities, worksheets and quizzes. Some materials are available in Spanish, French, Russian, Portuguese and Catalan. Topics can be tailored for students from elementary through high school levels. Key areas include cancer education, genes and genetics, health-related fitness, nutrition and sun exposure.

E-newsletter
Interested in updates on timely science topics and new teaching materials? Subscribe to the monthly *Cancer Education for Children* e-newsletter. The subscription link is on the website.

Science Sound Bites Podcast
This fun podcast makes science real for students by sharing casual conversations among St. Jude postdoctoral researchers, their colleagues and world-renowned scientists from St. Jude and other institutions. Visit *stjude.org/science-sound-bites.*

A global VISION

A NEW APP in clinical trials at St. Jude has the potential to save lives WORLDWIDE.

BY ELIZABETH JANE WALKER

"In every aspect, our future is focused on giving children everywhere the greatest hope for their future."

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

Four-year-old Lela Moody is a little ray of sunshine—singing, playing with her stuffed owl and spreading joy in her wake. Ironically, the little girl may be alive today because a ray of light hit her eye in just the right spot at just the right time.

In April of 2012, Mandy Moody noticed a whitish

PETER BARTA

Lela Moody's cancer was found early, but thousands of other children worldwide lose their lives each year because of late diagnosis and poor access to medical care.

reflection in her baby's eye. That tiny glare offered the only clue that 6-week-old Lela had an advanced case of the eye cancer retinoblastoma. At St. Jude Children's Research Hospital, surgeons removed her left eye but managed to preserve vision in the right eye.

Lela is fortunate, because her cancer was found before it spread further. But thousands of children in developing countries lose their lives each year because of late diagnosis and poor access to medical care.

As St. Jude extends its research and clinical care to the farthest reaches of the globe, a new clinical trial is harnessing the power of the mobile phone to provide early diagnosis—and to save the lives of children like Lela.

Early detection is key

Retinoblastoma is a rare cancer of the retina, the thin membrane at the back of the eye. If untreated, the cancer can spread to the optic nerve, brain, bones and bone marrow. The disease is usually discovered by parents who notice an abnormal glare in flash photos of their children. In a healthy child, the center of the eye may appear red in response to a bright light, but in retinoblastoma, the pupil may look white. That glow is known as leukocoria.

Carlos Rodriguez-Galindo, MD, chair of St. Jude Global Pediatric Medicine, says every child should have a light-reflex exam with an ophthalmoscope at every routine well-child visit at the pediatrician's office.

"If this were done properly, all kids with retinoblastoma would be diagnosed very early in the clinic," he says.

And yet, that rarely happens because of how difficult it is to perform this test in the clinic.

"In my years of seeing retinoblastoma patients—and I have seen hundreds of them—I have only seen a handful who came because a pediatrician or a nurse practitioner in the clinic detected the cancer with the light-reflex exam," he says. "All others are found when a parent said, 'Doctor, there's something wrong with my child's eye.'

"By the time a parent can see leukocoria, the tumor has already filled two-thirds of the eyeball," Rodriguez-Galindo adds. "That makes it more difficult to treat and save the eye."

Saving eyes and lives

About eight years ago, 4-month-old Noah Shaw was found to have retinoblastoma after his mom spotted a white reflection in photographs. As a result of that experience, Noah's dad, scientist Bryan Shaw, PhD, and his colleagues at Baylor University designed a program called CRADLE (Computer-Assisted Detector of Leukocoria) to scan photos for the tell-tale white reflex.

"When I analyzed my own family photo album of 9,000 pictures," Shaw says, "I found that my son's leukocoria started showing up when he was 12 days old. If he had begun treatment then, he might have been able to keep his right eye."

Not only will the app scan existing photos on a user's phone, but it can also evaluate a video taken by a clinician during an exam.

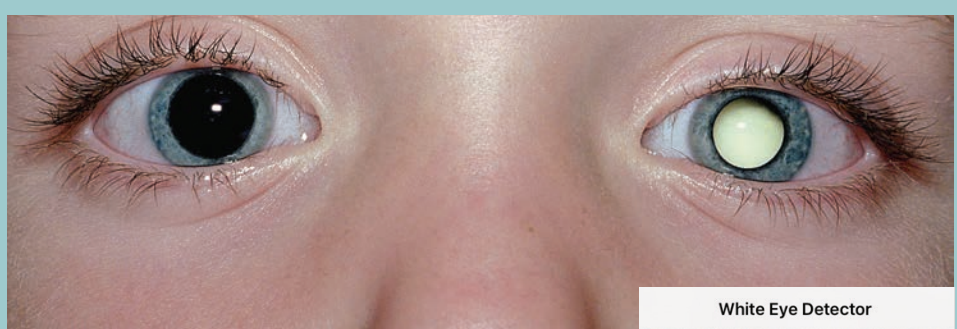
Now Rodriguez-Galindo, with the help of Harvard Medical School student Alexandra Power-Hays, is heading a St. Jude clinical trial to validate the app's sensitivity and determine how it works best. The long-term goal is to provide health care workers worldwide with a free tool they can use with confidence.

"In America, the proper use of this app may save eyes," Rodriguez-Galindo says. "But in countries with limited resources, the proper use of this app could actually save lives."

As soon as the clinical trial is complete and the tool has been validated, St. Jude will use the app to screen children worldwide. Plans are already in place to use the app in Guatemala and the Philippines, where St. Jude has an established early-diagnosis campaign for eye diseases and other health issues.

Lela Moody's mom says she's excited about the app's potential.

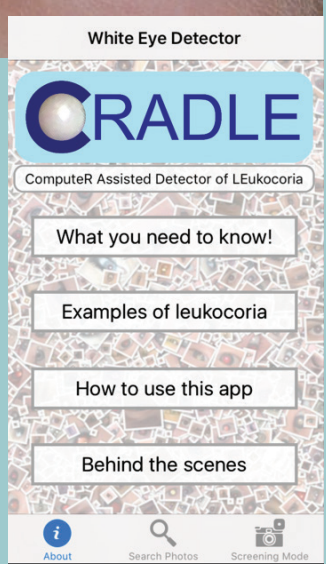
"Wouldn't it be great to harness technology in that way?" Mandy asks. "I look at Lela, and she's so full of life and energy and excitement. We're thankful for all the little things we get to experience with her. If this app can be used to save other children's lives, it would be huge." ■



THE GLOW TO KNOW

Most cases of retinoblastoma are discovered when parents glimpse an odd, white glow in flash photos of their children. Carlos Rodriguez-Galindo, MD, chair of St. Jude Global Pediatric Medicine, says by the time that reflection is visible, the tumor may have already filled two-thirds of the eyeball.

"In America, the proper use of this app may save eyes," says Rodriguez-Galindo about the white-eye detector software. "But in countries with limited resources, the proper use of this app could actually save lives."



HIGH HIGH

In St. Jude labs and clinics, scientists work day and night to find cures for children with high-risk leukemias.

By Elizabeth Jane Walker

All parents believe their babies are exceptional. But when doctors at a respected medical center told Dustin and Crystal Ellwood their daughter was the "rarest of the rare," their hearts did not soar with happiness. Four-year-old Stella had an extremely uncommon form of cancer called acute megakaryoblastic leukemia, or AMKL.

The day before Stella was scheduled to start treatment, the Ellwoods asked the oncologist a simple question: "How many children with this subtype have you taken care of?"

The physician responded, "Well, honestly, none."

Upon learning that St. Jude Children's Research Hospital had extensive experience treating children with this type of leukemia, the family obtained a referral. Within 24 hours, they were on a plane to Memphis, Tennessee.

"If we've got the rarest of the rare and nobody knows much about it, we want to go to a place that's thinking outside the box and doing research," Dustin explains. "As St. Jude helps Stella, the research they do will help others, as well. We felt 100 times more comfortable coming here."

Tackling the toughest cases

Since 1962, St. Jude clinicians and researchers have made dramatic progress in increasing the survival rates for childhood leukemias. But despite their best efforts, some children still die of their disease. Teams of scientists at St. Jude are working nonstop to find cures for those children, many of whom have rare subtypes that do not respond to chemotherapy.

Tanja Gruber, MD, PhD, is one of those scientists. Long before Stella was born, Gruber and her colleagues were teasing out the origins of AMKL, which is a form of acute myeloid leukemia (AML).

RISK REWARDS

"In 2012, we identified a fusion gene that had a poor prognosis," Gruber recalls, referring to a gene that is created when pieces of broken genes fuse together. "But we were still left with a lot of cases for which we didn't know the underlying genetic cause of the cancer."

To increase the amount of available data, Gruber led the world's largest study of the genetic changes that cause AMKL.

In the past, clinicians assumed that bone marrow transplants were required to cure AMKL. But a transplant also has risks, as the immune system is wiped out and replaced with donor cells.

Gruber and her team found several genetic alterations that can help determine which children will likely be cured with chemotherapy alone and which ones must have blood stem cell transplants. A lab test can show whether a child has one of three particular fusion genes. If the test is negative, then that child can likely be cured by chemotherapy alone. If the test is positive, the child requires a transplant.

"All institutions can now take this prognostic data and act on it," Gruber says.

Motivation, inspiration, collaboration

When Gruber arrived at St. Jude in 2009, she had already conducted research on a high-risk subtype of acute lymphoblastic leukemia (ALL) called Philadelphia chromosome-positive ALL. At St. Jude, she turned her sights to infant ALL, identifying drugs and designing therapies for babies with a subtype called MLL-R. Eventually, her research expanded to AMKL.

"I've always been interested in high-risk subtypes," says Gruber, who notes that more than 25 AML subtypes have been identified thus far.

"When you take care of high-risk patients in the clinic and they do not do well, it motivates you to work harder," she explains. "If I lose a patient, I take it as a personal failure. I know intellectually you're not supposed to do that, but it makes me want to work even harder."

This year, Gruber will head a new AML clinical trial. Patients from 10 institutions will have their genes sequenced so clinicians can identify which mutations are present. Gruber says she hopes the study will shed even more light on AML and its subtypes.

In addition, the hospital is developing a St. Jude-funded clinical research consortium to create international clinical trials for children with high-risk leukemias and other rare diseases.

"Each institution might see only a couple of cases a year, so nobody makes progress toward cures," says James R. Downing, MD, St. Jude president and chief executive officer. "But with this coordinated approach, we can make that progress."

New insights into rare leukemias

Only a small number of children have the form of AML Stella has. Another subtype, known as core-binding factor acute myeloid leukemia (CBF-AML), accounts for about 20 percent of childhood AML cases. Recently an international team headed by St. Jude scientists created a detailed map of the genetic variations that drive CBF-AML.

Researchers had already identified two genes affected by chromosomal rearrangements in CBF-AML. Until recently, scientists did not know what other mutations worked with those rearrangements to cause disease.

Jeffery Klco, MD, PhD, of St. Jude Pathology, teamed up with Downing; St. Jude Computational Biology Chair Jinghui Zhang, PhD; and other scientists to identify the genetic changes that contribute to this cancer.

The findings were an outgrowth of the St. Jude – Washington University Pediatric Cancer Genome Project, an unprecedented initiative to uncover the genetic origins of childhood cancer.

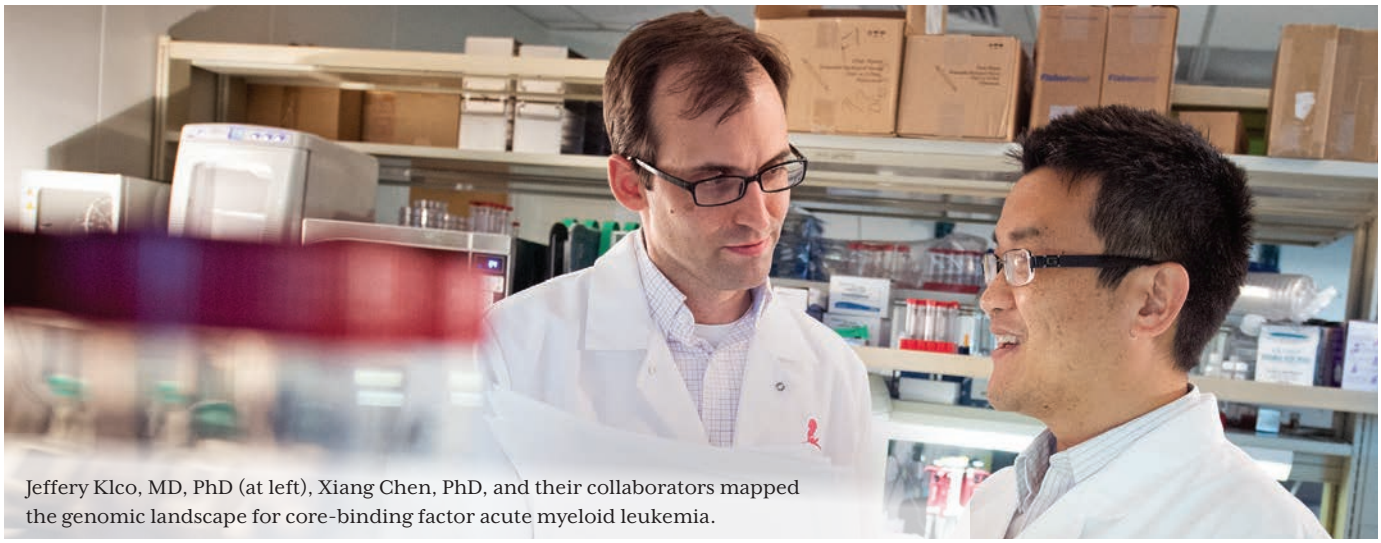
"This study highlights how the Pediatric Cancer Genome Project continues to generate new insights into genetic alterations and cooperating mutations that give rise to diseases like AML," Downing says.

Scientists are already at work to determine the precise roles of the genetic changes discovered as part of that study.

PETER BARTA

Stella Ellwood listens to the heartbeat of oncologist Tanja Gruber, MD, PhD. Long before Stella was born, Gruber and her colleagues were hard at work teasing out the origins of AMKL, the cancer Stella is fighting.

PHOTOS BY SETH DIXON



Jeffery Klco, MD, PhD (at left), Xiang Chen, PhD, and their collaborators mapped the genomic landscape for core-binding factor acute myeloid leukemia.

Homing in on ALL

As teams of researchers toil to solve the mysteries of AML, scientists in nearby labs and clinics study rare ALL subtypes. ALL is the most common childhood cancer, so even though its overall survival rate is 94 percent, it remains one of the top causes of childhood cancer deaths. The 6 percent of children who are not cured often have high-risk subtypes or have disease that is initially identified as standard-risk and yet fails to respond to treatment.

"Every person is important, so obviously we want to cure every child with ALL," says St. Jude pathologist Charles Mullighan, MD, MBBS, who has spent most of his career identifying new subtypes of the disease. His work has led to many new approaches to diagnosis and therapy, with several of his discoveries incorporated into precision medicine trials.

Last fall, the American Society of Hematology honored Mullighan for his success in providing insights into the genetic basis of ALL, particularly high-risk forms of the disease.

And yet, for all his expertise even Mullighan cannot yet identify exactly how many high-risk subtypes are in existence.

"There's still an appreciable chunk of leukemia cases—both in children and adults—that don't fall into one of the subgroups historically defined by conventional methods," says Mullighan, who predicts the main subtypes of ALL will soon be mapped.

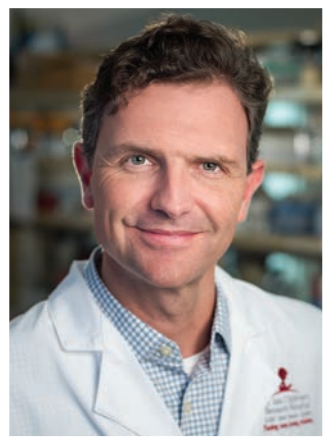
"There will always be more to learn," he says. "You'll always find another gene or another type of mutation or another fusion partner, but the overall grouping will be largely resolved in the next year or two as some very large studies come to completion."

The best place

Mullighan and his colleagues have experienced great success in uncovering new information about high-risk subtypes.

Last October, Mullighan led an international team that discovered the genetic origins of one subtype of B-precursor ALL. The researchers described a unique mechanism showing how one genetic change or rearrangement—in this case, a gene called *DUX4*—can trigger another change in regulation of a second gene, *ERG*, which then results in leukemia. That paper is the culmination of research Mullighan began when he was a postdoctoral fellow in 2004.

"The study highlights the importance of detailed genetic study to fully understand how the disease develops," he says. "While we advanced our understanding over several years, it wasn't until the advent of genome sequencing that we could crack the case."



Charles Mullighan, MD, MBBS, says he's in the best place to make discoveries about rare leukemia subtypes. "St. Jude offers the perfect convergence of opportunity and resources and expertise," he says.

A month after that paper published, he and his colleagues revealed new details about a new, high-risk ALL subtype called MEF2D-rearranged ALL. The team also found a promising targeted therapy for patients with that disease.

Also in November of 2016, Mullighan's lab announced that the prevalence of Ph-like ALL remains high among adults of all ages with ALL. The researchers found that the outcome for these patients may be improved by using medications that are already available.

Mullighan says he's in the best place to make those kinds of discoveries.

"St. Jude offers the perfect convergence of opportunity and resources and expertise," he explains. "There's the hospital's mission and its strategic direction; the infrastructure and resources; the historic biorepository of tumor samples; our leading role in frontline leukemia trials; our collaborations with investigators around the world; and our culture of very careful annotation, follow-up and uniform treatment of children with leukemia.

"Those things are often done elsewhere," he adds, "but it's rare that everything is under the same roof like it is here."

Reasons for the research

All of those discoveries are occurring on the same campus where Stella Ellwood is pursuing equally important activities.

While she's fighting for her life, she's making jewelry and painting pictures. Reading books and playing practical jokes on her mommy. Swinging on the playground and playing dress-up. Making plans to be a pediatrician when she grows up.

If all goes according to schedule, Stella will undergo a bone marrow transplant in the summer of 2017. Then this bright and intelligent little girl will return home to Maryland with her loving family—who have always known, after all, that Stella truly is the rarest of the rare. ■

PETER BARTA

Stella Ellwood is one of only a small number of children to have AMKL, a rare subtype of acute myeloid leukemia. St. Jude researchers recently led the world's largest study of the genetic changes that cause this subtype. The scientists' findings can now be used worldwide by clinicians treating children with AMKL.

Saving Kids in Your COMMUNITY

The St. Jude Give thanks. Give hope. campaign helps support St. Jude, whose treatment plans can save lives in hometowns like yours.

By Leigh Ann Roman

Like many 8-year-olds, T.J. Lipscomb enjoys playing Pokémon. The second-grader from Baltimore, Maryland, is also passionate about animals and music.

"He loves music, playing music and dancing to music," says his father, Tremayne Lipscomb Sr.

Seeing him today, you would never guess that five years ago T.J. was fighting for his life against acute lymphoblastic leukemia (ALL). As Lipscomb considered treatment options at his local hospital, he noticed the words "St. Jude Children's Research Hospital" printed at the top of one of the treatment plans.

Lipscomb knew about St. Jude through his employer, DTLR Inc., an urban apparel, footwear and music retailer. DTLR is involved in a fundraising campaign known as "St. Jude Give thanks. Give hope." Customers who donate at the cash register receive personalized St. Jude pinups that are then hung in the store. Involving about 100 retail partners nationwide, the spring giving program has raised more than $7.35 million since it began in 2009.

The Lipscombs chose the St. Jude treatment plan for their son. They say they are grateful it was offered at their local hospital, because it was the only option that allowed T.J. to avoid radiation.

"The doctors said that St. Jude found a way to treat his ALL without radiation," Lipscomb says. "They explained to me that St. Jude is a special hospital and that they share their research with other hospitals."

St. Jude freely shares the discoveries it makes, and every child saved at St. Jude means doctors and scientists worldwide can use that knowledge to save thousands more children.

With his cancer in remission, T.J. now has check-ups every three months and is a healthy big brother to his little sister, Autumn.

Lispcomb shares his family's story with DTLR employees every year as the company prepares for St. Jude Give thanks. Give hope.

"My story is a living testament that you don't have to go to St. Jude to benefit from the hospital," says Lipscomb, DTLR community outreach manager. "People benefit from the great work St. Jude does, even if they don't come to Memphis." ■

T.J. Lipscomb

A SECOND CHANCE AT A FIRST START

By Mike O'Kelly

The St. Jude Early Childhood Clinic helps babies and toddlers achieve developmental milestones during treatment.

PHOTOS BY SETH DIXON

PHOTOS BY SETH DIXON

Speech-language pathologist Angela Eftink works with 2-year-old Gideon Purchase. "I was astounded," Gideon's father says, "at how much emphasis is placed on not only trying to get Gideon well but making sure he is as developmentally normal as possible."

often come fleetingly, but create a lifetime of memories for new parents: happy moments ranging from a baby's first words to a toddler's first steps. These events signify important developmental milestones.

For children with cancer or other diseases, such achievements may be delayed due to illness, treatment or time away from home—factors that can keep children from learning and growing normally.

Children younger than 3 years old who are at risk for such delays often receive early-intervention services from government agencies in their home states. These programs provide access to supportive services like physical therapy, occupational therapy or speech therapy.

In late 2015, Sharnelle Toledo sought the help of early-childhood intervention services in her New Mexico hometown for her 2-year-old son, Jericho Tsosie, when he did not meet growth and cognitive milestones for his age.

Therapists who visited Jericho at his home noted he wasn't tracking moving objects with his eyes. Days later, Sharnelle noticed an odd reflection in her son's eyes. An MRI scan revealed he had retinoblastoma, a cancer of the retina, in both eyes.

Sharnelle wanted to explore all available options for his treatment. After researching retinoblastoma, she obtained a referral to St. Jude Children's Research Hospital.

Shortly after arriving at St. Jude, Jericho became one of the first patients in the St. Jude Early Childhood Clinic, which helps babies and toddlers learn, grow and develop as much as possible while undergoing treatment.

A starting point

The St. Jude Early Childhood Clinic was created in 2015 with a family-centered focus that brings together experts from psychology, rehabilitation services, social work and child life. The team assesses patients and then forms individualized interventions to help ensure that young patients do not fall behind their healthy peers.

"Infant mental health is vital to development, and it permeates everything for these young children. It's their starting point,"

SETH DIXON

Andrew Molnar, PhD (center), and Jennifer Harman, PhD, helped Jericho Tsosie learn, grow and develop as much as possible while undergoing treatment.

says Jennifer Harman, PhD, a clinical psychologist in St. Jude Psychology.

Each patient in the clinic first receives a 90-minute assessment with Harman or her colleagues, Andrew Molnar, PhD, and Lisa Jacola, PhD. The team uses these initial sessions to conduct age-appropriate testing related to problem-solving skills, language abilities, motor and social skills, and school readiness.

In a newborn or young infant, psychologists look for eye contact, vision tracking, and startle and reflex responses, but they also examine the parents' role in the child's development.

"We look at how parents are coping with their child's treatment, and we make sure they feel supported. We emphasize that, even in a hospital environment, there are ways to interact with your newborn and use the environment around you to promote their ongoing development," Harman says.

The assessments vary by age, diagnosis and patient. While a wealth of information can be gathered from more active patients, psychologists rely heavily on the parental interview for children who display few signs of interaction or communication, as was true when Jericho initially came to St. Jude.

Tailoring treatment

St. Jude clinicians referred 10-month-old Gideon Purchase to the clinic in February of 2016. Gideon had neuroblastoma, a tumor that generally develops in the adrenal glands. His assessment revealed problems related to motor functioning, which later turned into instances where he hit himself.

"Dr. Harman was extremely helpful in guiding us through Gideon's issues and how we could be responsible and discipline him appropriately, knowing that normal techniques aren't going to be appropriate due to his treatment," says Gideon's father, Gary Purchase.

"I was astounded at the number of services St. Jude has for young patients," he continues, "and how much emphasis is placed on not only trying to get Gideon well but making sure he is as developmentally normal as possible."

Implementing the plan

After forming an overall evaluation from the assessment, an interdisciplinary team of psychologists, rehabilitation therapists, social workers, child life specialists and school teachers creates a comprehensive strategy for each patient.

"These plans are generally modeled after intervention service plans available in the community with specific goals to allow for a smoother and guided transition to services once a child returns home," Molnar says.

St. Jude Rehabilitation Services plays a huge role in implementing the plan. Jericho's developmental interventions focused on speech therapy, occupational therapy and physical therapy. Physical therapist Angela Corr worked with Jericho, setting goals to guide him toward crawling and standing while speech-language pathologist Angela Eftink worked with his language skills.

"We measure progress with a standardized measure widely used across the country so that physical therapists in the patients' hometowns can also track progress when they return home," Corr says.

Jericho battled through rehab sessions three times each week. His persistence and the support of his mother paid off. Today, he can nearly stand by himself.

"He learned to sit on his own without catching his fall and how to bear weight on his arms and knees," Sharnelle says. "It's great to know he is able to learn, but that it's just going to take time."

Jericho isn't talking yet, relying on hand signals and exclamations to communicate. Sharnelle says if he's unable to learn how to speak, she would eventually like for him to learn sign language.

Meanwhile, Gideon recently returned home to his community in East Tennessee, where he is now walking and easing into developing the skills of a growing 2-year-old.

The return home

The Early Childhood Clinic's goal is to smoothly transition patients from their time at St. Jude into early intervention and preschool programs in their hometowns. Programs vary by state and community, so the St. Jude team coordinates with local officials, administrators and health care providers to make sure all aspects of the child's development are considered. Some schools and programs may initially lack vital resources if they have never before encountered children who require specialized services related to the medical diagnoses treated at St. Jude.

"We encourage families to be their child's strongest advocate, and a lot of them already are," Molnar says. "In the case of Jericho, his mom went home, took the road map we provided and implemented it."

Jericho is now off treatment and returns to St. Jude every eight weeks for check-ups. Back in New Mexico, he's enrolled in afternoon classes four days a week at a child care center.

"I felt like I was at a dead end as far as Jericho being able to do the types of things that other kids do, but the Early Childhood Clinic gave him a different outlook on what he could do and what he could accomplish," Sharnelle says. "Sometimes I pop my head in at his child care center to see how he is reacting, and if the other kids are playing with him and being nice. He's doing well, and he is right alongside the other kids." ■

ST. JUDE EARLY CHILDHOOD CLINIC BY THE NUMBERS

42% are infants
26% are age 1
30% are age 2
1% are age 3

Average age of new patients:
21 months old

Joshua Wolf, MD (at left), and Jason Rosch, PhD

Scientific Sleuths

Why wouldn't Milah's infection respond to antibiotics? Two scientists set out to solve the mystery. The answer offers hope to other children with compromised immune systems.

By Chris Pennington

Milah Kimber was only 2 weeks old when her mother, Marketia, noticed red spots on her baby's skin. Doctors immediately sent Milah to St. Jude Children's Research Hospital, where she began chemotherapy treatments for acute myeloid leukemia, a cancer of the white blood cells.

Complications arose when Milah developed a bloodstream infection. No matter which antibiotics were used, the infection wouldn't go away.

Antibiotics helped the little girl survive during treatment, says Joshua Wolf, MD, of St. Jude Infectious Diseases, but there was still the issue of the infection's resistance. For nearly a month, Milah battled both her cancer and the infection.

PETER BARTA

"We moved into the hospital," Marketia says. "Milah kept going in and out of the ICU."

"She just stayed ill," Wolf says. "Eventually, her immune system recovered, and she cleared the bacteria."

Milah's cancer went into remission, and regular checkups since have been reassuring. Now she is a happy, healthy 2-year-old—but until recently clinicians could not explain why the infection had persisted. It simply had not responded to antibiotics.

In search of answers

Wolf and his colleagues were determined to solve the mystery.

"After Milah recovered and I met with her mom to get permission, we began researching the issue," Wolf says. "We saw it as an opportunity to learn from her case and derive information we can use to help future kids."

> "The mutant bacteria responsible for her prolonged infection had never been described before."
>
> —Joshua Wolf, MD

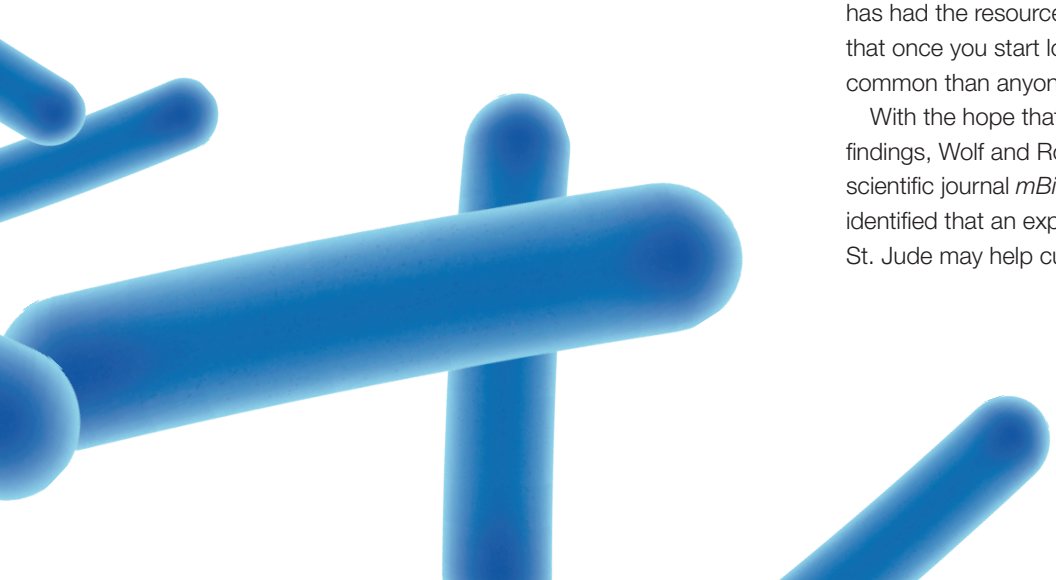
The bacteria, known as vancomycin-resistant *Enterococcus faecium* (VRE), normally lives inside the gut. But in Milah's case, the bacteria entered her bloodstream.

"What happened when the bacteria moved into this new place?" Wolf asked. "How did it adapt?"

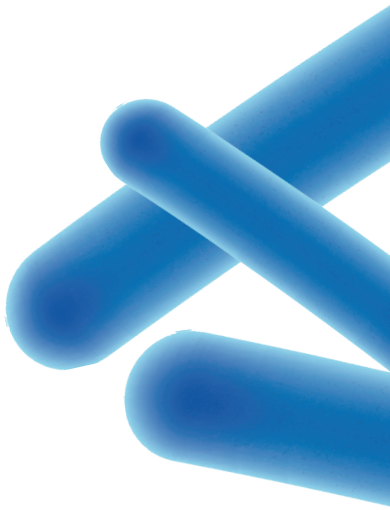
To find out, he enlisted the help of Jason Rosch, PhD, of St. Jude Infectious Diseases. Using samples taken from Milah each day of her infection, Rosch looked at the genetic sequences to see how the bacteria changed.

He had no idea what to expect.

"One mutation kept showing up intermittently throughout the course of treatment," Rosch says. "It came up early and was there at the end, which surprised us a little bit."



A haystack of needles



The mutation occurred in one of the bacteria's genes. This gene, known as *relA*, affected the bacteria's alarm system when the bacteria were growing in what is called biofilm.

"Like slime on rocks in a river," Rosch says. "That's a biofilm. It's just a complex community of bugs."

Most bacteria live in your body by forming such communities. Like many children undergoing cancer treatment, Milah had a central venous catheter implanted in her body. Medicines, blood products and fluids could be delivered through this tube.

"The infections Milah had were probably related to the catheter," Rosch says. "Bacteria don't just sit there and float; they attach to surfaces and stick there."

Rosch and his colleagues spent nearly a year investigating the bacteria. The scientists found that when floating freely, bacteria could be treated with antibiotics. But in biofilm, mutant bacteria couldn't be killed.

"Part of the challenge is finding the mutation," Rosch says. "The consequences of that could be a needle in a haystack of needles."

Lessons from Milah

Milah's parents, Marketia and Andrew, are grateful their daughter is now healthy and doing well. They recall the first few months of Milah's life as a blur—from seeing red spots on her skin to visiting a local hospital to entering St. Jude. Both mother and father remained hopeful during those weeks of doubt.

"It was an experience," Andrew says. "I thank God. It was a bad thing to have cancer, but we also understand it can be cured. It takes a lot of patience by the doctors."

Milah's case was a first.

"The mutant bacteria responsible for her prolonged infection had never been described before," Wolf says. "Part of that is nobody has had the resources and the opportunity to look. And it may be that once you start looking for these things, they're much more common than anyone ever thought."

With the hope that other children might benefit from their findings, Wolf and Rosch shared results of their research in the scientific journal *mBio*. As part of their work, the researchers also identified that an experimental compound being investigated at St. Jude may help cure such infections in the future.

PETER BARTA

Lessons scientists learned from Milah Kimber may someday save the lives of other children worldwide.

Looking to the future

"With Milah, we had a young child with an aggressive cancer, who received aggressive chemotherapy and had a very, very prolonged infection," Rosch says. "It's like three strikes. It speaks to the quality of doctors here that they were able to cure her."

Wolf met the family again during their recent visit to St. Jude. The last time he'd seen Milah, she was just a few weeks old.

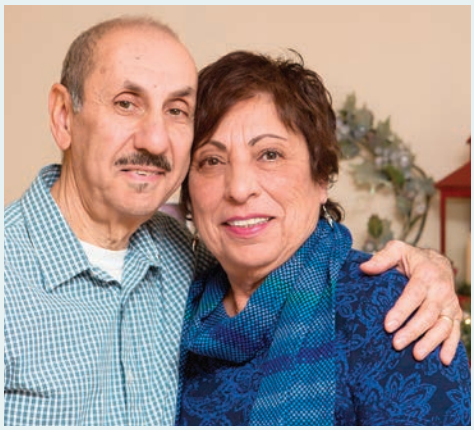
"This was an opportunity to learn," Wolf says. "We've now started talking about looking for such prolonged infections in other patients."

In other words, how often do antibiotic-tolerant bacteria develop in patients like Milah? And what does this mean when it happens to a patient whose immunity is diminished because of chemotherapy?

"If you look at the literature, there is really not all that much information available," Rosch says. "That's an important question not only for the patients, but also from a public health perspective."

"We're going to use this as a jumping-off point to start thinking more about how VRE evades antibiotics," Wolf says. "As we go forward, understanding that phenomenon in a patient is going to be important." ■

Helping the Children



"It is just simple giving," says Patrick Pompeo of his philanthropy. "We are contributing to a great organization to help children."

By Rachel Schwartzberg

Patrick Pompeo says the reason he and his wife, Caroline, give to St. Jude Children's Research Hospital is simple: "I know St. Jude is going to use my gift to do the right thing."

Strong supporters of St. Jude for many years, the New Jersey couple directs some of their generous giving through their donor-advised fund, which they established with a major financial services firm.

Pompeo retired in 2001 from Blimpie, an international sandwich shop chain. When his brother-in-law founded the company in the 1960s, Pompeo was working at the New York Stock Exchange, but his relative wanted him to join the growing business.

"I had experience working at an Italian deli for five years," he says. "I knew cold cuts. I knew food."

Finally, in 1975, he joined Blimpie, beginning a second career that spanned more than two-and-a-half decades.

He originally began giving to St. Jude because of Danny Thomas.

"I watched *Make Room for Daddy,"* Pompeo explains. "I loved the show, and I loved Danny Thomas. One day he was doing an interview, and he shared his story about praying to St. Jude to make it in show business—and how he built the hospital as a shrine to St. Jude. Danny Thomas made such an impression on me."

Years later, Pompeo decided he should also do something for St. Jude.

"I discussed it with my wife," he says, "and we have been contributing to the hospital since then."

Today, the couple volunteers at their parish food pantry and say they feel blessed to have their daughter, Annemary, and three granddaughters nearby.

Pompeo visited St. Jude for the first time last year with his daughter and one of his granddaughters. They were impressed by how St. Jude is "so full of love and hope."

He explains that in giving to St. Jude, he and his wife never had goals or ambitions.

"It is just simple giving," he says. "I never doubt St. Jude and how they use the money. We are contributing to a great organization to help children." ■

research
highlights

Second cancer risk declines in survivors of childhood cancer

SETH DIXON

Greg Armstrong, MD

Survivors of childhood cancer are living longer. Now research shows they are also less likely to develop second cancers while still young. The decline followed a sharp drop in the use of radiation therapy for treatment of childhood cancers.

In the Childhood Cancer Survivor Study (CCSS), the percentage of pediatric cancer patients treated with radiation fell from 77 to 33 percent between the 1970s and the 1990s. The average radiation dose also dropped. Their chance of having second cancers within 15 years of the first fell, as well.

The study included 23,603 five-year survivors from the CCSS. They were treated at 27 medical centers in the U.S. and Canada. The federally funded study is based at St. Jude. Greg Armstrong, MD, of the St. Jude Department of Epidemiology and Cancer Control, is the principal investigator for CCSS and is a co-author on this study.

"The most ominous late effect of pediatric cancer treatment is a second malignancy," he said. "This study shows efforts to reduce the risk of this late effect are paying off."

The research appeared in the *Journal of the American Medical Association*.

Les Robison, PhD, receives national award

CHRIS HAMILTON, COURTESY AMERICAN CANCER SOCIETY INC.

Les Robison, PhD

Les Robison, PhD, St. Jude Epidemiology and Cancer Control chair, was recently awarded the American Cancer Society's Medal of Honor. The medal is awarded to individuals who have made the most valuable contributions and impact in saving lives from cancer through basic research, clinical research and cancer control. Robison received the award for his work in cancer control.

Past recipients of the Society's Medal of Honor include Donald Pinkel, MD, first St. Jude director; former U.S. President George H.W. Bush and and First Lady Barbara Bush; Edward Kennedy, senator from Massachusetts; George Papanicolau, MD, inventor of the Pap test; and former U.S. Surgeon General C. Everett Koop, MD.

Biostatisticians build a better analytic tool

The right tool makes any job easier. That is especially true when the job involves sifting through millions—sometimes billions—of pieces of genetic information to uncover the basis of disease, including the role inherited genetic variations play in disease risk, treatment success or the likelihood of treatment-related side effects. Generating data through whole-genome sequencing and other techniques is just the beginning.

St. Jude biostatisticians partnered with colleagues in the U.S. and China to develop such a tool. This new statistical approach, called the set-valued method, can help scientists learn more from genomic data.

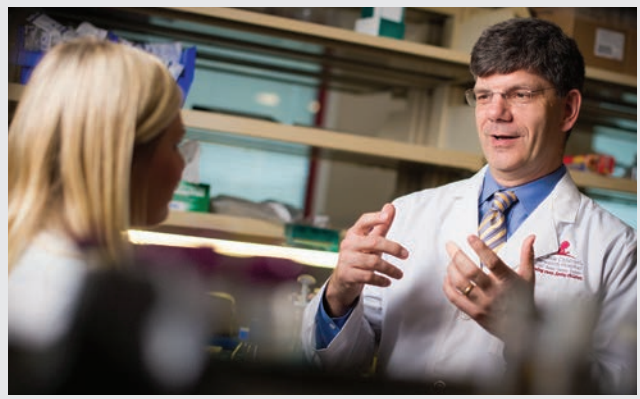
The researchers showed that for certain studies the new method is better than current analytic tools at identifying rare variations associated with secondary traits that may provide clues about disease risk. The tool was designed for case-control studies, an approach to find differences between two groups of people.

"This new method has such profound advantages compared with current approaches that we strongly recommend using it to analyze secondary genetic traits in sequencing studies with a case-control design," said Guolian Kang, PhD, of St. Jude Biostatistics. A report on this approach appeared in the journal *Genetics*.

SETH DIXON

Guolian Kang, PhD (at left) and Wenjian Bi, PhD

Loss of ARID1A protein drives colon cancer



PETER BARTA

Charles Roberts, MD, PhD

Not all cancers are caused by direct changes in the genetic code. Cancers also arise from events that influence gene expression in other ways. Now, St. Jude researchers and their collaborators have discovered how a tumor-suppressing protein interacts with genetic enhancers to silence cancer genes.

As became clear from the St. Jude – Washington University Pediatric Cancer Genome Project and other studies, genes that encode epigenetic regulators are often mutated in cancer. These genes are thought to work by altering the structure of chromatin, the protein packaging that surrounds DNA, to determine which genes are on, or off, in different cells. Until now, the way these gene mutations lead to cancer has been poorly understood.

The newly published research sheds light on the process. The ARID1A protein is part of the SWI/SNF chromatin remodeling complex. Scientists found that loss of ARID1A drives the onset and progress of colon cancer.

The new findings were reported in the journal *Nature Genetics* by Charles Roberts, MD, PhD, St. Jude executive vice president and director of the Comprehensive Cancer Center, and his colleagues.

Why do some leukemia patients relapse?

Pediatric acute lymphoblastic leukemia (ALL) is one of the 20th century's cancer success stories. Today, about 94 percent of children with ALL become long-term survivors. Some patients, however, still relapse and die of their disease.

Research suggests ancestry plays a role in why some cancer returns.

St. Jude researchers recently led a study to better understand the role inherited genetic variation plays in relapse. They used a library of more than 11 million gene variants to screen patient DNA. The scientists found four associated with relapse and ancestry.

"These genetic variants were markers of patients at high risk of relapse regardless of ancestry, but they were twice as common in patients with African and American Indian ancestry as in Europeans," said Seth Karol, MD, of the St. Jude Comprehensive Cancer Center. The four variants identified more than half of African-American and Hispanic patients who relapsed.

"Going forward, it will be important to track the contribution of these four genetic variants to relapse risk to determine if they can help guide treatment intensity," Karol said. The study was published in the journal *Leukemia*.


SETH DIXON

Seth Karol, MD (at left), and Mary Relling, PharmD


PETER BARTA

Thirumala-Devi Kanneganti, PhD

Mystery molecule is a key to thwarting colon cancer

St. Jude immunologists have discovered that a protein called NLRC3 plays a central role in inhibiting colon cells from becoming cancerous. This protein is one of a large family of proteins that regulate immune and other cell functions.

"NLRC3 is important for protecting from abnormal colon cell growth, and when it is not present, tumors will develop," said Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology.

Kanneganti said that NLRC3 likely plays a broader role than only preventing tumors. "We really do not know its role in infectious and inflammatory diseases," she added.

She and her team also identified key components of the NLRC3 tumor suppressing pathway. These mechanisms offer targets for new drugs that would restore the protective mechanism to treat colon cancer. Until now, the role of NLRC3 in protecting against cancer development had been unknown.

A report on this study appeared in the journal *Nature*.

Research provides insights into adolescents' care-planning needs

SETH DIXON

Megan Wilkins, PhD (at left) and Ronald Dallas, PhD

St. Jude-led research shows that HIV-infected adolescents and their families benefit from tailored, advanced-care planning with trained facilitators. Participants in a recent clinical trial called the process worthwhile and helpful. The study suggests that other young people with life-limiting conditions may benefit from this approach to planning care at the end of life.

"These are difficult discussions to have, but we found that adolescents as young as 14 wanted to be part of the conversation about end-of-life care, and that families wanted to hear from their children," said Ronald Dallas, PhD, of St. Jude Infectious Diseases.

The research appeared in the journal *Pediatrics*.

An estimated 400,000 U.S. children have life-limiting conditions such as cancer or HIV/AIDS.

"The findings should help allay clinicians' fears about initiating these discussions with adolescents," Dallas said.

SETH DIXON

J. Paul Taylor, MD, PhD

Discovery linked to two neurological diseases

St. Jude researchers have discovered the way toxic proteins linked to two neurological diseases target the integrity of membraneless organelles and trigger disease.

The discovery had implications for the most common forms of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). ALS, also known as Lou Gehrig's disease, attacks the nerve cells responsible for muscle control. The average life span after diagnosis is two to five years. FTD is a dementing illness caused by loss of nerve cells in the brain. Neither of these diseases has a cure.

Scientists found that toxic peptides directly interfere with assembly and function of membrane-less organelles. The peptides do that by disturbing the normal process that allows the membrane-less organelles to assemble and function.

The study's results help account for the many cellular abnormalities present in both ALS and FTD. J. Paul Taylor, MD, PhD, a Howard Hughes Medical Institute investigator and chair of St. Jude Cell and Molecular Biology, says the discovery sets the stage for future studies to look at new drug interventions.

The study's findings appeared in the journal *Cell*.

On Top of the World

After he vanquished cancer, Tim Wigginton sought new mountains to climb.

By Elizabeth Jane Walker

Legs and lungs burning, Tim Wigginton climbs upward, squinting into the sun and inhaling the cold, heady scent of evergreens. At the pinnacle, he takes a moment to revel in his achievement.

Then he begins to plan his next ascent.

"I've always loved mountains," Tim says. "I like to be at the top—and then look down and see everything below."

Tim acquired his tenacity and drive as a small boy, when faced with a diagnosis of non-Hodgkin lymphoma. He says St. Jude Children's Research Hospital provided him with the tools and inspiration to scale that mountain, and he's never looked back.

Tim and his family arrived at St. Jude in 1977. Throughout chemotherapy and radiation treatments, his parents constantly emphasized the importance of a positive attitude, encouraging their son to focus on the future.

That optimism and determination extended to his professional life, where he achieved the position of sales director at a global health care company.

"Cancer made me the way I am," he says. "I had to fight for my life at 10 years old. I experienced things that children never are supposed to go through. But as a result, if someone tells me I can't do something, I say, 'No, get out of my way. I'll show you I can do it.' I think that makes me want to climb a higher mountain the next time."

Through the St. Jude LIFE long-term follow-up study, he helps the next generation of cancer survivors while learning to maintain his own health.

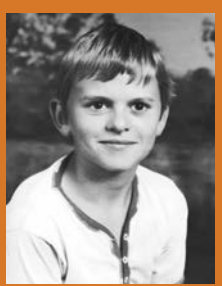
"The St. Jude LIFE study has educated me a lot," says Tim, who keeps scrupulous records of medical screenings and makes a conscious effort to pursue a healthful lifestyle.

He continues to set lofty goals. Next up is Mt. Whitney, the highest summit in the contiguous U.S. And his long-term objective?

"I'm turning 50 years old, and you'll have about 50 more out of me," he says. "I told the doctor at St. Jude LIFE that I'm going to be the oldest living St. Jude survivor." ■

"I had to fight for my life at 10 years old. I experienced things that children never are supposed to go through."

—Tim Wigginton



Tim Wigginton acquired his tenacity and drive as a small boy, faced with a diagnosis of non-Hodgkin lymphoma.

A gift from your donor-advised fund helps us make a major difference in the fight against childhood cancer. Treatments invented at St. Jude have helped push the overall childhood cancer survival rate from 20 percent to more than 80 percent since it opened more than 50 years ago. St. Jude is working to drive the overall survival rate for childhood cancer to 90 percent, and we won't stop until no child dies from cancer. But we can't do it without you.

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Out of this world

Five-year-old Kevin Hunter embarks on a virtual-reality adventure during an event celebrating an $18.2 million gift made possible by Best Buy customers. Children joined Best Buy employees in creating crafts, playing with mini robots and mixing tunes as part of the hands-on event. Since 2013, Best Buy customers have donated nearly $40 million to the hospital as part of the St. Jude *Thanks and Giving* campaign.

ANN-MARGARET HEDGES

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