

# promise

St. Jude

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When it comes to **cancer**, children aren't **little adults**  
*pg. 4*

**Virtual reality** and pain management  
*pg. 12*

Why does **Hodgkin lymphoma** recur in some families? *pg. 14*

# promise

a quarterly publication of the Communications Department  
St. Jude Children's Research Hospital | 262 Danny Thomas Place  
Memphis, TN 38105-3678



## Cover Story

### 04 Children Aren't Little Adults

Kids and adults often have different mutations driving their diseases.

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# BACK TO SCHOOL



## A class act

With a little help from St. Jude, eighth-grader Evans Culpepper has returned to his community school, welcomed by his friends and classmates.

By Keith Crabtree, PhD

Evans Culpepper experienced a relapse of acute lymphoblastic leukemia (ALL), a cancer of the blood, when he was 8 years old. He needed a bone marrow transplant. While confined to his hospital room at St. Jude Children's Research Hospital, he learned how to play chess.

Justin Gardner, a teacher and school liaison in the St. Jude School Program by Chili's, taught Evans the game.

"Evans was in such pain," says Evans' mother, Malise Culpepper. "He was on a morphine drip. He couldn't do math, but chess was a great way for him to use his brain."

Today, 14-year-old Evans is back at home, leading an active life and attending eighth grade with his friends.

The treatment for ALL and other pediatric cancers can affect learning and thinking. Patients often need Individual Education Plans (IEPs) or 504 Plans, which are required by federal law for students with specific educational needs. Evans has such a plan.

"He needs a little more time on math," Culpepper explains.

In fact, Gardner often recommends extra time for assignments and tests, including standardized tests such as the ACT and SAT.

"I'm trying to advocate for our patients," says Gardner, describing his work as a school liaison. "Advocacy is particularly needed during school transitions."

For example, the transition from elementary to middle school can often result in a lapsed IEP or 504 Plan when parents and school officials opt to discontinue the plan for an ostensibly healthy child. But the cognitive late effects of cancer treatment—from chemotherapy, radiation or surgery—can still interfere with learning.

Fortunately, school transitions for Evans have proceeded without difficulty—thanks, in part, to the liaison work of Gardner.

"Anything for Justin," responded a grateful Evans, when his mom asked if he wanted to be in this story with Gardner.

"He got me to where I am. He put in the time for me, so I'm putting in the time for him." ■

**You can go home again, but it takes preparation to make a seamless transition back to the classroom. St. Jude school liaisons help ease children back into their community schools.**



WHEN IT COMES TO CANCER,

# Children Aren't Little Adults

By Maureen Salamon

**New research proves that children and adults with cancer often have different mutated genes driving their diseases. This reinforces the need for pediatric-specific precision therapies.**

Only faulty logic would lead someone to look at a child and merely see a small adult. So why should a child with cancer receive the same medication as an adult with cancer?

New research led by St. Jude Children's Research Hospital is perfectly poised to transform this way of thinking. Studying a core group of a half-dozen pediatric cancers, scientists showed for the first time that malignancy in children and adults frequently arises from different genes with different mutations.

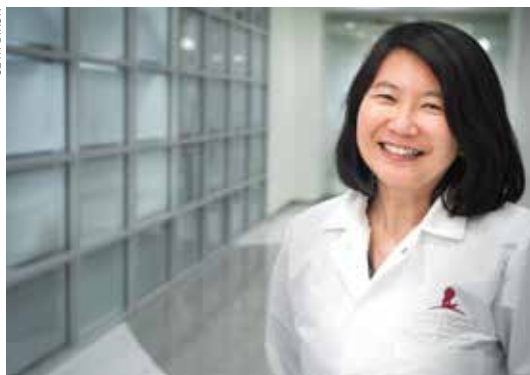
The results, St. Jude experts contend, should prompt shifts in how new drugs are evaluated. Instead of limiting the study of drugs in children only to those already deemed effective and tolerable in adults—meaning some novel therapies are never tried in pediatric patients—the research hammers home how this prevailing strategy is likely a missed opportunity.

## **A new resource for clinicians**

Overall survival rates for pediatric cancer currently exceed 80 percent, thanks to treatment advances pioneered at St. Jude and elsewhere. Yet, cancer remains the leading cause of disease-related death among U.S. children ages 1 to 19. The new findings highlight the need to develop targeted medications for pediatric patients and also provide a more accurate roadmap for researchers to accomplish this, says Jinghui Zhang, PhD, St. Jude Computational Biology chair.

“Very few drugs are specifically developed for pediatric

Caleb Brown



“Very few drugs are specifically developed for pediatric cancer, because the adult cancer population is much bigger. This information will provide a great resource for researchers and clinicians, giving them the ability to develop new therapies and devise new treatment protocols for children.”

– Jinhui Zhang, PhD

cancer, because the adult cancer population is much bigger,” Zhang explains. “This information will provide a great resource for researchers and clinicians, giving them the ability to develop new therapies and devise new treatment protocols for children.”

Ching-Hon Pui, MD, Oncology chair at St. Jude, vigorously agrees with Zhang.

“All the new drugs are tried in adults first, with few exceptions,” he says. “This is wrong. Just because a drug doesn’t work in adults doesn’t mean it won’t work in children.”

### Computer crunching on a massive scale

Recently published in the journal *Nature*, the research by Zhang and her colleagues is the most comprehensive so far to identify the genetic alterations influencing pediatric cancers. Its top finding: Only 45 percent of the mutated genes driving cancer in children matched the genes driving malignancies in adults.

Conducted in partnership with the National Cancer Institute as part of the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) project, the vast effort combined gene sequencing and computer data crunching on a massive scale. Six cancers were spotlighted, including acute lymphoblastic leukemia (ALL), both the B- and T-cell types; acute myeloid leukemia; the bone cancer osteosarcoma; the kidney cancer Wilms tumor; and neuroblastoma, a tumor of the sympathetic nervous system.

The study was especially comprehensive because it implemented three types of gene sequencing on both tumor tissue and normal tissue from 1,699 children and adolescents. These included whole genome sequencing of each person’s entire complement of DNA; exome sequencing of the DNA that encodes cells’ instructions for making proteins; and transcriptome sequencing of genes being expressed in the tumor tissue.

### DNA distinctions come to light

Aside from the startling lack of genetic overlap between adults’ and children’s cancers, Zhang says she was also struck by several other distinctions. About 62 percent of mutations in pediatric cancer were either “copy-number” alterations—leaving patients with too many or too few copies of particular genes—or gene rearrangements. Conversely, gene changes

in adult cancers typically involve what scientists call “point mutations”—only one point, or a few points, of genetic variation, Zhang explains.

An additional surprise was that eight of the 689 pediatric patients with B-cell ALL carried genetic changes previously linked only with skin cancer caused by ultraviolet (UV) radiation. This suggests that exposure to UV light may be a previously unrecognized risk factor for some cases of childhood leukemia. However, this finding needs further experimental confirmation, Zhang notes.

All told, Zhang says these inconsistencies point to another gaping void: Currently, genetic testing in pediatric cancer patients is the same as that done in adults. But these tests shouldn’t be identical.

“The fact that there’s only limited genetic overlap with adult cancer suggests we have to develop genetic testing specifically designed for pediatric cancer,” Zhang says. “This is one of the most important messages we want to address.” ■

Trinity Cunningham  
and Woods Garrett







# A Second Chance

**A ground-breaking gene therapy pioneered at St. Jude has curative potential for infants born with XSCID.**

*By Jane Langille*

One of life's most precious moments for parents is snuggling a newborn child. For Ricardo and Simone Evangelista of Sao Paulo, Brazil, the birth of their son Samuel was especially sweet, as they had already lost two babies to unknown causes.

But Samuel's life was in danger. At 3 months old, he was diagnosed with X-linked severe combined immunodeficiency (XSCID). In this rare disorder, also known as bubble boy disease, the body lacks the immune cells necessary to fight off harmful viruses, bacteria and fungi.

Most children with XSCID die within the first two years of life.

After learning about St. Jude Children's Research Hospital, the Evangelistas and their doctor spoke with Ewelina Mamcarz, MD, of St. Jude Bone Marrow Transplantation and Cellular Therapy. The couple immediately agreed to take part in the world's first lentiviral gene therapy trial for infants with XSCID.

"When we arrived at St. Jude, we knew we were in the best place in the world," Ricardo says. "Brazil doesn't have anything that comes close."





### Round of applause

During his last visit before returning home to Brazil, tiny Samuel Evangelista celebrates with (from left) Ewelina Mamcarz, MD; interpreter Marc Friedman; and Katie Birdsell, a nurse practitioner in Bone Marrow Transplantation and Cellular Therapy.

### Re-engineering human genes

XSCID is an inherited disorder that occurs almost exclusively in males. Affecting about one in every 200,000 newborns, XSCID is caused by a mutation in the *IL2RG* gene that encodes a protein critical for developing the body's immune cells.

To date, bone marrow transplantation has been the most effective treatment for XSCID. With a transplant, a patient receives healthy blood-forming cells from a matched donor. Those cells settle into the patient's bone marrow and make immune cells. Unfortunately, more than 80 percent of patients with XSCID lack fully matched donors. Among those who do receive transplants, one-third develop immune problems that continue for years.

To find a safer and more effective way to cure children with XSCID, Brian Sorrentino, MD, director of St. Jude Experimental

Hematology, worked tirelessly for more than a decade to perfect a novel gene therapy. Leading a team of scientists, he successfully created what is known as a lentiviral vector. This type of virus can insert a healthy copy of the *IL2RG* gene into a patient's blood-forming cells.

The vector is made in the Children's GMP, LLC, an on-campus facility that produces biological products in accordance with FDA regulatory regulations. The GMP is the only facility in the world to both make a lentiviral vector and re-engineer cells to carry the healthy gene. The vector includes features designed exclusively to enhance safety and effectiveness.

"It's been an enormous amount of work, but we're thrilled to be producing a stable cell line using a vector that's never been used in a clinical trial before," Sorrentino says.

## A novel clinical trial

Samuel is the sixth of seven infants under the age of 2 to take part in the Phase I trial. The treatment involves removing the patient's bone marrow, filtering and purifying the child's blood stem cells and incubating them with the lentiviral vector to insert a healthy copy of the *IL2RG* gene. The re-engineered cell line is then transfused back into the patient. The objective is to reconstitute T cells as well as natural killer cells and B cells, creating broad immune-system function.

Mamcarz and Sorrentino head the multisite clinical trial, which includes Benioff Children's Hospital at the University of California, San Francisco, and Seattle Children's Hospital. For patients at the other institutions, bone marrow cells are shipped to the GMP facility for re-engineering and then are sent back for infusion.

Before infusion, patients receive a low dose of the drug busulfan, roughly one-third of the amount used in transplants.

"Using chemotherapy in infants is controversial, especially in those with non-malignant disorders," Mamcarz says.

"But in previous clinical studies where it was not used before transplantation or gene therapy, patients only achieved T cell correction.

"As a result, many were still prone to recurrent viral infections and diarrhea and required expensive monthly infusions of intravenous immunoglobulin."

## Promising responses

Results have been promising among the seven infants treated to date.

"So far, our patients have tolerated chemotherapy well, showing only mild suppression of blood cell count for a few days and recovering to normal levels by three weeks, well ahead of our safety target of six weeks, allowing them to be discharged from the hospital and followed on an outpatient basis," Mamcarz says. "In addition, we have not needed to provide any of the babies with blood products while they awaited cell recovery."

Six of the seven babies treated achieved reconstituted immune systems within three to four months after gene therapy.

"We've stopped giving intravenous immunoglobulin treatments when the babies started making their own immunoglobulin around six to nine months after treatment," Mamcarz says. "This is truly an achievement over prior gene therapy trials, where B cell reconstitution did not occur and patients required intravenous immunoglobulin for life."

The trial's first patient arrived at St. Jude with complex issues, including a viral infection. Maternal immune cells the baby had acquired before birth prevented him from achieving immune recovery after treatment with the lentiviral vector.

"We gave him a second treatment, without chemotherapy, and



## Designing a cure

To find a safer and more effective way to cure children with XSCID, Brian Sorrentino, MD, director of St. Jude Experimental Hematology, worked tirelessly for more than a decade to perfect a novel gene therapy. Leading a team of scientists, he successfully created a lentiviral vector that can insert a healthy copy of the *IL2RG* gene into a patient's blood-forming cells.

it worked," Mamcarz says. "The maternal cells disappeared, part of his immune system already recovered, and the infection that he had had for over a year and a half is now gone."

To date, two babies have been taken off immunoglobulin infusions and one has started receiving routine vaccinations. The patient responded well to immunizations, producing significant immune responses to numerous types of *Streptococcus pneumoniae* strains within six weeks of vaccination.

## Samuel's surprising results

Within two days of traveling to St. Jude, 11-month-old Samuel spiked a fever caused by an infection in his shoulder. Mamcarz

discovered the infection was caused by bacteria used in a vaccine commonly given to newborns in Brazil to prevent tuberculosis. Serious side effects of the vaccine in healthy babies are rare, but for Samuel it had caused a life-threatening

complication because he lacked an immune system.

Surgeons at St. Jude performed an operation to remove the infection from his shoulder before Samuel was treated with his own genetically re-engineered cells to treat XSCID.

"Samuel surprised us quite a bit. At first, his gene marking of the infused cells was lower than those of other children in the study. But our vector must be quite powerful, because he went on

**The St. Jude trial for infants with XSCID may provide insights for treating other disorders, including Wiskott-Aldrich syndrome and sickle cell disease.**



to reconstitute just like other patients who had very strong marking,” Mamcarz says.

Gene therapy has given Samuel a second chance to live. He received his last immunoglobulin infusion in January 2018. The 16-month-old returned home with no activity restrictions.

“Sam’s a fighter,” says his mom, Simone. “He loves playing with little cars...and with my cell phone.”

She and Ricardo will bring Samuel back to St. Jude every three months for checkups.

### Teamwork and collaborations

As more infants are treated in the clinical trial, Sorrentino and Mamcarz eagerly await results regarding the long-term durability and potential side effects of the gene correction therapy.

The researchers credit multidisciplinary teamwork for developing the treatment protocol, manufacturing the lentiviral vector and establishing collaborations with partner sites to open the ground-breaking trial.

Lentiviral vector technology has also been used to help patients who only partially benefited from previous bone marrow transplants. A recently published study by the National Institutes of Health used a lentiviral vector developed at St. Jude to successfully reconstitute the immune system in several patients.

### Looking beyond XSCID

Sorrentino anticipates that the St. Jude XSCID clinical trial will provide insights for treating other disorders. These include Wiskott-Aldrich syndrome, a disorder that causes infections and reduces the ability to form blood clots, and sickle cell disease, which affects about 100,000 Americans.

“We care for almost 1,000 sickle cell patients at St. Jude,” Sorrentino says. “Our gene therapy platform could potentially be curative for these patients as well as for many other devastating immune disorders in the future.”

“Every time one of these babies turns the corner, we are so gratified,” adds Sorrentino, who has dedicated his career to translating gene therapy technology from bench to bedside. “I’m convinced that many of the children Dr. Mamcarz has treated on this protocol would not have lived without receiving this experimental therapy.”

“We give huge credit to the families who trust us to treat their newborn infants,” Mamcarz says. “I’m excited for patients like Samuel, who can go home with a new lease on life.” ■

### Going home

The world’s first lentiviral gene therapy trial for infants with XSCID has given 16-month-old Samuel Evangelista hope for a bright future. He returned home to Brazil in January 2018 with no activity restrictions.



# The EXTRA Mile



## Through a charitable gift annuity, one donor receives payments for life while helping St. Jude kids.

By Zack McMillin

As a former marathoner who remains an avid runner, Joe Hollis knows something about going the extra mile. The mission of St. Jude Children's Research Hospital motivates him to keep a relentless pace of giving.

In 2010, while running with his St. Jude philanthropic adviser, Hollis learned how a charitable gift annuity could benefit him while helping St. Jude kids. He loves the simplicity of this unique giving vehicle, which provides payments for life at a set rate and can provide tax benefits for some donors.

"This is a big plus to me, to have the peace of mind of the additional income and also know that I'm helping the children," says Hollis, a semi-retired car dealer from Missouri. "I'm trying to increase it as much as I can, every year. I've set some big goals."

Hollis, who is in his late 60s, has put St. Jude in his will. Every spring he tries to attend the Danny Thomas – St. Jude Society event for supporters who have included the hospital in their estate plans.

"I tell everyone, this is an awesome place and you really need to see it to get your head around how big their plans are for saving these children," Hollis says. "Every time I go, it seems like I pick up something new."

Ever the salesman, Hollis always sports a St. Jude logo on his hat or shirt.

"It's a great way to get someone to ask about St. Jude," he says. "I'll give them my 10-minute pitch."

Hollis says he always points out that families never receive a bill from St. Jude for treatment, travel, housing or food.

"And I always talk about how the research is shared with everyone in the world," he says. "Things like that are what sets St. Jude apart."

A few years ago, Hollis honored his parents by dedicating a plaque in the St. Jude Biomedical Library. The inscription reads: "Attitude is the crayon that colors the world." He felt the quote, one he's seen on signs during his runs, captured the hope and resilience of St. Jude patients and families.

"You hear those stories, and you've got to get that box of Kleenex out," he says. "So inspiring." ■

**For details about charitable gift annuities or other ways to support St. Jude, call 1-800-910-3188 or email [giftplanning@stjude.org](mailto:giftplanning@stjude.org).**



# The *Heartbeat* of the *Hospital*

For the employees who dedicate their lives to St. Jude, working at the hospital is more than a job. It's a calling.

By Elizabeth Jane Walker

They've come from 50 states and more than 80 foreign countries, inspired by the mission, awed by the phenomenal scientific facilities. These dedicated individuals marshal their intellect, their compassion and their energy toward one goal: finding cures and saving children.

They are the employees of St. Jude Children's Research Hospital.

Thousands of faculty and staff work together night and day to make discoveries and advance cures. Whether they're practicing medicine and science, calibrating state-of-the-art machinery or cooking gourmet food, St. Jude employees offer families a light in the darkness.

"It is our diverse and talented workforce that makes us who we are," says James R. Downing, MD, St. Jude president and chief executive officer.

Long celebrated for its clinical and scientific merits, St. Jude now heads

many lists as one of the best workplaces in America.

The reason?

"Our patients and their families inspire us to continue searching for cures and improving treatments," explains Dana Bottenfield, vice president of St. Jude Human Resources. "Our employees connect to our mission, and we're focused on fostering a culture that allows them to do their best work."

*"Our employees connect to our mission, and we're focused on fostering a culture that allows them to do their best work."*

— Dana Bottenfield

For the past eight years, St. Jude has been named one of the "100 Best Companies to Work For" by *Fortune* magazine. In 2018, Glassdoor named the hospital to its listing of the nation's best

places to work. *People* magazine has touted St. Jude as one of the "Companies That Care." *Fortune* also praised the institution as one of the best workplaces for women and millennials, as well as for diversity and health care. And the federal government has lauded St. Jude for the support it offers employees who serve in the military.

Those accolades inspire St. Jude employees to work harder. The hospital's workforce features many who are the best in their fields—including Howard Hughes Medical Institute investigators, a Nobel laureate and members of the Institute of Medicine and the National Academy of Sciences.

These employees are drawn by the mission and the unparalleled resources, but they stay because of the collaborative environment—a place where they can save the lives of children today, while discovering the cures of tomorrow.

"We must be bold and ambitious, chasing big dreams and pursuing scientific and medical excellence," Downing says. "It is our legacy and our future." ■

PHOTOS BY JUSTIN VENEMAN



## Selfie time

A small group of St. Jude faculty and staff gather for a photo to celebrate the most recent *Fortune* magazine award.



### Exploring new depths

Tirrell Ross immerses himself in the virtual reality experience.

# A Virtually Painless Experience

St. Jude explores virtual reality as a distraction technique for children and teens undergoing the pain crises of sickle cell disease.

BY MIKE O'KELLY

Patients in a new St. Jude Children's Research Hospital study will soon dive deep into the ocean for a marine experience alongside tropical fish, friendly seals and curious dolphins. While launching multi-colored bubbles at a variety of aquatic life, they'll navigate an underwater terrain of sunken ruins and stone columns.

Swimsuits, scuba gear and beach towels won't be necessary—the underwater journey is part of a new virtual reality experience designed to distract children with sickle cell disease who have acute pain crises.

People with sickle cell disease have red blood cells that are sickle-shaped and hard, making it difficult for their cells to move through blood vessels and deliver oxygen to body tissues. Pain crises are the recurring episodes that occur when normal blood flow is disrupted.

### Engulfing approach

The pain is different for each individual. Some children get complete relief from routine pain medicines while others need more time or increased dosage before the pain subsides.

Three years ago, Doralina Anghelescu, MD, director of the hospital's Pain Management Service, began a clinical trial to see if adding the drug gabapentin to the standard regimen would lessen acute pain from sickle cell crises more quickly or completely. The study is ongoing, but when presented with the opportunity of including virtual reality technology as a distraction tool, the researchers decided to try it.

The virtual reality project will include 76 patients—half will receive virtual reality sessions and the other half will receive standard treatment. St. Jude is partnering with the Memphis-based Methodist Comprehensive Sickle Cell Center on the clinical trial. This is the first study at St. Jude to use virtual reality, helping further position the institution as a leader in pain management for pediatric patients.

"I think St. Jude can be on the front line and be a champion for this new concept of integrative medicine—a combination of pain medications, working with psychologists, using relaxation techniques and technology-based approaches such as virtual reality," Anghelescu says.





### Under the sea

Children and teens in the study's virtual reality arm will slip on a headset and headphones and grasp a video controller before they are launched into the 15-minute undersea experience. While receiving IV medications, participants dive into the water from a virtual boat and either navigate through the ocean or sit back and enjoy an automated ride.

Entering a 360-degree underwater world, patients can launch an unlimited arsenal of multi-colored orbs at passing marine life and strategically placed objects such as genie lamps, treasure chests and shimmering targets. Sea creatures such as jellyfish, orca whales and sea turtles glow brightly when the bubbles make contact, a harmless game of target practice that cumulates in a score posted at the end of the session.

Patients will meet a baby seal eye-to-eye at the journey's halfway point. With relaxing music as a backdrop, the seal swims away to reveal an underwater castle of columns and archways.

"Overall, it's a soothing experience, and it really does immerse you virtually," says Latika Puri, MD, of St. Jude Hematology, the study's principal investigator. "I thought 15 minutes might be a long time at first, but every few minutes you see something different, which makes you curious about what is going to happen next."

St. Jude Hematology clinical research associates and nurses observe the session and help participants complete a short satisfaction survey. Participation in the study is a one-time occurrence.

Swimsuits, scuba gear and beach towels won't be necessary—the underwater journey is part of a new virtual reality experience designed to distract children with sickle cell disease who have acute pain crises.

### A broader scale

Virtual reality has been used as a distraction technique for burn patients undergoing painful dressing changes, but St. Jude is one of the first institutions to use it for sickle cell crises in a study.

While virtual reality is a newly explored form of distraction, patients and families are already adept at using technology to alleviate pain or nervousness prior to medical procedures. It could be as simple as a child playing a game on a smart phone when receiving chemotherapy.

"Patients and families instinctively use distraction tools. This is just a bit more advanced intervention," Anghelescu says.

The technology could potentially be used at St. Jude to help an even wider range of patients.

"It's great because virtual reality as a distraction tool has broader applicability than just for pain, especially in oncology patients with port access and routine needle sticks," Puri says. "At St. Jude, there is a real interest in making advancements by integrating cutting-edge science and technology with clinical medicine." ■



# WHEN LIGHTNING STRIKES TWICE

**WHY ARE SOME FAMILIES STRUCK WITH MULTIPLE CASES OF HODGKIN LYMPHOMA? RESEARCH TO PINPOINT GENETIC CAUSES COULD LEAD TO TARGETED TREATMENTS.**

By Maureen Salamon

The old adage that looks can be deceiving certainly applies to Kaden and Kristian Knecht. On the surface, the brothers seem strikingly different.

Light-haired Kaden, nearly 18, is serious, driven and goal-oriented, while slightly darker-featured Kristian, 15, sports a laid-back and fun-loving demeanor.

But the teens have one thing in common that neither would have chosen: Both were diagnosed two years apart with Hodgkin lymphoma, a cancer of the white blood cells in the lymph nodes. Now clinicians at St. Jude Children's Research Hospital are determining whether the Knecht brothers also share a genetic mutation that may have caused the cancer to develop.



This St. Jude study, known as the FAMHL clinical trial, is on track to be the largest study ever conducted for families with a high frequency of Hodgkin lymphoma. It's also the only such effort using whole-genome sequencing, which provides the most comprehensive DNA analysis possible.

The Knecht boys' mother, Laura Duthu, was told that lightning doesn't strike twice. She hated learning it actually could, but is thrilled that St. Jude may unearth the reason two of her four children developed the same type of cancer. Both underwent chemotherapy treatments at St. Jude and are now in remission.

"If they can figure out if there's a genetic link, or what's causing this, maybe in the future we could prevent something like this from happening to another family," Duthu says. "You don't often hear of the same type of cancer in siblings like this. I thought the study was a great idea."

### A gathering storm

Established research has shown that Hodgkin lymphoma—diagnosed in about 8,300 people in the U.S. each year—may run in families. But scientists have never identified possible genetic underpinnings of the condition, even in families where multiple cases strongly suggest an inherited risk.

St. Jude treats about 30 new Hodgkin patients each year. More than 20 families throughout the years have had more than one person diagnosed with the disease, including parents and children, says oncologist Jamie Flerlage, MD. She is running the FAMHL trial with colleagues Monika Metzger, MD, of St. Jude Oncology and Jun J. Yang, PhD, of Pharmaceutical Sciences.

Flerlage says there's a two- to six-fold increase in the risk of developing Hodgkin lymphoma when a close family member has also had it. But she's been stymied in her desire to explain why. Exposure to the Epstein-Barr virus—which causes mononucleosis—is a known risk factor (and one the Knecht brothers share), but not everyone who's exposed to the virus gets

Hodgkin. And little else would suggest the malignancy might occur more frequently in certain people.

"We don't know the genetic risk—we just know from large population studies that there is a genetic link," Flerlage says. "Right now, there's no way to test anyone to say, 'You don't have it; you don't have to worry.' Even if you have someone



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### Sibling support

Kristian Knecht (at left) and his brother, Kaden, both received treatment for Hodgkin lymphoma at St. Jude. The teens are also participants in a clinical trial designed to discover the disease's origins.





### Examinations and investigations

Jamie Flerlage, MD, talks with 11-year-old Shamaria Smith during a checkup. Flerlage and her colleagues want to learn how to predict whether a child's family members will develop Hodgkin lymphoma. The research may help scientists create targeted drugs based on the disease's biological and molecular features.

in your family with Hodgkin, there's nothing we can do except watch for clinical symptoms."

### Glimmers of sunlight

Fortunately, survival rates for Hodgkin lymphoma remain quite high as the St. Jude research—expected to bear fruit in three to five years—continues.

"Today, more than 90 percent of patients survive and go on to lead normal, productive lives," Flerlage says.

Like the Knechts, the vast majority of Hodgkin patients are adolescents or young adults, and the disease almost never strikes before age 10. Incidence peaks in the 20s and falls in the 40s, peaking again around age 65. Most Hodgkin lymphoma

**"We're comparing genomes in each family, and comparing one family to another, to see if there's a common gene or if there are specific genes in each family."**

— Jamie Flerlage, MD

patients find telltale lumps or bumps, often in their necks, Flerlage says. Other key symptoms include unexplained fevers, weight loss and drenching night sweats. A tissue biopsy is needed to confirm diagnosis.

The Knecht boys' treatment path mirrored that of most patients, who undergo two to six months of chemotherapy. Some patients also

receive radiation, though Flerlage says doctors skip it whenever possible to avoid side effects and the associated risk of patients developing secondary cancers.

"In the past, everybody used to receive radiation as part of their treatment," she says. "It's only in recent years that we've found there are certain groups of patients who respond well

# The FAMHL clinical trial is on track to be the largest study ever done on families with a high frequency of Hodgkin lymphoma. It's also the only such effort using whole-genome sequencing, which provides the most comprehensive DNA analysis possible.

enough to chemotherapy to not need radiation. And St. Jude was one of the institutions that led the effort.”

## Research sparks discovery

Enrolling more than a dozen families so far since late 2016, the FAMHL study is centered around families in which the patient is 21 or younger and has a parent, sibling or child who has also had Hodgkin lymphoma. DNA samples are taken from those with a history of Hodgkin as well as from family members who've been unaffected in order to compare any differences. The study is being conducted in collaboration with the National Cancer Institute, which is also contributing samples collected over the last four decades from at least 30 families affected by Hodgkin lymphoma. This collaboration will expand the St. Jude efforts, strengthening the eventual findings.

Whole genome sequencing, a technique that deciphers every letter of a person's genetic code, has been used by St. Jude investigators to identify potential disease-causing variants in participants' germline DNA. Germline mutations are present in every cell of the body since birth, including tumor cells and normal cells, while so-called somatic mutations are only present in tumor cells.

## A common current

Unaffected family members participating in the study are mostly close relatives, but can include cousins if a particular family tree suggests an aunt or uncle may have also had the disease, Flerlage notes. But every family in the study has at least one first-degree relative with Hodgkin lymphoma.

“We're comparing genomes in each family, and comparing one family to another, to see if there's a common gene or if there are specific genes in each family,” Flerlage explains, adding that this part of the process should take one to two years. The analysis will be done through Yang's group and experts in the St. Jude Cancer Predisposition Division, who are specialists in identifying novel genetic variants.

All the families happen to be similar in at least one other aspect: They're united in their commitment to the research.

“Every single family has been more than willing to participate, because they all have more than one person affected and have been asking the question ‘why’ the entire time,” Flerlage says.

“Families also have the option to learn about their own

results, and every family wants to do that because it may have implications for others in their family, or their kids. They're worried about this already.”

## Cause and effect

Flerlage and her colleagues believe that understanding the origins of Hodgkin lymphoma—whether critical genetic defects or variations related to risk—will accomplish several goals. Chief among them are the ability to proactively predict whether a patient's family members will develop the cancer, as well as to create targeted drugs based on its biological and molecular features.

If researchers do find a particular mutation running in a family that places members at a higher risk for cancer, those consenting to receive that information may benefit from genetic counseling, she says.

Flerlage specifically hopes a gene defect is discovered that definitively means Hodgkin will develop in an affected person. Such a clear cause-effect link would translate into less gray space in helping families understand what to expect and how to cope.

“Because Hodgkin is widely curable,” she says, “it's less of a goal to prevent it than find a way to offer predisposition counseling to other family members and offspring and then to find a new target for treatments.”

## An eye on the sky

After ushering two children through cancer treatments, Duthu is justifiably worried that Hodgkin lymphoma may strike yet another of her offspring, who include a 20-year-old daughter and 7-year-old son. But she says she's relieved that St. Jude clinicians are doing everything possible to figure out whether that's a possibility.

“They may find something, they may not...maybe 10 years down the line, maybe never, maybe tomorrow,” she says. “My hopes are they are able to come to some conclusion on why this is happening or what caused this, but if they don't, I'm OK with that.”

“Despite the cancer, the whole St. Jude experience has been God-sent,” she adds. ■

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

# 6 Ways

## TO HELP TEEN PATIENTS NAVIGATE LOSS

Know teens or young adults who have cancer?  
Here are some tips for helping them deal with grief.



By Elizabeth Jane Walker

For teens and young adults with cancer, life may seem more complex than it is for younger children or adults.

As they undergo treatment, teenagers must also cope with separation from their school and friends. Unlike younger children, teens are acutely aware of the long-term implications of a cancer diagnosis. But perhaps the most difficult challenge can be the loss of friends to death.

To help patients traverse the landscape of loss, St. Jude Children's Research Hospital oncologist Liza-Marie Johnson, MD, conducted research in which she spoke with teens and young adult patients at St. Jude.

Thirty-seven percent of the study's participants had lost friends, with 66 percent of those deaths related to cancer. Many of the patients admitted they rarely, if ever, discussed those losses. A full report on Johnson's research findings recently appeared in the journal *PLOS One*. ■

The following insights may help you support a teen patient who is experiencing loss:

- 1. Recognize the depth of the bond:** Teens with cancer share a unique connection. Who better understands the reality of hair loss, nausea or other issues than someone who is also going through those events? Teens often bond quickly over their shared experience with illness and then contemplate their own mortality when a friend passes away.
- 2. Understand the range of emotions:** In addition to grief, a teen may feel shocked, depressed, lonely, angry, guilty, disbelieving, hopeless or vulnerable. The survivor may also have difficulty sleeping or harbor feelings of emptiness.
- 3. Talk it out:** Silence may make a friend's death more difficult to process and increase the survivor's risk of depression, anxiety or the physical symptoms of stress, such as headaches or stomach pain.
- 4. Jumpstart conversations:** Acknowledge a teen's relationships with other patients and ask about those relationships as a way to begin a discussion about death.
- 5. Listen:** Attend to the teen's concerns rather than ignoring the loss. Encourage the patient to interact with peers instead of seeking solitude.
- 6. Seek professional assistance:** Consider seeking support from a trusted child life specialist, hospital chaplain, social worker or member of the psychology team.



# Country Cares

## And So Does Dad

### A longtime supporter recalls the day the hospital's mission got personal.

By Richard J. Alley

For nearly 30 years, the country music industry has helped support the mission of St. Jude Children's Research Hospital through its Country Cares for St. Jude Kids program. In that time, country music radio stations have marshalled their audiences, organized radiothons and raised more than \$750 million for the hospital.

An early pioneer of the Country Cares movement was Don Langford. While working as program director for a California radio station, he was summoned to the hotel room of Randy Owen, lead singer of legendary group ALABAMA. Owen was the spark that ignited Country Cares.

Langford says he had no interest in working with the initiative at the time.

"I drove to the hotel rehearsing all of my reasons why I was not going to be a part of Country Cares—it's a hospital in Memphis, it doesn't affect me on the West Coast—and 10 minutes later, I'm on the board," Langford says.

Then Langford visited St. Jude, where he saw firsthand the dream St. Jude founder Danny Thomas had envisioned and Owen advocated.

Seven years later, the unthinkable happened: Langford's daughter, Analise, was diagnosed with Hodgkin lymphoma.



#### Living the dream

Country Cares pioneer Don Langford and his daughter, Analise, a St. Jude cancer survivor.

"Three days later, we were in Memphis," he says. "When I walked into the hospital, I was no longer a member of the board, program director of a radio station or chairman of the Academy of Country Music. I walked in the door as a father, so it was a whole different experience."

The experience reaffirmed his original commitment to St. Jude and drove home the mission he'd spent so much time broadcasting.

Today, Analise is healthy and has a family of her own. Her father is semiretired, still on the board of Country Cares and taking every opportunity to raise awareness for St. Jude.


"I think we'd all like to say, at the end of our day, that we did something that will leave a mark," Langford says. "And this is something I can say: That, in a small way, I was part of something that got very big, very fast." ■

*To learn more about Country Cares, the hospital's other radio programs or the newest fundraising campaign, Music Gives to St. Jude Kids, visit [stjuderadio.org](http://stjuderadio.org).*



# The MISS Cont

By Amy Wolff Sorter



**Thirteen-year-old Dylan Thomas** used to spend hours executing secret missions, infiltrating enemy lines and proving his valor through action-adventure video games. When he wasn't dashing through battlefields or vanquishing the forces of evil, he was embroiled in a battle with an even more insidious adversary: a particularly aggressive form of acute myeloid leukemia (AML).

Nearly two years ago, Dylan underwent two grueling rounds of chemotherapy and a bone marrow transplant at a North Carolina hospital. Eventually, his leukemia returned. A second transplant held his only hope for a cure.

Dylan's doctor suggested that he consider a new clinical trial, called VENAML, at St. Jude Children's Research Hospital. The study features a drug called venetoclax, which has shown promise in treating adults with leukemia.

# PROMISE: continues

Discoveries emerging from a lab in Cell and Molecular Biology are now moving into the clinic to help children with an aggressive form of leukemia.



PETER BARTA



## Gallant gamer

Video game ace Dylan Thomas participated in the VENAML clinical trial, which helped him achieve remission so that he could undergo a second bone marrow transplant for acute myeloid leukemia.

## A dramatic response

In August of 2017, Dylan enrolled in the clinical trial.

"When we arrived, Dylan had a tumor on his leg, and cancer had infiltrated into his sinuses," explains his mom, Cloie Thomas, RN. "It was starting to spread down his throat. He could barely speak. But after the third day of taking venetoclax, he was talking again. Within a week, it was like the tumor in his leg completely melted away."

Cloie says the treatment was much less traumatic than the chemotherapy Dylan had previously undergone.

"Venetoclax got his disease to the lowest point it had been since the day he was diagnosed," she says.

By October, Dylan had been in remission long enough to undergo a second transplant.

## Bold collaboration

The drug that helped Dylan achieve that remission has been a focus of the lab of Joe Opferman, PhD, of St. Jude Cell and Molecular Biology.

At St. Jude, the paths and goals of laboratory and clinic often merge to improve patient outcomes. Basic-science discoveries Opferman made in his lab have recently moved into the clinic through the VENAML study.

Opferman joined forces with Jeffrey Rubnitz, MD, PhD, of St. Jude Oncology, for the study, which launched in July 2017. It marks the first time Opferman and Rubnitz teamed up to bring lab results into the clinical setting.

## Assessing the foe

Pediatric leukemia isn't a singular disease. The most common is acute lymphoblastic leukemia, or ALL.

This disease generally responds well to treatment.

But AML is different.

This leukemia has many different subtypes and is more difficult to treat. Fewer children are diagnosed with the disease, and fewer drugs are available to combat it.

"We've been stuck at a 70 percent survival rate for the past 10 to 15 years," Rubnitz says, "so we need to find new therapies for AML."

## Call of duty

For many years, Opferman has been studying how certain proteins enable cancer cells to evade death—and how to obstruct that process.

His particular interest is in the MCL1 protein and the BCL2 family of proteins. Expression of the BCL2 protein is often elevated in hard-to-treat leukemias, including AML. Opferman's research has been instrumental in testing venetoclax, a BCL2 inhibitor.

To pinpoint which proteins boost cancer cells, he uses another technique, called BH3 profiling.

"It's a rapid way to take a mixture of cancer cells and assess which pro-survival molecule it's addicted to," he says. "By knowing that, you could postulate that if you added an inhibitor of that specific family member, then you would get a therapeutic benefit."

Using this method, it's possible to find out whether a certain cancer depends on BCL2 for survival.

"If you find that a cancer cell is supported by BCL2," Opferman says, "you can predict that it would respond well to something like venetoclax."

## The one-two punch

Another important aspect of Opferman's research involves combining new therapies with existing chemotherapy. Many cancer treatments rely on combination therapies. The benefits are that different agents attack various pathways in the same cancer cell.

"The more stress you put on cells from different pathways, the less chance that the patient ends up resistant to a single drug," he says.

Venetoclax is the first FDA-approved drug targeting the BCL2 protein in cancer cells. Because the drug had not yet been approved for use in childhood leukemia, the next logical step was to introduce venetoclax to children who have undergone standard chemotherapies for AML and have relapsed.

That's where the clinician stepped in.



SETH D. XION

## Triumphs in the lab

Joe Opferman, PhD, of St. Jude Cell and Molecular Biology, has spent years studying how certain proteins enable cancer cells to evade death—and how to obstruct that process. Discoveries he made have recently moved into the clinic.

## Joining forces

Rubnitz learned about Opferman's research when the latter made a presentation about how inhibiting the BCL2 protein might reduce cancer development. Rubnitz knew there had been long-term efforts to inhibit BCL2 and related proteins. He thought the relatively new drug venetoclax might be useful in targeting AML among children.

The resulting clinical trial, VENAML, is a two-phase trial. The first phase tests the safety of venetoclax, when combined with a standard chemotherapy regimen.

Patients in the study have AML that never responded to treatment or that returned after receiving standard therapy. Rubnitz expects up to 30 children to participate in the first phase. The study's second phase will roll the drug out to a larger group of children.

But Rubnitz and Opferman have even higher aspirations.

## Inspiration and determination

The eventual plan is to collect a sample from a patient with relapsed AML and send it to Opferman and his lab.

"He can then tell us, 'This patient is likely to respond to venetoclax,' or 'This patient would not,'" Rubnitz says. "We'd use venetoclax in patients Joe predicts would respond well to it."

The hope, Rubnitz goes on to say, is that venetoclax, or a similar drug, could one day be used in patients newly diagnosed with AML, rather than only for those who relapse.

The VENAML trial helped Dylan achieve remission so he could undergo a second bone marrow transplant. But sadly, the cancer cells returned a few months after transplant, and Dylan eventually lost his valiant battle.

Heartbreaking losses like these make Opferman and Rubnitz even more determined to find a cure for this insidious disease.

## The ultimate goal

Opferman says he envisions a rapid screening system that would allow

clinicians to predict responsiveness to specific drugs.

"I think in the next five to 10 years, we'll have a broader palette of drugs to use, so that you could tailor a given therapy based upon how the cells are in the patient," he says. "You could say, 'Aha, this patient is very MCL-1 dependent, so we'll add this drug to the standard chemo versus that drug.'"

The long-term goal is to be agile in tailoring that treatment.

"If the patient initially responded well to the venetoclax and had a BCL2-dependent BH3 profile, but then had a recurrence later, we could check to see if the cells that recurred had changed their addiction," Opferman explains. "Are they now dependent on a different protein for their survival? Then we could plug in other drugs as necessary."

## Making a difference

Both researcher and clinician emphasize that the trial is in its early days. Still, the first step is to proceed with VENAML, centered on the only approved BCL2 drug.

"One of the cool things about St. Jude is that you are here to improve treatments and cures for patients," Opferman says. "For a basic scientist like me, being involved in a clinical trial is as close as you can get to doing that. I'm excited about it, because it obviously brings us that much closer to making a difference." ■

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



### Taking aim at AML

Oncologist Jeffrey Rubnitz, MD, PhD, is dedicated to saving the lives of children such as 6-year-old Briza Ramirez, who has acute myeloid leukemia.

**"We've been stuck at a 70 percent survival rate for the past 10 to 15 years, so we need to find new therapies for AML."**

— Jeffrey Rubnitz, MD, PhD



### Dynamic duo

Laboratory researcher Joe Opferman, PhD, has joined forces with clinician Jeffrey Rubnitz, MD, PhD, to find a way to cure AML that has relapsed or is difficult to treat.



## DNA approach reveals a 'hijacking'

Changes in DNA cause cancer. The DNA in cells is usually coiled and packed more tightly than a commuter train at rush hour. Researchers have had to uncoil the molecule to find and study the changes that lead to cancer.

St. Jude scientists have used a new method to study DNA when the molecule is coiled. By studying DNA in 3-D, they found previously hidden changes that drive cancer.

The approach helped researchers identify a mechanism that drives about 10 percent of high-risk cases of neuroblastoma, a cancer of the sympathetic nervous system. The scientists showed how a rearranged chromosome allowed a cancer-promoting gene to "hijack" segments of DNA.

Those segments normally rev-up expression of other genes. In this case, the hijacking leads to increased expression of a cancer-promoting gene. The findings suggest a possible new treatment approach for neuroblastoma.

"Studying DNA in 3-D will help us identify, understand and ultimately address other changes that are driving tumor growth and spread," said Jinghui Zhang, PhD, St. Jude Computational Biology chair.

The research was done in collaboration with scientists at Dana-Farber Cancer Center and the Whitehead Institute of Biomedical Research. The findings appeared in the journal *Cancer Discovery*.



From left: John Schuetz, PhD, and Aaron Pitre, PhD

## AN ACHILLES HEEL in a lethal leukemia

Scientists have discovered how a link between two proteins in acute myeloid leukemia (AML) enables cancer cells to resist chemotherapy. Disrupting that link could render the cells vulnerable to treatment.

John Schuetz, PhD, of St. Jude Pharmaceutical Sciences, and his colleagues knew a protein called ABCC4 is elevated in aggressive cases of AML. The team searched for other proteins that might interact with ABCC4 and enable its function. By screening hundreds of proteins, they found one called MPP1, which was greatly increased in AML.

The findings could help clinicians identify patients with high levels of ABCC4 and MPP1. Such patients might benefit from drugs that disrupt those proteins.

The findings could also lead to drugs to enhance chemotherapy in patients with colon and breast cancers and the brain tumor medulloblastoma.

A report on this research appeared in the journal *Nature Communications*.



## IMPROVING VACCINATION rates in hospitals

A St. Jude quality improvement initiative that greatly increased the employee vaccination rate for pertussis, or whooping cough, offers a model for other health care institutions nationwide.

Previously, about 58 percent of St. Jude health care workers with patient contact had received the Tdap (tetanus, diphtheria, acellular pertussis) vaccine, said Elisabeth Adderson, MD, of St. Jude Infectious Diseases. That percentage is about double the national average for health care workers. Yet, Adderson and her colleagues believed they could improve that rate.

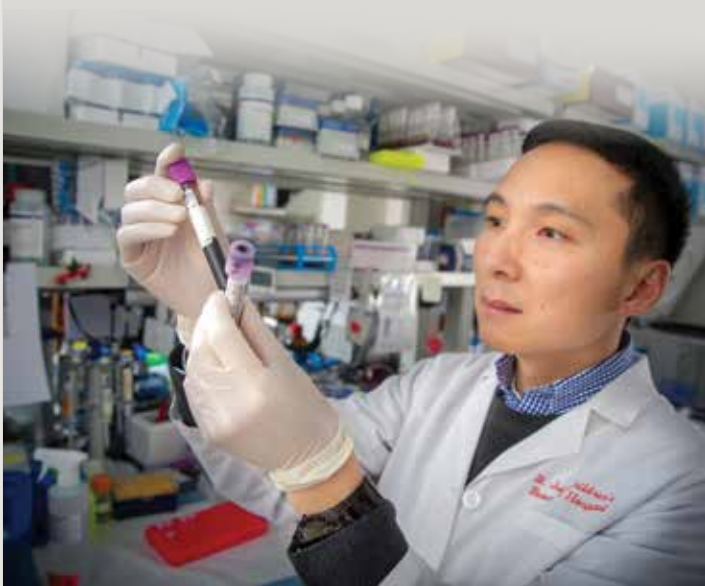
Through a robust campaign, she and her team increased the vaccination rate to 90 percent.

The researchers shared their techniques with other hospitals in the scientific journal *Vaccine*.



Elisabeth Adderson, MD

PHOTOS BY SETH DIXON



Jun J. Yang, PhD

## A DOUBLE WHAMMY for leukemia patients

St. Jude scientists have discovered new germline variations in a tumor suppressor gene called *TP53*. Children with these variants are at risk of developing leukemia. They also have a one-in-four chance of developing another cancer later in life.

Germline variations are carried in the DNA of every cell, not just in the DNA of tumor cells.

“These germline variations are a double whammy for carriers,” said Jun J. Yang, PhD, of the St. Jude departments of Pharmaceutical Sciences and Oncology. “Not only is their risk of developing leukemia very high, they are also more likely to relapse or develop another cancer subsequently.”

The association between the high-risk variants and second cancers is so significant that researchers are exploring how to help patients and families manage their risk.

A report on this study appeared in the *Journal of Clinical Oncology*.



### The buzz about the garden

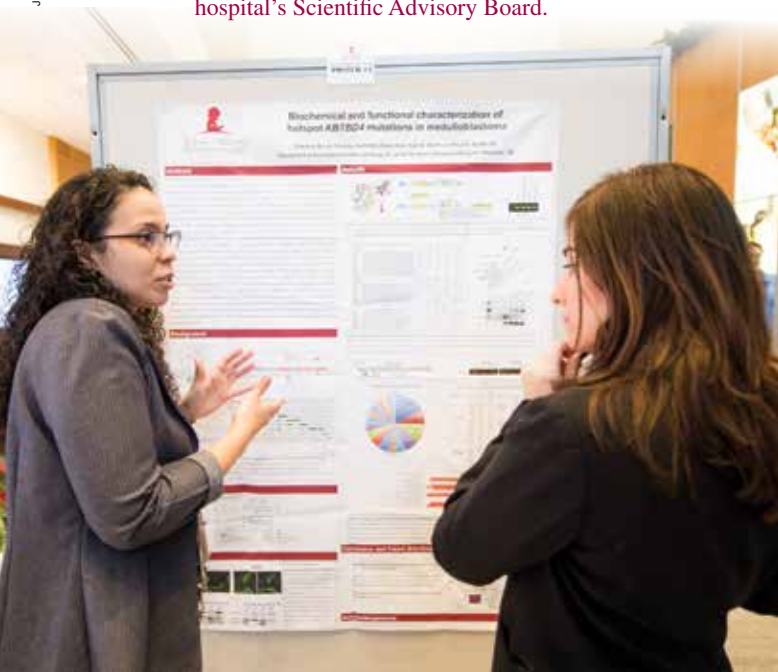
During the past year, about 20,000 bees have been added to the St. Jude Garden to improve pollination in the space. St. Jude was one of the nation's first hospitals to create a garden dedicated to growing vegetables and herbs for consumption by patients, families, staff and visitors. Most of the garden's bounty is consumed in the hospital's cafeteria. The garden team expects to harvest more than 7,000 pounds of produce from the garden in 2018.



From left: Ben Youngblood, PhD, and Hazem Ghoneim, PhD

### Sharing science

During the hospital's recent Faculty Postdoctoral Poster Session, Himy Muniz-Talavera, PhD (at left), of St. Jude Developmental Neurobiology explains her research to Fatima Rivas, PhD, of St. Jude Chemical Biology and Therapeutics. The annual event features a variety of posters from St. Jude faculty and coincides with a visit of the hospital's Scientific Advisory Board.



## ORIGINS REVEALED for immune system's 'smart soldiers'

White blood cells called memory T cells are the rapid reaction force of the disease-fighting immune system. These cells recognize and respond when previously vanquished viruses, cancer or other threats try to stage a return.

But where do these smart soldiers come from? Scientists have long debated the origin of memory T cells.

Researchers from St. Jude and Emory University have the best evidence yet about the answer.

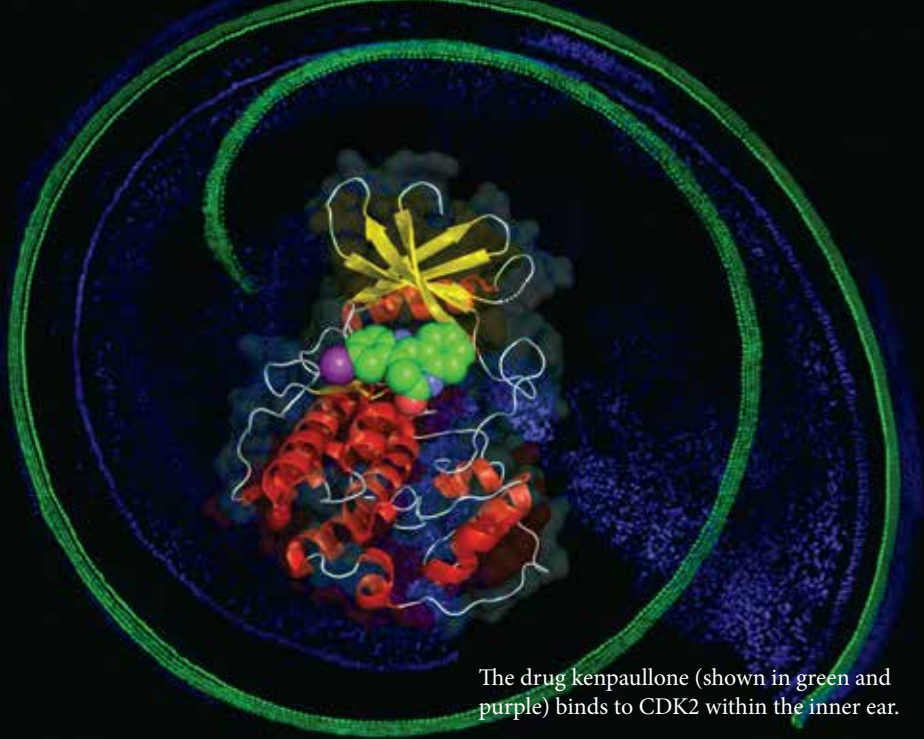
The scientists showed that certain memory T cells develop from T cells originally made by the body for another role. Called effector T cells, these cells fight viral infections and other threats. Usually, these cells complete their job and then die.

But researchers found that a small percentage of effector T cells turn back the developmental clock and live on as memory T cells. Memory T cells move throughout the body, always ready to recognize an attack and mount a defense.

"These results have provided new insights into memory T cell differentiation and may help researchers generate more effective vaccines or cancer immunotherapies," said Ben Youngblood, PhD, of St. Jude Immunology.

The research appeared in the journal *Nature*.





The drug kenpaullone (shown in green and purple) binds to CDK2 within the inner ear.

## A NEW AVENUE to prevent hearing loss

The chemotherapy drug cisplatin may help save a child's life. But that same medication can also damage a child's hearing. Now, St. Jude scientists have found a compound that prevents hearing loss caused by cisplatin in laboratory models.

The drug is known as kenpaullone. It works by binding to and inhibiting the enzyme CDK2. Researchers showed that reducing the activity of CDK2 preserved hearing, in part by protecting hair cells in the inner ear. The hair cells are irreplaceable and are essential for hearing.

Currently, there are no approved drugs in the U.S. to prevent or treat hearing loss. Fifty to 70 percent of cancer patients treated with cisplatin experience hearing loss.

Jian Zuo, PhD, of St. Jude Developmental Neurobiology says more studies are needed before kenpaullone or related compounds are ready for clinical trials. A report on this study appeared in the *Journal of Experimental Medicine*.

## DOUBLE THE REWARDS for exercise

An online "game" that rewards players for physical activity may help motivate young cancer survivors to be more active. That's vital, since they are more likely than their peers to be overweight and physically inactive.

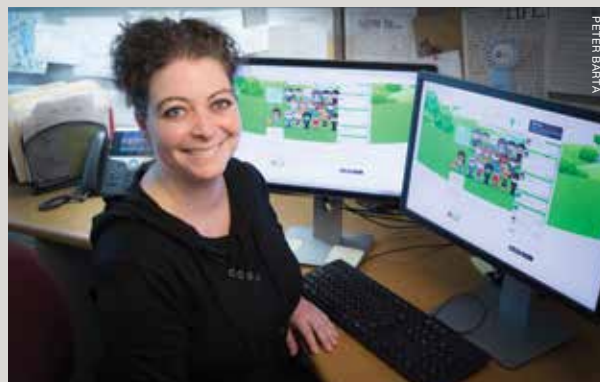
In a recent study, cancer survivors ages 11 to 14 received activity monitors and education about physical activity.

Average weekly exercise rose slightly for those who could earn stickers, T-shirts, gift cards and other rewards by increasing their activity levels. Those survivors showed small gains in fitness and cognition.

But physical activity decreased among those who had no chance to earn rewards.

"We were looking for engaging and creative ways to motivate them to do something to get their heart rates up. Based on these early results, we may have found an approach," said Carrie Howell, PhD, of St. Jude Epidemiology and Cancer Control.

St. Jude researchers are now testing this technique in a larger national study.



Carrie Howell, PhD



## Creative expression

Eighteen-year-old Serafin Garcia displays his artwork during the 2018 Teen Art Show. Garcia and other teenagers described their creative works in detail before a crowd of family members and St. Jude employees. The pieces are now on display in the hospital's Teen Art Gallery.



# Incorrigible Optimism

**Looking back 40 years, one survivor explains how cancer shaped his life.**

**By Clay Johnson**

I was 8 years old in 1978, when I arrived at St. Jude Children's Research Hospital for treatment of acute lymphoblastic leukemia (ALL). Back then, all kids with leukemia received cranial irradiation to eliminate cancer cells in the brain and spinal fluid. This treatment often caused severe learning problems. During my therapy, I received 2,400 rads of radiation.

The future was uncertain, but my family are incorrigible optimists. We focused on the present and didn't look too far down the line, trusting God to get us through each day.

I grew up and earned advanced degrees in law and divinity. I even learned to read Greek and Hebrew. Thankfully, the therapy I'd received hadn't impaired my ability to learn, work or have a family. Today, my wife and I have five children, ranging in age from 9 to 19.

In 2009, St. Jude invited me to join a long-term follow-up study for cancer survivors.

One of my motivations for joining the St. Jude LIFE study was that I was one of the earlier survivors of ALL. I used to ask doctors, "Hey, I had all this treatment as a child. What happens now?" and they'd say, "We don't know. You tell us." They didn't have enough people who had survived long enough to know what would happen.

I want patients to be able to know. So it wasn't a question of why I would join the study. It was more the question, "Why wouldn't I?"

On my first return visit for St. Jude LIFE, I also got a glimpse of what my parents had gone through. I realized parents at St. Jude have to live in two worlds—one is the world of encouragement and realistic optimism for their kid. The other is the reality that they might lose one of the most precious people in their lives.

My parents offered me constant encouragement. Their support, and the support of St. Jude, was steady enough that although I knew I was seriously ill, I wasn't constantly thinking about the risks. I was just a kid. And that's a great gift.

The experiences I had at St. Jude made me who I am today: an incorrigible optimist. And for that, I'm profoundly grateful. ■

## Then and now

Clay Johnson with St. Jude founder Danny Thomas in 1978; and today, with his wife and family.



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for kids like Azalea.

St. Jude patient Azalea,  
*rhabdomyosarcoma*

## Your gift has the power to change lives—and save them.

Your partnership in our lifesaving mission can make a difference in the lives of children battling cancer and other life-threatening diseases. Funding a research program, naming a space in the hospital or establishing an endowment fund are a few ways your support could help St. Jude accelerate progress and transform childhood cancer research and treatment.

**Learn more from a St. Jude representative.**

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### Colors of caring

The magic number changes from day to day, but currently it's 520. That's how many colorful wristbands have been given to Ron Hardin, RN, by St. Jude patients and staff. The pediatric oncology nurse wears the bracelets on his arms as well as attached in bunches to a belt around his waist. Each band has special significance, because it represents a person who has touched Hardin's life.

"It's not the number of bands that's important," he says. "It's who they're from."

Current and former patients often greet Hardin with the words, "Mr. Ron! Have you still got mine?" And he always does.

"I do this to keep my buddies with me," says Hardin, who has worked in the hospital's Medicine Room for 22 years. "They've graced me and blessed me, and it's a privilege to have them with me every day."



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