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St. Jude

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have a higher leukemia risk?

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Untangling a Lethal **Brain Tumor**

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making the impossible
POSSIBLE

By including St. Jude in his will, one donor furthers his legacy.

By Zack McMillin

Not long before Jack Vosse left home to begin an Air Force career, he was among those who gathered in downtown Memphis February 4, 1962, to witness the opening of St. Jude Children’s Research Hospital by founder Danny Thomas.

Nearly 50 years would pass before Vosse set foot on campus again, as a retiree devoted to the St. Jude mission.

“I was astounded to see all that has been done,” he says. “To know so many people have made it possible to save these kids, when 50 years earlier Danny Thomas was told it would be impossible.”

A longtime supporter of St. Jude, Vosse says his involvement deepened when he reached retirement.

Shortly after his wife, Lee, passed away, he received a letter explaining how individuals could leave a legacy and help future generations of children by including St. Jude in their wills.

“Not only had I considered it, but I already had put St. Jude in my will,” Vosse says. “So I called to let them know.”

That led to a meeting with a St. Jude philanthropic adviser. Andrew Ellis explained that by notifying St. Jude of the generous bequest, Vosse had helped the hospital better plan

for future needs. Ellis also connected Vosse to volunteer opportunities and offered him the option of funding a bench with a plaque inscribed in memory of Lee.

Vosse’s planned bequest granted him membership into the Danny Thomas–St. Jude Society. These supporters, who have included St. Jude in their estate plans, are invited to an annual event that includes special hospital tours, as well as presentations from patient families, doctors and researchers.

It was such an event in 2009 that brought Vosse back to campus. Almost every year since, he has returned, and his wonder has grown.

“I love to hear the scientists, doctors and nurses talk about what they do – you see how they are so passionately wrapped up in it,” Vosse says. “It’s an amazing experience.” ■

To include St. Jude in your estate plans or obtain information about how your charitable goals may align with the hospital's mission, call 1-800-910-3188 or email giftplanning@stjude.org.



Fifty-seven years later
Jack Vosse was in the crowd when Danny Thomas celebrated the hospital’s grand opening. A bequest by Vosse helps ensure the hospital’s future.

By Carole Weaver Clements, PhD

BETTER TOGETHER

The St. Jude Comprehensive Cancer Center highlights the power of team science in getting things done.

Pretend you're the most incredible trumpet player in the world. You live in a neighborhood next to the country's top pianist, bassist and drummer.

Any one of you can thrill an audience. But as a quartet, you can make even richer music by learning and playing off each other's strengths.

Now say that instead of a trumpet player, you're a cancer biologist. And instead of a quartet, you

have an orchestra consisting of a world-leading oncologist, a pathologist, a geneticist, and dozens of other top experts in cancer research and treatment. Every one of you leads a stellar individual research program. But how do you blend your talents in a symphony that takes on childhood cancer as a whole?

You do it through the St. Jude Comprehensive Cancer Center.

Perfect harmony

As the only National Cancer Institute (NCI)-designated Comprehensive Cancer Center dedicated solely to children, the St. Jude Comprehensive Cancer Center is deliberately designed to foster collaboration among high achievers across the hospital.

Marking the success of this approach, the center recently earned a second consecutive "exceptional" ranking – the highest possible distinction – from the NCI, once again distinguishing St. Jude as one of the nation's elite cancer research institutions.

Because St. Jude is a pediatric specialty hospital focused on cancer and other life-threatening diseases in children, its Cancer Center differs from most, as it is completely integrated into the fabric of the entire organization.

"Cancer is remarkably complex," says Charles Roberts, MD, PhD, director of the center. "To beat it, we need collaboration. NCI-designated Cancer Centers bring together oncologists, surgeons, pathologists and many other scientists to focus on a shared problem.

"We ask, 'What are the critical issues we want to attack? What are children dying from? Where is the opportunity for greatest impact?' After identifying the most pressing problems and greatest opportunities, we develop a collaborative strategy to address them."

From lab to bedside to the world

Five Cancer Center research programs, led by world-renowned experts and composed of investigators from diverse

disciplines, drive progress in key areas: blood cancers, brain tumors, solid tumors, basic cancer biology and childhood cancer survivorship. These individuals meet regularly to exchange ideas and are supported by shared resources and seed funding for promising research.

"There's a natural opportunity for cross-pollination," notes Victor Santana, MD. As senior vice president of St. Jude Clinical Trials Administration and the center's associate director for clinical research, his responsibility is to oversee all clinical trials at St. Jude.

"Although my clinical duties are in the solid tumor group, I have interactions with investigators across all the Cancer Center programs," he says.

St. Jude research, spanning the spectrum from lab to clinic,







SETH DIXON

Playing off strengths

"The strength and innovation of the basic science, and how that science gets translated into clinical trials, allow St. Jude to have real impact on patients' lives," says Victor Santana, MD, pictured with St. Jude patient Luis Rodriguez Gutierrez.

ST. JUDE COMPREHENSIVE CANCER CENTER RESEARCH PROGRAMS

-  Cancer Biology
-  Cancer Control and Survivorship
-  Developmental Biology and Solid Tumor
-  Hematological Malignancies
-  Neurobiology and Brain Tumor



PETER BARTIA

Working in concert

"Cancer is remarkably complex," says Charles Roberts, MD, PhD (right), shown with Charles Mullighan, MBBS, MD. "NCI-designated Cancer Centers bring together oncologists, surgeons, pathologists and many other scientists to focus on a shared problem."



Collaborating for cures

Martine Roussel, PhD (at right), co-leads the Cancer Center's Cancer Biology Program, which explores fundamental scientific questions about pediatric cancer. Investigators in this program collaborate with others across the center to help move new basic science discoveries into the clinic.

turns scientific discoveries into innovative clinical trials that give young patients the best chance of healthy adulthoods.

"Because of the remarkable science coming out of our programs, we enroll a lot of patients on studies; in fact, 98 percent take part in clinical trials during their time at St. Jude," Santana says. "This offers patients the opportunity to improve their outcomes and care – and to feel they're advancing science and helping others."

To share knowledge and advance cures, the center's members also collaborate extensively with other NCI Cancer Centers; help train the next generation of cancer researchers; and educate the community about cancer, cancer prevention and healthy living. A core team led by Dana Wallace, associate director for Cancer Center administration, organizes regular meetings, seminars and events for members.

"An NCI Cancer Center is meant to be a whole greater than the sum of its parts," she says. "Our job is to make sure that happens. It's awesome to see the great collaborative science that comes out of these discussions."

An exceptional center

The St. Jude Cancer Center was established in 1977 when the hospital received its first Cancer Center Support Grant from the NCI. Funded by the NCI ever since, the center earned comprehensive status in 2007 and its first exceptional rating in 2013.

Every five years, the center must renew its NCI grant funding and designation. During the most recent cycle, Roberts, Wallace and groups throughout the center began preparations 18 months in advance. A 2,300-page application was followed by a full-day, on-site visit by NCI reviewers.

The result? As well as a second consecutive "exceptional" rating, the center earned its best numerical score to date.

"I honestly could not be prouder of the incredible team of Cancer Center members, leaders and staff that made this achievement possible," Roberts says.

National treasure

Renewal years are a valuable time to pause and reflect on the center's direction and contributions at a national level.

"It was a tremendous honor for the center to be called a 'national treasure' by the reviewers, and the fact that our score is the best it's ever been shows our impact," Santana says. "Going through the review process also allows investigators and leadership to identify areas where we can work together even better."

The review process is constructive, says Charles Mullighan, MBBS, MD, who co-leads the Hematological Malignancies Program with oncologist Ching-Hon Pui, MD.

"We looked back on what we've accomplished over the last five years," Mullighan says, "but now are thinking about where we're headed, and planning strategically about areas where we need to grow our research efforts and expand our treatment programs."

Unique responsibility

Fifty-five percent of pediatric cancer cases are caused by genetic changes that are never seen in adult cancers. This recent discovery, led by center member Jinghui Zhang, PhD, working with scientists from the NCI, the Children's Oncology Group and other centers, underscores the importance of pediatric-focused research efforts.

"In these cases, the old model of developing drugs first for adults and then moving them down to children just won't work," Roberts says.

St. Jude has a responsibility to develop new cures especially made for children, he says.

Examples of key breakthroughs made possible through Cancer Center collaborations include increasing survival rates for acute lymphoblastic leukemia to 94 percent; creating a better immunotherapy that doubled the rate of

"We ask, 'What are the critical issues we want to attack? What are children dying from? Where is the opportunity for greatest impact?' After identifying the most pressing problems and greatest opportunities, we develop a collaborative strategy to address them."

– Charles Roberts, MD, PhD

treatment response in children with high-risk neuroblastoma; and launching the first clinical trial for medulloblastoma, a common childhood brain tumor, that matches treatments to the molecular features of individual patients' tumors.

"The strength and the innovation of the basic science, and how that science gets translated into clinical trials, allow St. Jude to have real impact on patients' lives," Santana says.

Planning for tomorrow

Now that most young cancer patients survive their disease, research to help alleviate the long-term side effects of cancer treatment is essential.

"It's important to look at the entire continuum, from diagnosis to survivorship," Santana says. "Our Cancer Center does that exceptionally well."

To more rapidly advance progress, Cancer Center members have also taken the lead on other large-scale projects in new or innovative areas.

"The center has become the vehicle for strategic planning related to childhood cancer," Mullighan says.

"Some of the most forward-looking initiatives have been launched through direction and vision from the center – such as, how will we expand our efforts in immunotherapy? How do

we best position ourselves for precision medicine? What does the next generation of clinical trials look like?

"It's the natural home for those questions, because you can rapidly pull together the key people from the Cancer Center to get new initiatives off the ground," he continues.

Unparalleled mission

Roberts says it's a compelling time to be a cancer researcher.

"We still have a long way to go, but thanks to emerging technologies, we now have a better understanding of cancer and therapies – and thus have the opportunity to advance cures for children more rapidly than ever before," he says.

And just as science moves the Cancer Center forward, the hospital's mission provides the inspiration.

"It's being in the clinic and seeing a 7-year-old who was playing soccer two days earlier, but then finds out his bruises weren't from soccer but from leukemia; or a toddler who was meeting all of her milestones, but now she's battling for her life," says Roberts, who is also a practicing pediatric oncologist and scientist.

"There's nothing that brings more motivation and drive." ■



PHOTOS BY PETER BARTA

OVERCOMING *the* ODDS

By Elizabeth Jane Walker

RESEARCHERS MAKE DISCOVERIES ABOUT A RARE BONE MARROW DISORDER.

Imagine winning the Powerball jackpot – more than once. To Danni and Brent Treu, that scenario may actually sound plausible. After all, their three children have a condition so rare that doctors have compared its odds of occurrence to that of winning the lottery.

Several years ago, the couple learned their 5-year-old son, Brady, had a bone marrow disorder called monosomy 7 syndrome. The condition occurs when a child's bone marrow cells have only one copy of chromosome 7, instead of the usual two.

"The doctor told us, 'There's one of two things that will happen. It's either going to turn into leukemia, which will be really hard to get rid of with monosomy 7, or Brady's going to go into full-blown marrow failure and quit making blood,'" Danni recalls. "The only cure was a bone marrow transplant."

Sobering surprises

Brady's younger siblings underwent tests to see which one might be a bone marrow donor.

The answer was "neither."

All three children had both monosomy 7 and myelodysplastic syndrome (MDS). In MDS, bone marrow cells don't produce the normal blood cells that transport oxygen, clot the blood or fight infections. Children with familial monosomy 7 syndrome and MDS are also apt to develop an aggressive form of acute myeloid leukemia (AML).

"It's really rare for one kid to have MDS, or for one kid to have monosomy 7," Danni says, "but when you hit all three of them in the same family, basically it's unheard of."

It's a lottery no one would choose to enter. But St. Jude Children's Research Hospital has helped this family overcome the odds.

Now, new research may help other children born with the condition.



Rare trio

(From left) Brady, Charlee and Bentley Treu were born with a bone marrow disorder called monosomy 7 syndrome. "It's really rare for one kid to have MDS, or for one kid to have monosomy 7," their mom says, "but when you hit all three of them in the same family, basically it's unheard of."



Hope through research

Jeffery Klco, MD, PhD, of St. Jude Pathology and his colleagues recently made important discoveries about the disorders that affect the Treu family. The findings may help some patients avoid the risk, stress and expense of bone marrow transplantation.

Two genes, many possibilities

Jeffery Klco, MD, PhD, of St. Jude Pathology and his colleagues recently made important discoveries about the disorders that affect the Treu family. The findings may help some patients avoid the risk, stress and expense of bone marrow transplantation.

For decades, researchers searched for the origin of familial monosomy 7 syndrome. Then Klco and his team, as well as investigators in Europe, discovered the condition is caused by germline mutations in the genes *SAMD9* or *SAMD9L*. Usually inherited, germline mutations occur in the DNA of every cell.

As a result, scientists are developing guidelines to pinpoint which children require transplants and which can avoid them.

Three success stories

The Treu children were not a part of Klco's recent study, but their experience mirrored that of the participants. To head off AML development, Brady and his younger sister, Charlee, underwent bone marrow transplants from unrelated donors. But the symptoms of their little brother, Bentley, simply melted away like snow in the sunshine.

SAMD9 and *SAMD9L* have now been identified as cancer predisposition genes, so St. Jude includes them in genetic screenings for patients who have bone marrow abnormalities or leukemia. Klco's team also identified other mutations that, when paired with *SAMD9* or *SAMD9L* alterations, cause AML.

He predicts many more exciting advancements in the future, as the hospital opens a new clinic for patients with bone marrow failure disorders such as MDS.

The search continues

To answer even more questions, Klco is dedicated to working with researchers worldwide, including St. Jude colleagues Jason Schwartz, MD, PhD, and Marcin Wlodarski, MD, PhD, of Hematology.

"Now we're trying to figure out how the mutations ultimately lead to monosomy 7 and MDS," Klco says. "What are the triggers? Why do some children have spontaneous recoveries? There's still a lot to do."

Danni says she's thankful Klco and other researchers continue their quest.

"It's so important to do research on rare disorders like this one," she says. "If you don't do research, how can you ever detect the disease or develop better treatment plans for it?" ■

"It's so important to do research on rare disorders like this one. If you don't do research, how can you ever detect the disease or develop better treatment plans for it?"

– Danni Treu

Scientists from St. Jude and the University of California, San Francisco, led by Kevin Shannon, MD, studied 16 patients from five families with *SAMD9* or *SAMD9L* mutations. Some of the children had monosomy 7, a few developed MDS and even a couple got AML. But the scientists were astounded that some of the children regained normal bone marrow function without therapy.

"Historically, these kids usually get bone marrow transplants," Klco says. "Now we know that in children with these mutations, sometimes the monosomy 7 cells go away."

Secrets Beneath the SURFACE

What hidden hazards lie beneath the surface of genome editing? One scientist develops tools to make detailed maps of uncharted territory.

By Keith Crabtree, PhD

The human genome, our complete set of DNA, contains about 3 billion base pairs within 23 chromosomes. In 2003, scientists completed a project to sequence the human genome. Yet, scientists still don't fully understand the roles of the estimated 22,000 genes and other sequences within those 23 chromosomes.

"Even though we now have the human genome sequence, our ability to interpret its function is still limited. It's like having the full text of a book where you don't know what many words mean," says Shengdar Tsai, PhD, of St. Jude Children's Research Hospital.

Why is it crucial to understand that information?

Well, many human diseases — including life-threatening disorders like childhood cancer — arise from mutations, or changes, to the body's DNA.

A nautical map

Through genome-editing technology, scientists like Tsai can directly change the DNA of living cells. Genome editors are like tiny molecular scissors that can be programmed to cut precise locations in the genome. As cells naturally repair these cuts, DNA at these spots can be added, deleted, replaced, or, in other words, edited.

"Genome-editing technologies are amazing because they can enable curative therapies, where a patient's own cells are permanently genetically changed to treat the disease," Tsai says.

If proven to be safe and effective, genome-editing technologies may soon deliver cures for pediatric cancer, HIV, sickle cell disease and many other diseases.

But these scientific breakthroughs depend on a deeper understanding of the 'global' effects of genome editing.

Tsai, who enjoys sailing, came to the St. Jude Hematology Department from Boston. He likens scientists' current understanding of genome-editing effects to an incomplete nautical map. Scientists can see locations of potential hazards, but their depth and danger remain unknown.

A pioneer in understanding genome-editing technologies, Tsai is developing tools to make better maps.

Tsai likens scientists' current understanding of genome-editing effects to an incomplete nautical map.

Setting sail

Many headlines in recent years convey the same point: "New genome-editing technique transforms human medicine."

In fact, genome editing today has been remarkably simplified. The editing technology that has garnered this attention and excitement is called Clustered Regularly Interspaced Palindromic Repeats — or CRISPR-Cas9. "Cas9" refers to an enzyme that can be easily programmed to cut DNA at specific locations.

CRISPR is a powerful tool.

"Any gene you're interested in, you can mutate in a cell and study the effects of that mutation quickly," says Mitch Weiss, MD, PhD, St. Jude Hematology chair. "But to do something clinically," he adds, "is much more difficult because there are lots of things you have to worry about."

A sharp lookout

One of the things Weiss, Tsai and other scientists worry about is malignant cell transformation.

During gene editing, some cells might experience accidental cuts in their DNA and mutations may result in unwanted cell growth.

"For any genome-editing target, we wanted the capability to ask, 'What areas of the genome are we really changing?'" Tsai explains.

Tsai recalls early work in his field using computational predictions to find the location of unintended, off-target mutations. It was a guessing game, like losing your keys in the dark and looking for them only where it's well-lit.

To search completely, Tsai developed sensitive and unbiased experimental tests. One of these methods — Genome-wide Unbiased Identification of Double-stranded breaks Enabled by Sequencing (GUIDE-seq) — has been adopted by many large companies and institutions as the go-to method for defining genome-editing activity across the human genome for clinical applications.

Tools for discovery

“Genome-editing technologies are amazing because they can enable curative therapies, where a patient’s own cells are permanently genetically changed to treat the disease,” says Shengdar Tsai, PhD. He and his team have developed new tools to perform rapid large-scale testing of genome editors.



JUSTIN VENNAN

Wide berth

Still, a daunting challenge remains: making a map that enables scientists to know the depth of the dangers below, the functional effects of unintended off-target mutations.

“What we need to do is see beneath the surface,” Tsai explains.

New methods under development in his lab will help scientists detect possible adverse effects related to genome-editing, speeding the development of safe, effective therapies.

Tsai was recently awarded an NIH grant from the Somatic Cell Genome Editing program, a National Institutes of Health Common Fund program designed to improve methods for editing the human genome.

The grant will support development of a new way to test the safety of genome editors with human T cells. Scientists commonly use T cells to develop genome editing therapies for cancer and other diseases.

“T cells are unique cells, in that they rearrange their DNA to produce genetic diversity for adaptive immune recognition,” Tsai says. “Each cell’s genomic rearrangements can be a cellular barcode we can use to identify potential threats. For us, T cells are like the canary in the coal mine to identify genome-editing-associated dangers.”

All hands on deck

Tsai and his team have developed new tools to perform rapid large-scale testing of genome editors. Immense datasets are required to navigate the depths of the genome

and accurately predict activity using cutting-edge deep learning and artificial-intelligence technology.

“Now we can look at a large number of targets to learn important principles about genome-editing safety,” says Tsai, explaining his excitement about the promise of his research.

While these studies progress, Weiss and Tsai are developing a CRISPR gene-editing effort to translate lab results to clinical care — and perhaps, one day soon, cures. Joining forces with St. Jude hematologist-oncologist Akshay Sharma, MBBS, and Shondra Pruett-Miller, PhD, Center for Advanced Genome Engineering director, their team uses CRISPR-Cas9 to edit blood stem cells to induce fetal hemoglobin, a possible cure for sickle cell disease and other blood disorders.

“Genome editing is an amazing technology that has changed the way we work in the lab,” Weiss says. “It will eventually change patient care as well.”

Tsai and his colleagues from St. Jude, the National Institute of Standards and Technology, and Carnegie Mellon University hope their work will ultimately help scientists safely navigate the vast unknown territories of clinical genome-editing. ■



A Taste of Home



Family feast

Chef Adrianne Calvo prepares a gourmet meal for St. Jude patients and families.

Chef Adrianne Calvo’s holiday meal for St. Jude is ‘Hispanic at heart.’

By Grace Korzekwa

If you walk into St. Jude Children’s Research Hospital on the day of Chef Adrianne Calvo’s annual visit, you know something amazing is in the works. You know it because of the smell: smoky, rich and comforting, wafting through the halls.

“It’s a big menu. Lots of flavor,” Calvo says.

Chef Calvo, TV and internet personality, author of five cookbooks and a Miami restaurant owner, presses pause on her busy life for a few days each year to serve St. Jude families. For the past 11 years, she and her team, including her mom, have prepared a huge, Cuban-inspired feast for hundreds of patients and staff. At St. Jude, it’s a holiday in its own right.

There are yuccas, beans, plantains, rice, flan and bread pudding. And there’s that Cuban pork roast, the source of the intoxicating smell. Calvo says the meal is, like her: “Hispanic at heart. I think we have enough food to feed half of the globe, pretty much.”

As a young woman growing up in Miami, Calvo considered becoming a journalist. After taking a high school cooking

class because of a scheduling fluke, she focused her storytelling instincts on food.

“My mom and my grandmothers, they always cooked for me, and I always looked at food as love, as caring,” she says.

After her sister, Jenny, died from cancer at 19, Calvo adopted her sister’s life’s mission: “Make it count.” Shortly thereafter, she connected with St. Jude.

“I saw the wonderful things St. Jude was doing,” Calvo says, “how they saved lives and what that means for the families. I thought, ‘How can I be of help here?’”

In 2008, Chef Calvo’s team prepared its first St. Jude feast. The pork roasts were nearly sizzling, their aromas filling the halls. During a quick break, Calvo overheard a patient exclaim: “Mom! Mom! It smells just like grandma’s house.”

Calvo knew she had established an important tradition.

“It’s cooking for a purpose,” she says. “And what greater purpose than love and family?”

For more on Chef Calvo and others who support St. Jude, visit stjude.org/inspire. ■

IN SEARCH OF THE SWEET SPOT

BY JANE LANGILLE

A new study aims to reduce long-term effects of Hodgkin lymphoma treatment.

As the goalkeeper for a competitive soccer team, Tyler Kingsbury knows how to strike the ball on the sweet spot to send it exactly where he wants it to go.

Last November, the 16-year-old found an unexpected yellow-card warning – a little lump under his armpit. It was an inflamed lymph node that flagged a need for further tests.

Shortly after Thanksgiving, a pediatrician in Florida diagnosed Hodgkin lymphoma. The cancer was in his chest and a lymph node in his neck.

“A friend and mom of another player on Tyler’s team strongly recommended St. Jude Children’s Research Hospital. Her daughter participated in a clinical trial for Hodgkin lymphoma at St. Jude four years ago and is still cancer-free and doing

well,” says Tyler’s mom, Kimberlee Kingsbury. “Everyone we spoke to said that if it were their child, they would go to St. Jude. But the final decision was Tyler’s.”

Tyler chose St. Jude and also volunteered to be patient No. 1 in a new clinical trial for children, adolescents and young adults with Hodgkin lymphoma.

“Three months at St. Jude for chemotherapy and an additional month for radiation, only if needed, sounded better than four to six months of treatment in Tampa,” Tyler says.

The new study builds on strong evidence from previous trials that have focused on hitting the sweet spot – maintaining high survival rates while minimizing the long-term problems that can show up decades later with conventional therapy.

The new study builds on strong evidence from previous trials that have focused on hitting the sweet spot – maintaining high survival rates while minimizing the long-term problems that can show up decades later with conventional therapy.

Staying sharp during treatment

Tyler Kingsbury, the first patient to enroll in a new Hodgkin lymphoma clinical trial at St. Jude, practices soccer moves during a break from treatment.

SETH DIXON

Saving lives with fewer side effects

“Our main objective is to test whether we can reduce radiation and steroids for patients who respond very well to the initial two cycles of chemotherapy while keeping survival rates the same,” says Tyler’s oncologist, Jamie Flerlage, MD.



SETH DIXON

Team of experts

Hodgkin lymphoma is a cancer that begins in the lymph system. Abnormal cells called Reed Sternberg cells multiply, causing the lymph nodes to get larger. The disease can spread to the lungs, spleen, liver or bone marrow.

In the United States, up to 8,500 individuals are diagnosed with Hodgkin lymphoma each year. The disease mostly affects children over the age of 15 and young adults up to the age of 39 years, with another peak occurring in older adults.

Because of advances in chemotherapy and radiation techniques, five-year survival rates for children with Hodgkin lymphoma are very good – between 90 and 95 percent for early diagnoses and close to 90 percent if the disease has spread. But here’s the catch: treatment carries an increased risk of cardiovascular and lung problems, and a significant risk of secondary cancers due to historically extended radiation fields. Prolonged treatment with steroids puts patients at risk for bone fractures because of low bone density, high blood pressure, obesity and secondary diabetes.

In 1990, researchers from St. Jude, Stanford University Medical Center and Dana-Farber Cancer Institute formed a consortium to find a way to keep cure rates high while limiting the late effects of treatment.

St. Jude oncologist Jamie Flerlage, MD, is the primary investigator for the newest consortium study, called cHOD17. The trial locations include St. Jude, Dana-Farber, Stanford, Massachusetts General Hospital and two of the hospital’s

affiliates – the St. Jude Affiliate Clinic at Novant Health Hemby Children’s Hospital in Charlotte, North Carolina; and the Jim and Trudy Maloof St. Jude Midwest Affiliate Clinic in Peoria, Illinois.

“Our main objective is to test whether we can reduce radiation and steroids for patients who respond very well to the initial two cycles of chemotherapy while keeping survival rates the same,” Flerlage says.

Eye on the ball

Similar to previous studies, children in the new trial receive risk-adapted therapy. That means they’re placed into one of three risk groups depending on the extent of their disease. They receive radiation therapy depending on how their cancer responds.

All patients receive two cycles of chemotherapy that includes steroids. Those in low- and intermediate-risk groups receive a proven combination of five drugs known as the Stanford V regimen, but with bendamustine substituted for mechlorethamine, which is no longer available.

“This is the first time bendamustine will be tested in front-line therapy in children. We expect it will work well, because it works beautifully and is very well tolerated in both adult and pediatric patients who have relapsed,” Flerlage explains.

Another plus: Bendamustine is widely available, while the other drug is not. Results from this study may provide support for other countries around the world to adopt the protocol.

Patients with high-risk disease receive a different chemotherapy combination tailored to their larger extent of disease,

following promising results from a trial that ended last year.

Tyler is in the intermediate-risk group. Between weekly appointments in the first cycle of chemotherapy, he is attending virtual classes online.

“Tyler is living a very normal life during treatment,” says his dad, Jeff Kingsbury. “One of the researchers put us in touch with a local soccer club in Memphis, so he can keep training.”

Early game strategy

The cHOD17 trial is one of the first studies in pediatrics to rely solely on an early PET scan after the initial cycles of chemotherapy to determine the next step of treatment. The scan allows doctors to check how many active lymphoma cells remain in the body.

If no active cells are found, patients forgo radiation therapy. Patients in the intermediate-risk and high-risk groups who must receive more chemotherapy after that scan will no longer receive steroids with treatment. Although steroids work well to decrease cancer cells, these drugs are now being removed from further cycles for patients whose active cancer cells are gone. By reducing steroid exposure, clinicians help children avoid problems such as obesity and joint issues.

If active cancer cells are present after two cycles, further treatment involves targeted radiation to the specific lymph nodes. Low-risk patients receive radiation therapy, while those in the intermediate and high-risk groups receive more chemotherapy, with steroids, and then complete their radiation treatment.

Goalkeeping

“The reason for this trial is to keep moving the field forward with less therapy for those with an adequate response,” Flerlage says. “We assume we are over-treating groups of patients because so few patients relapse. We need to find the sweet spot.”

Flerlage says most patients who relapse can be cured with more chemotherapy and radiation therapy.

The cHOD17 study is also the first to screen patients before treatment and two years later for side effects that may affect their quality of life, such as attention, memory and sleep problems.

“We hope to identify when the issues begin so that we can make adjustments to therapy and help more patients avoid them in the future,” Flerlage says.

Tyler is itching to get back to goalkeeping in Florida once he finishes cancer treatment. After high school, he has his sights set on college and wants to see how far he can go with soccer.

He seems relaxed about being the first patient in a study that may help children with Hodgkin lymphoma achieve cures with fewer late effects. “It’s probably the best cancer center in the world for kids with cancer,” he explains. ■

St. Jude Saved My Life Twice



Historically, children with Hodgkin lymphoma received the same cancer treatment as adults. Back in 1985, when he was 16 years old, Nick Dustman discovered that a lump under his ear was actually Hodgkin lymphoma. Doctors at St. Jude found cancer in his neck and performed a major abdominal operation to assess whether it had spread to other lymph nodes and organs.

His nodes were all negative for cancer. He received radiation to a broad area of his body from the bottom of his rib cage to his neck. This form of radiation is rarely used today but back then, it successfully boosted cure rates for Hodgkin lymphoma.

After treatment, Nick returned to his life. When he grew up, he became a national sales director for a pharmaceutical company and an avid biker. Then at age 41, Dustman began having trouble breathing after biking a couple of miles.

He enrolled in St. Jude LIFE, a research study that brings long-term childhood cancer survivors back to St. Jude for regular health screenings. St. Jude doctors discovered he had serious heart problems and immediately referred him to a cardiologist.

“My cardiologist found that my left main artery was almost 100 percent blocked. He was surprised I could make it up a flight of stairs, let alone ride a bike,” Dustman says. “I had a six-way bypass procedure.”

Nick has also managed other late effects from his childhood cancer treatment, including esophageal stricture, thyroid problems and hearing issues.

Today, at age 50, he bikes an average of 20 miles per day and 45 miles on Saturdays.

“I’m extremely fortunate,” he says. “St. Jude saved my life twice.”

FIELD OF GENES

WHEN IT COMES TO LEUKEMIA, THE RISKS ARE HIGHER FOR HISPANIC CHILDREN. SCIENTISTS DISCOVER WHY.

By Mike O'Kelly

EIGHT-YEAR-OLD JOHAN ANTIGUA is a switch-hitting, hard-throwing shortstop with a major-league smile. His love of baseball stems from an early age. The youngest of five ball-playing brothers, he took his first steps on a baseball diamond. It's no surprise that he's most at home at the ballpark. Since January 2018, however, he's been a spectator, unable to join his team on the field.

In December 2017, Johan's mother, Jessica, grew concerned when he developed fever, a dry cough and a swollen face. Johan soon recovered, but the symptoms returned a few weeks later during a January baseball practice. Jessica took him to the hospital immediately, where physicians initially diagnosed lymphoma. A few days later, further tests revealed that Johan had acute lymphoblastic leukemia (ALL), the most common childhood cancer.

"The first thing I thought was that I was going to lose him," Jessica says. "When you hear the word cancer, you think the worst."

Johan was referred to St. Jude Children's Research Hospital, where his clinicians explained the course of treatment: two-and-a-half years of chemotherapy. He's currently approaching the midway point of therapy.

Johan, who is of Puerto Rican descent, is the first member of his family to have pediatric cancer. Because of his Hispanic ethnicity, Johan may have had a higher risk of developing ALL. Researchers at St. Jude are trying to find out why.

Full count

For the past decade, St. Jude scientists have examined racial disparities in children with ALL. Jun J. Yang, PhD, of St. Jude Pharmaceutical Sciences, has looked at gene variations to explore why Hispanic children have an increased risk of leukemia. The most recent study from his lab is one of the largest efforts yet focused on Hispanic patients with ALL.



PETER BARTA

Home run

Jun J. Yang, PhD, and his colleagues have discovered a new gene associated with an increased risk of acute lymphoblastic leukemia in Hispanic children.

Researchers found a new gene associated with an increased risk in these children. The gene, *ERG*, was already known to play a role in childhood leukemia.

"We looked at the entire genome, and out of the 20,000-plus genes sequenced, *ERG* emerged as the one at the top in the Hispanic population," Yang says.

High-risk variations in *ERG* were associated with a 1.56-fold increased risk of ALL in Hispanic children.

Although the individual risk remains low, Yang says the finding shows that abnormalities in *ERG* are critical for the development of this cancer.

On deck

One of the challenges researchers faced when studying why Hispanic patients are more likely to develop ALL is the diverse makeup of the population. Hispanic children come from many geographical areas, but they still have the highest

incidence of this cancer in the U.S. and are less likely than other children with ALL to survive.

In the study, Hispanic ethnicity was defined as having more than 10 percent Native American genetic ancestry. Yang and his colleagues confirmed previous findings that variations in three other genes – *ARID5B*, *GATA3* and *PIP4K2A* – were more common in Hispanic children and were linked with an increased chance of developing ALL.

The risk was highest for children with the highest percentage of Native American ancestry. Scientists found no significant increase in the ALL risk of African-American children with the high-risk *ERG* variations and a small increase in children of European ancestry.

That was surprising, because for previously discovered leukemia genes, the effects on ALL genetic risk have usually been consistent across ancestries.

"St. Jude has taken a comprehensive and genomic approach to look into the biology behind the racial disparities in this disease," Yang says. "In terms of looking at ALL in Hispanics, I think we are at the forefront of scientific discovery."

Extra innings

Researchers collaborated with the Children's Oncology Group and scientists from 15 other institutions in the U.S. and Guatemala. Through the new St. Jude Global program, the institution has partnerships in Central and South America to further study Hispanic populations with ALL. Additional research is needed to determine whether environmental or other factors might trigger *ERG* to cause cancer more often in these children.

"We are looking into performing genomic research in those populations, not only to have a better understanding of the biology of ALL, but to identify factors that might improve treatment outcomes for Hispanic patients and children with high Native American ancestry everywhere in the world," Yang said.

That's good news for children like Johan, who is interested in returning to the activities and games he loves.

"His coaches and teammates have been asking about him," Jessica says. "He's used to being active, and he just wants to play baseball again." ■

Play ball

Eight-year-old Johan Antigua looks forward to the day when he can return to the baseball diamond.



SETH DIXON

Untangling

DIPG

AFTER DECADES WITH NO NEW THERAPIES, PIVOTAL NEW ST. JUDE RESEARCH INTO A LETHAL BRAINSTEM CANCER FUELS HOPE FOR MORE EFFECTIVE OPTIONS.

By Maureen Salamon

The moment has long been seared into Darrel Adkins' memory: Arriving at St. Jude Children's Research Hospital with his daughter, Mandy, the frightened father thrust his hand forward to greet the check-in nurse. But his handshake was rebuffed in the best possible way. "The nurse told me, 'We hug here. We're family,'" Darrel recalls. "And that's what we were."

The family feeling embodied at St. Jude has never left Mandy's parents in the years since their vibrant daughter died of a rare brainstem tumor called glioblastoma in November 2000. Darrel and Phyllis Adkins dedicated an annual music festival in their home state of Ohio to Mandy's memory. Almost all of the nearly \$1 million they've raised from the event thus far has been donated to brain tumor research at St. Jude.

Such great intentions have now begun to pay off in pivotal ways. St. Jude researchers are beginning to untangle

the deepest secrets of devastating brain tumors – which confounded scientists for decades – offering new hope for effective treatments.

"Our money is seed money, that's what we call it," says Darrel, who regularly travels with Phyllis to St. Jude to glimpse the technology and talent their donations help fund. "People still ask what it's going to take to find the cure for cancer. After seeing what goes on at St. Jude, my answer is 'money.' Money pays for research. I'm so glad we did this."

A scientist's greatest hope

Building on years of dogged discovery, Suzanne Baker, PhD, director of the hospital's Brain Tumor Research Division, recently led a team that generated a lab model for another brain malignancy known as diffuse intrinsic pontine glioma (DIPG). Baker and her colleagues discovered how one gene mutation changes the expression of other genes in this lethal brainstem tumor's development.

"My greatest hope is that our research would show us how to stop this terrible disease," she says.

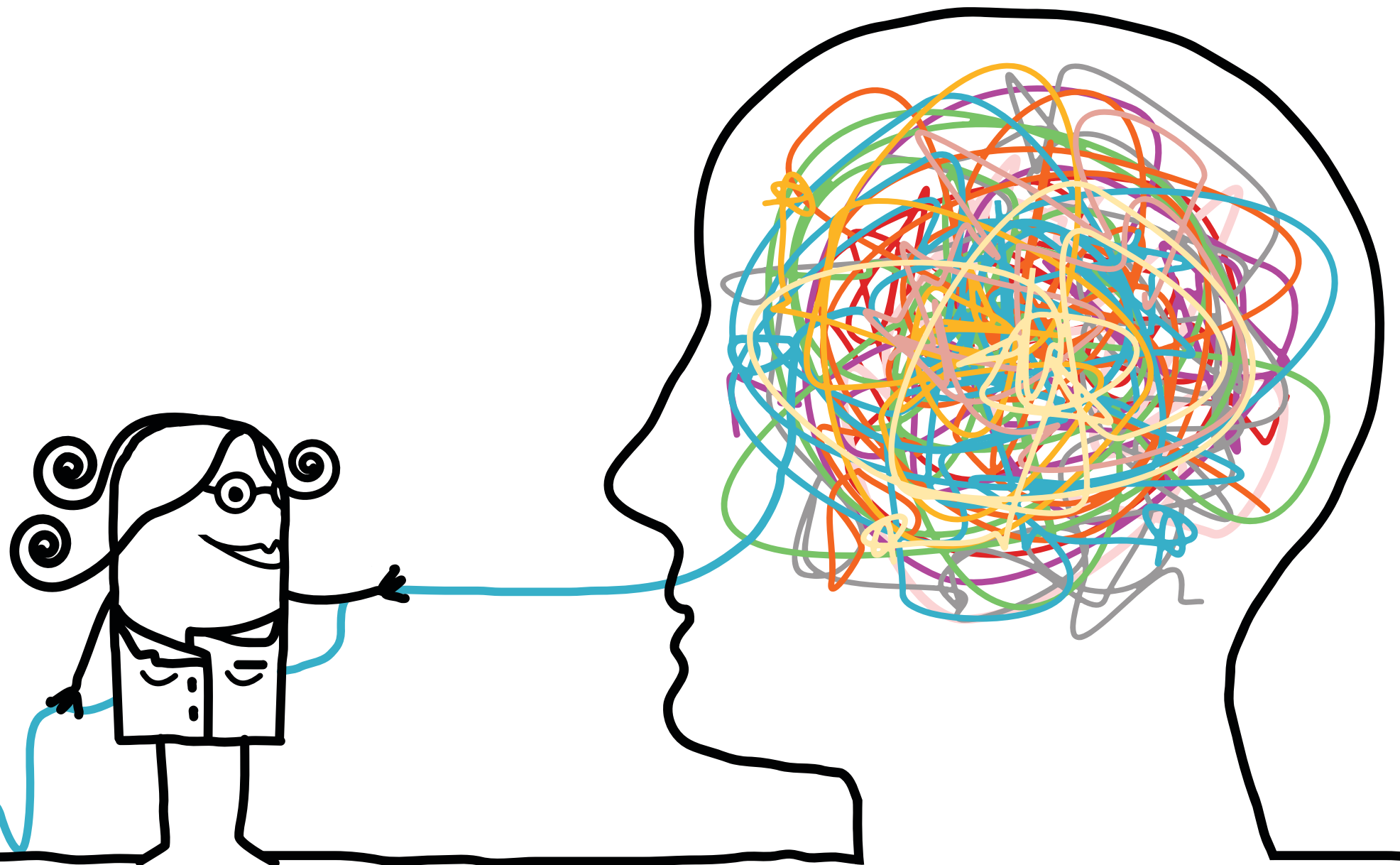
Although Baker has spent most of her lab career focusing on DIPG and other deadly high-grade gliomas, the human toll of brain tumors has never escaped her.

As a doctoral student in the 1980s, she attended a bluegrass festival organized by Darrel and Phyllis Adkins. Baker vividly remembers spotting a dancing Mandy Adkins onstage, a little girl lost in the music.

"It was a really surprising connection – much more than a researcher typically would have to a patient's family," says Baker, who now meets with the couple every time they visit St. Jude and has spoken at their annual festival, Musicians Against Childhood Cancer.

Challenges to effective treatment

Baker's new studies, published in the journals *Cancer Cell* and *Acta Neuropathologica*, provide potential pathways



to accomplish her goal of eradicating DIPG. Diagnosed in several hundred children each year in the United States, DIPG comes with an especially grim prognosis: Young patients survive only nine months on average, with fewer than 10 percent living longer than two years after diagnosis.

But surgery isn't a treatment option because the brainstem, which controls vital functions such as breathing, swallowing and heart rate, can't be removed. And while radiation and chemotherapy can help extend the lives of DIPG patients, the disease is exceptionally resistant to these therapies. More-effective options haven't emerged in the last 50 years.

"The tumors do respond initially to radiation, but then they recur. And in children, there's still not a standard of care for chemotherapy because there's not clear proof that any chemotherapy consistently extends survival in childhood high-grade glioma whether it's in the brainstem or not," Baker explains.

"Part of the problem is that our brains have a natural barrier to keep toxins out. We call it the blood-brain barrier, and it actually does a good job keeping a lot of drugs out of the brain," she adds. "So if we find a drug we think is promising, but it doesn't get to the tumor, it's not going to help. It's a challenging situation."

Discovery of key mutation

In 2012, Baker and St. Jude colleagues in seven departments revealed a web of related genetic alterations essential to understanding how DIPG develops. While many types of cancer arise from gene mutations that drive uncontrolled cell growth, mutations influencing DIPG stem from deviations in the cell's so-called epigenetic machinery, which oversees how genes are turned on or expressed.

The researchers pinpointed a key mutation called H3 K27M that occurs in most cases of DIPG. This mutation arises in a gene that codes for histones. Histones are molecules that help to package the DNA in cells. Chemical changes in the histone proteins can influence whether genes are activated or kept inactive.

"There had never been a histone mutation identified in human cancer before," Baker explains. "It really tells you that this is something that's very, very important for this disease."

Because histones are crucial to every cell of the body, Baker wondered why the H3 K27M mutation showed up so often in brain gliomas. To solve the mystery, the St. Jude researchers used genetic engineering to create a lab model that selectively switched on the mutation in the same type of brain cell that gives rise to DIPG in children.

The project unveiled critical ways the mutation causes DIPG. For instance, the mutation triggers immature cells known as stem cells from the developing brainstem to multiply abnormally, but only during a narrow window of development. This short-lived effect on stem cells may help explain why most DIPGs develop in early childhood.

"We thought it would be important to try to model this as accurately as we could because the actual tumors are already telling us that the K27M mutation is really only playing a critical role in a very specific developmental context," Baker says.

Brakes and accelerators

Baker and her colleagues also learned that the H3 K27M mutation works together with a pair of other gene mutations that are known to drive DIPG tumors. One mutation removes a "brake" on cell growth, while the other sparks a cell growth "accelerator" to work overtime. Adding the histone mutation accelerated the speed of brain tumor formation and caused most of the tumors to form in the brainstem. The lab-generated tumors closely resemble those from children with DIPG – making this the most accurate effort yet to portray DIPG in lab conditions.

"Now we have a much cleaner comparison, where it's easier to see what the contribution of the histone mutation is without all of that variation you typically get from one person to another," Baker says.

In a different model system, the researchers turned off the H3 K27M mutation and showed that it slowed tumor growth and made some of the tumor cells develop into more mature cell types that stop multiplying. In both model systems, the researchers showed that the histone mutation turned on a collection of genes related to brain development – likely contributing to DIPG growth by keeping tumor cells in a more primitive state when they continue to multiply.

The new revelations were built on years of research by Baker and others to identify gene mutations involved in high-grade gliomas, which account for up to one in five brain

In memory of Mandy

Although 22-year-old Mandy Adkins died of a brain tumor in 2000, her parents continue to support research that may save lives of other children in the future. "People still ask what it's going to take to find the cure for cancer," says Mandy's dad. "After seeing what goes on at St. Jude, my answer is 'money.' Money pays for research."



Game-changing discoveries

"This is a long game," says Suzanne Baker, PhD (center), "but the last few years of basic research have completely changed the way we view DIPG. We understand things we never imagined before in terms of the mutations that drive this disease."

and spinal tumors in children. Through advances in genomics made possible in the early 2000s, scientists identified genetic missteps driving the tumors.

A highly publicized St. Jude collaboration with the Washington University Pediatric Cancer Genome Project in 2014 linked recurring mutations in the *ACVR1* gene to a third of DIPG patients. That research also revealed an alteration in *NTRK* genes driving tumor development in young high-grade glioma patients whose tumors developed outside the brainstem.

A new era of discovery

Baker's research over the past decade would never have been possible without the generosity of St. Jude families affected by DIPG. She worked with a clinical colleague who devised a protocol that allows parents of an affected child to donate tumor tissue upon the child's death.

While the request proved excruciating, "a number of

families actually reported that this was important to them—that it was something that gave some meaning to what they had gone through," she says. "Without the tissue donations, we really would have had no way to look at the disease."

Now Baker's new lab model of DIPG will enable scientists to take the next step: testing new therapies for the malignancy, and even boosting understanding of other tumors triggered by such mutations. The connection between epigenetics and childhood brainstem tumors has also drawn the attention of researchers worldwide, she notes, expanding the number who devote their efforts toward the field.

"For us to be more effective with therapy for these tumors, we really have to understand what is going wrong, what caused the problem to start with," Baker says.

"This is a long game," she acknowledges, "but the last few years of basic research have completely changed the way we view DIPG. We understand things we never imagined before in terms of the mutations that drive this disease." ■

Precision care for a high-risk type of leukemia



Testing for minimal residual disease (MRD) can help some patients avoid bone marrow transplantation. MRD occurs when a low level of cancer cells remain after a patient has finished the initial therapy for cancer.

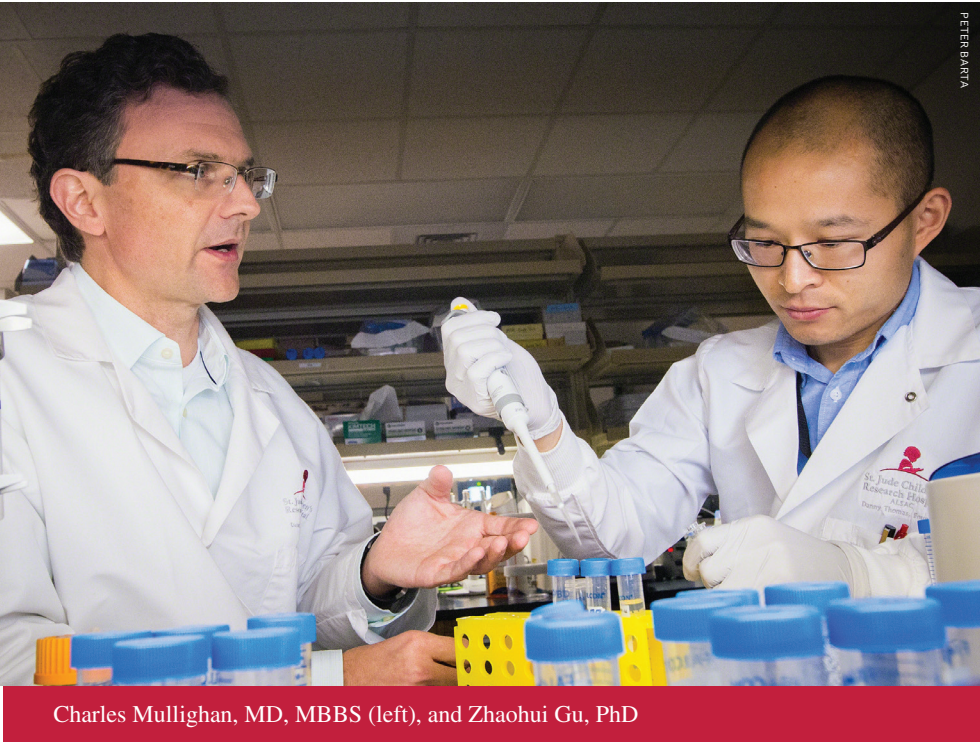
MRD can be used to guide care. It helps clinicians know when to intensify or reduce treatment.

Many physicians still use transplantation to treat hypodiploid acute lymphoblastic leukemia (ALL). This disease is rare and generally has poor outcomes.

St. Jude scientists compared treatment outcomes between hypodiploid patients treated with transplantation or chemotherapy based on their level of MRD. The study found that for patients treated with MRD-guided therapy, transplantation did not significantly improve patients' survival. This was especially true for patients with no MRD after therapy to induce remission.

"This study confirms our earlier observation that patients with hypodiploid ALL who have no evidence of MRD should not be transplanted," said Ching-Hon Pui, MD, St. Jude Oncology chair.

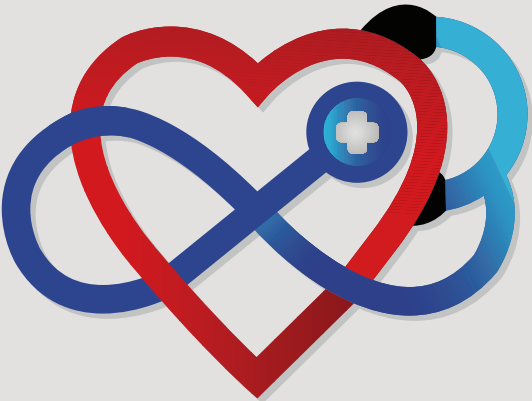
The findings appeared in the *Journal of Clinical Oncology*.



Setting new priorities for patient safety

St. Jude recently worked with the Solutions for Patient Safety (SPS) network to set research priorities for improving patient safety. SPS is a group of more than 130 children's hospitals.

Different safety research may be needed for kids as compared to adults.



Excited about the mission

For the ninth consecutive year, *Fortune* magazine named St. Jude to the "100 Best Companies to Work For" list. According to this year's survey, 93 percent of St. Jude employees believe the hospital is a great place to work, and 97 percent said they are proud to tell others about their work. "At St. Jude, it's critical to our success that we recruit and

retain the brightest and most talented individuals across scientific, clinical and administrative operations," said James R. Downing, MD, St. Jude president and chief executive officer. "Our dedication to employee satisfaction and well-being is integral to discovering cures and treating pediatric cancer and other catastrophic diseases."



Refining how leukemia is classified

St. Jude researchers are like explorers filling in a map. They identified new subtypes of the most common childhood cancer, B-cell acute lymphoblastic leukemia (B-ALL). The research will provide more information about the biology of B-ALL. This is likely to improve the diagnosis and treatment of high-risk disease.

Using genomic tools, the researchers studied nearly 2,000 children and adults with B-ALL. The findings show that B-ALL has 23 subtypes.

The St. Jude team identified eight new subtypes in this study. These subtypes have distinct genomic and clinical features and outcomes. Through this work, two-thirds of the previously uncharacterized B-ALL patients can be classified into subtypes.

"B-ALL has remarkable molecular diversity," said Charles Mullighan, MBBS, MD, of St. Jude Pathology. "This diversity helps drive precision medicine to improve B-ALL treatment and outcomes." The research appeared in the journal *Nature Genetics*.

The SPS network focuses on improving care for kids. The team relied on input from parents, clinicians and hospital leaders. This data helped identify 24 key pediatric safety topics in need of research. The topics cover issues like safety culture and communicating about care.

SPS network hospitals care for half of all hospitalized children each year. With this reach, the study results will be able to have an immediate effect on patient safety.

"The input of parents in this process was critical," said James Hoffman, PharmD, St. Jude chief patient safety officer. "We created a resource that other children's hospitals can use to guide research to improve pediatric patient care."

The study appeared in the journal *Pediatrics*.



Hongbo Chi, PhD

How to fight chronic inflammation

St. Jude scientists led a study that identified a subset of immune cells. These cells may be key to treating chronic, debilitating inflammatory disorders.

The study focused on a family of helper T cells called Th17 cells. Th17 cells launch the immune response against fungal infection and other threats. The cells are also known to fuel inflammation.

Researchers identified a new subset of Th17 cells distinct from the conventional Th17 cells that drive chronic inflammation. These two types of Th17 cells have their own unique functions.

The St. Jude team showed that metabolism and a protein complex called mTORC1 play important roles in regulating Th17 function.

“Identification of this new Th17 subset opens new avenues for developing effective treatment of chronic inflammatory conditions,” said Hongbo Chi, PhD, of St. Jude Immunology.

This work was published in the journal *Nature*.

Controlling protein factories within cells

Booming construction occurs inside cells. This includes the regulation and assembly of different parts of cells. Scientists at St. Jude are learning about what controls the construction of protein-making factories called ribosomes.

Ribosomes are made inside a part of the cell called the nucleolus. A protein called nucleophosmin helps organize the nucleolus. This protein also regulates the construction of ribosomes.

To study this protein, the researchers used protein-containing droplets that mimic the liquid-like properties of the nucleolus.

“This approach showed that nucleophosmin works with a molecular partner called SURF6,” said Richard Kriwacki, PhD, of St. Jude Structural Biology. “Together, these partners adapt and control the fluid structure of the nucleolus as it assembles ribosomes.”

Understanding this process may help researchers develop targeted cancer treatments. The findings may also influence research on amyotrophic lateral sclerosis, or Lou Gehrig disease.

This work appeared in the journal *Nature Communications*.



From left: Diana Mitrea, PhD; Mylene Ferrolino, PhD; and Richard Kriwacki, PhD



James Hoffman, PharmD

Reducing alert fatigue

St. Jude is helping improve electronic health record systems. These systems produce alerts when medicines might not work well together. The alerts are not always right, which forces clinicians to override the alert.

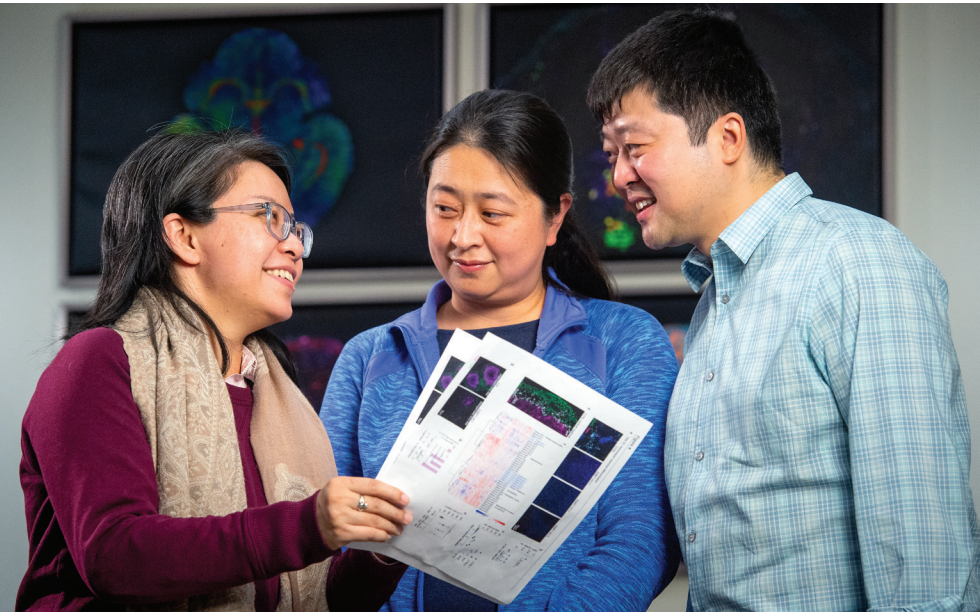
A constant stream of unneeded warnings leaves clinicians at risk for alert fatigue where they pay less attention to the warnings. St. Jude researchers evaluated alerts and found ways to safely reduce alert overrides by 40 percent.

This research presents an approach that other health care leaders can use to evaluate their own electronic health records systems.

“Customization to each local setting is key,” said James Hoffman, PharmD, St. Jude chief patient safety officer. “We provided a framework that other hospitals can adapt for their needs.”

A report on this work appeared in *Pediatrics*.

Brain development findings have clinical applications



From left: Jamy Peng, PhD; Xiaoyang Yang, PhD; and Beisi Xu, PhD

St. Jude researchers have discovered how two proteins interact to control hundreds of genes that build the developing human brain. The scientists found that the proteins UTX and 53BP1 link to activate the program by which the genes control the development of immature

pluripotent stem cells into functioning neurons and brain structures.

The protein UTX was known as an epigenetic regulator of chromosomes in brain development, but until now the other proteins involved in the process were unknown. Epigenetic controls manage switching genes on or off to orchestrate development from generic cells to specialized cells like neurons.

The genome of thousands of individual genes is like data stored on a computer disk, but the epigenome is like a computer program that controls how stored data are read.

The findings have potential clinical implications because abnormalities in the UTX function cause defects in brain development such as the rare Kabuki syndrome and the brain tumor medulloblastoma.

The findings appeared in the journal *Nature Neuroscience*.

“If you can find the good in the challenges that come your way, it’s not a setback – it’s a step toward where you’re supposed to be.”

Life After Treatment:

A STEP FORWARD

BY CANDICE STEVENS



Success story
Candice Stevens was 15 months old when she arrived at St. Jude. Today, she’s using her talents and skills to help other children cope with challenges they face.

Life can be hard. It’s not always positive and lovely. But you already know that, right? Allow me to share a secret: If you can find the good in the challenges that come your way, it’s not a setback – it’s a step toward where you’re supposed to be.

When I was 15 months old, a crying toddler with a swollen stomach, the pediatrician repeatedly discounted my parents’ concerns. He said they needed to let me “cry it out.” Finally, my mom demanded more tests.

Sure enough, I had a mass in my abdomen, which had already spread to my lymph nodes. I had less than 50 percent chance of survival. Would you call that a setback?

That same night I was flown to St. Jude Children’s Research Hospital. After surgery, 36 rounds of chemotherapy and a bone marrow transplant, I went into remission – a giant leap forward.

Potential setback No. 2 occurred when I lost my hearing from the treatment that had saved my life. But thanks to my hearing aids and speech therapy, I’m now able to enjoy music – especially country music – and even sing.

Throughout school, I had to work harder than many other students, but I persevered. Last year, I graduated from college with a degree in sociology. Today I’m in graduate school to be a school counselor. That’s two steps closer to my goal of having a career that will help people.

Everyone doesn’t have cancer, but everybody has their own struggles. Middle school is a pivotal time when kids may need extra support. Because of my experiences, I feel that’s the route I’m supposed to take.

Meanwhile, I’m grateful for my family and for St. Jude. I’m thankful that I’m able to take part in the St. Jude LIFE study for long-term survivors. What doctors learn from my experiences may help other children with cancer.

When I visit St. Jude, I look around and think, “Why did I make it? Why me?” I don’t know. But I definitely believe my experiences have led me to where God wants me today: moving forward. ■

ANN-MARGARET HEDGES

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More than words

Alabama's Randy Owen and his wife, Kelly, catch their first glimpse of a St. Jude patient family room dedicated in their honor in the hospital's Kay Research and Care Center.

The dedication celebrated the 30th anniversary of the Country Cares for St. Jude Kids® radio program. Since its inception by Owen, Country Cares has raised more than \$800 million through radiothons with more than 200 radio station partners and through other country music industry events.

"The most important thing I'll ever do, apart from being a father and a husband, is helping children at St. Jude," said the Country Music Hall of Famer.

"Over the past 30 years, I've watched children at St. Jude grow up to be happy, healthy adults. This room dedication shows that the country music industry has made a true impact, and I'm glad I could be part of that."

