St. Jude promise

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Mobilizing the **immune system** to attack cancer *pg. 5*

EXPLORE **new inpatient care floors** *pg. 16*

St. Jude Children's Research Hospital
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Cover story

Features

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AUTUMN 2016

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

On the cover:
Tyler Washington
Photo by Seth Dixon

SETH DIXON

Six-year-old Zoë Harrison and Amy Kennedy, a certified child life specialist, examine the mask Zoë will wear during radiation treatments. Play-based interventions can help children relax, avoiding anesthesia and reducing treatment time.

Practice and Possibilities

By Elizabeth Jane Walker

NEW RESEARCH SHOWS PLAY-BASED PREPARATION decreases sedation use and costs for children undergoing radiation therapy.

When it comes to martial arts, 6-year-old Zoë Harrison has all the right moves. She's strong. She's fearless. She's disciplined.

But Zoë's not too sure about the prospect of lying on a table with a mesh mask clipped to her face. It's a little scary—even for a karate kid.

At St. Jude Children's Research Hospital, Zoë will receive 30 radiation treatments for craniopharyngioma, a rare brain tumor. Precise positioning is crucial to ensure the radiation beam touches only the tumor, not healthy brain tissue. If Zoë is to avoid having anesthesia every day, she must learn to lie perfectly still.

The little girl needs someone who can offer guidance, focus and support. That's where the St. Jude Child Life Program comes in. Amy Kennedy, a certified child life specialist, will help Zoë prepare for radiation therapy.

Little girl, high stakes

"Familiarity is a huge thing, and it's important to give kids an opportunity to make this normal," Kennedy explains. "Get used to it, get comfortable, meet the people, feel settled."

Under Kennedy's guidance, Zoë has already successfully completed one diagnostic scan. But the stakes are higher for radiation therapy. If she cannot lie still, then Zoë must be sedated—a process that requires fasting beforehand and causes grogginess afterward. Daily sedation may also pose long-term health risks that include respiratory and learning problems.

"I've seen Zoë go through sedation back-to-back, two days in a row," says her mom, Cheila Rosencrans. "It was hard for me to watch. It takes a few hours for her to sleep the medication off, and then she's grumpy and not herself. So if we can avoid sedation, I'm all for it."

Confidence boosters

At St. Jude, Child Life Director Shawna Grissom leads a team of 18 professionals trained to work with children at different ages and developmental stages.

"We assess patients from the standpoint of age, previous hospitalizations and treatments, coping styles and temperament," Grissom says. "Then we prepare the children for what's going to happen. We show them pictures and walk them through the process. And then we actually practice in the treatment room."

Each patient is different. One child may require only 30

PETER BARTA

Shawna Grissom, St. Jude Child Life director, led research that explored ways to decrease sedation use in children undergoing radiation therapy for brain tumors.

or 45 minutes of preparation. Another may need a couple of weeks, easing into the process slowly.

"Maybe we work today for 10 minutes, lying still with the mask on," Grissom explains. "When the child gets restless, we get up, high-five each other, and do something fun for a while. Tomorrow, we lie still a little bit longer."

Grissom, Kennedy and their colleagues recently published a paper detailing how they decreased sedation use in children undergoing radiation therapy for brain tumors. These interventions not only reduced the children's anxiety, but also their clinical risk. By eliminating the use of anesthesia and reducing treatment time, the process also saved the hospital about $80,000 per patient.

A sense of control

When working with St. Jude patients, child life specialists rely on developmentally appropriate play, education and distraction. This may include music, recorded books, guided imagery and encouragement.

Before 7-year-old Addison Waldsmith began receiving radiation treatments for the brain tumor medulloblastoma, she met with Kennedy for two weeks. Kennedy introduced Addison to the room, the staff and the mask. Addison was delighted to learn she could eat breakfast before treatment if she did not have to undergo anesthesia. She could also complete the process in about 20 minutes, versus the two or three hours required for sedation and recovery.

Addison Waldsmith

Although Addison required sedation for the first couple of sessions, she completed the remaining treatments independently.

"Amy empowered Addison, boosting her confidence," says Addison's mom, Jenny.

"It's partly a control issue for these kids," Jenny continues, "and that's one thing Addison could personally control. She had her own little destiny there. She's 10 now, and she's so proud that she can do it."

Treatment practice

After working with Zoë for a couple of weeks, Kennedy is ready to introduce her to the treatment room. First, they look at photos of the facility.

"You'll lie on this table, and they'll make sure you're in the right spot," Kennedy explains. "We're going to go down there and show you how they do that. This machine is what will give you the radiation. You won't feel it or see it."

Arriving in the treatment room, Zoë scrambles onto the table.

"When the table moves around, it kind of sounds like an airplane," Kennedy warns. "We're going to show you how the machine moves so there won't be any surprises. All you'll have to do is hold still like you did the other day. Remember how well you held still? You were quite the rock star last week."

After asking a few questions, Zoë lies down. But moments after the mask snaps to the table, she shows signs of unease. When, after several adjustments, Zoë expresses continued anxiety, Kennedy reassures her.

"I don't want you to be scared and worried about this," Kennedy says, and guides the little girl back to the lobby, where her mom is waiting.

Because of Zoë's apprehension, Kennedy suggests scheduling a couple more practice sessions.

Moment of truth

In spite of their best efforts, some children still require sedation.

"Maybe they can't separate from their parents," Grissom explains. "Maybe they're just fidgety. Maybe there's something in the location of their tumor or the way they have to lie on the table that makes them uncomfortable or unable to lie still."

After a few more meetings with Kennedy, the day arrives for Zoë's first radiation therapy appointment.

"Zoë has been doing karate since she was 2," Kennedy observes. "I think a lot of the discipline that goes along with karate will help her be successful. She knocked it out of the park on the day of her simulation."

In the lobby, Cheila waits, hoping her daughter can complete treatment without sedation.

The minutes tick by. People come and go.

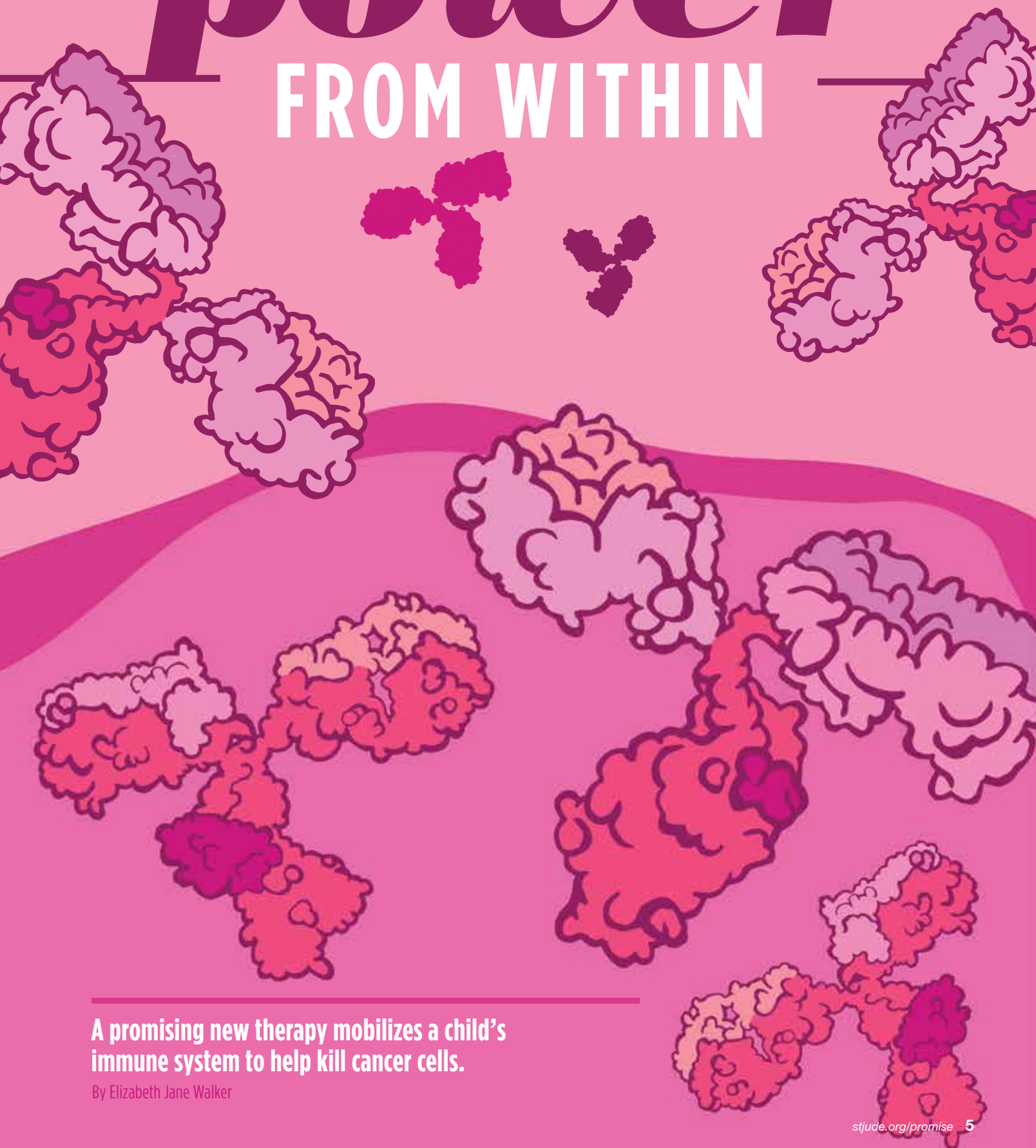
Finally, the doors open to reveal Zoë skipping down the hall, excited and proud of her accomplishment.

"That wasn't long at all," Zoë announces to her mom. And she does a little karate move to punctuate her victory. ■

SETH DIXON

Empowered by St. Jude Child Life, Zoë harnessed her inner warrior and vanquished her fears.

power FROM WITHIN



A promising new therapy mobilizes a child's immune system to help kill cancer cells.

By Elizabeth Jane Walker

PETER BARTA

VAISHALI (AT LEFT) AND **CHIRAG PATEL** TURNED TO ST. JUDE FOR THEIR DAUGHTER'S NEUROBLASTOMA TREATMENT. AS PART OF HER THERAPY, **KHUSHI** RECEIVES AN EXPERIMENTAL ANTIBODY THAT SIGNALS THE IMMUNE SYSTEM TO ATTACK AND KILL CANCER CELLS.

On a cold and rainy October evening last year, Chirag and Vaishali Patel discovered, to their horror, that intruders had infiltrated their happy home. Thieves had crept in, undetected, and attacked 6-year-old Khushi, a beautiful little girl whose passion for crafts was eclipsed only by adoration for her baby sister.

The invaders were, in reality, cancer cells within Khushi's body. Their attack had been stealthy—enabling the cells to evade discovery while their numbers multiplied.

In the months before, Khushi's tummy had hurt from time to time, but doctors had been unable to pinpoint the cause of her distress. Mild pain medicines offered only temporary relief. Finally a pediatrician detected a lump in Khushi's abdomen. Tests not only revealed tumors on her adrenal gland, but also on her liver and lungs. Khushi had neuroblastoma, a cancer of nerve tissue, and it was spreading quickly.

It was time to evict the trespassers. Khushi's physician sent her to St. Jude Children's Research Hospital.

A new type of therapy

"We arrived at St. Jude on a Sunday night," Chirag recalls. "It was pretty quiet at that time of day. But we felt some kind of spirit that we were at a good place."

During the following weeks, that impression was confirmed as the family met Khushi's treatment team. Chirag and his wife learned that clinicians could augment standard neuroblastoma treatment with a promising new therapy that would try to mobilize the power of Khushi's own immune system to help destroy her cancer.

This type of therapy is called immunotherapy.

Outsmarting wily cancer cells

The chief task of our immune system is to find and eliminate viruses, bacteria, cancer cells and other foreign substances. But when healthy cells mutate to become cancerous, they may outwit our body's natural defenses. The immune system may not recognize tumor cells as foreign or may not be strong enough to eradicate these dangerous cells.

What if we could strengthen that natural immune response? What if we could encourage the immune system to wage its own war on cancer cells?

Now we can.

"It makes perfect sense that we would try to unleash the immune system on cancer," says Khushi's oncologist, Sara Federico, MD. "If we can figure out how to harness it and help it attack cancer without making people too sick, we should be able to kill the cancer cells but spare the rest of the cells."

The secret weapon

Because Khushi's cancer was so aggressive, clinicians immediately waged an all-out assault on her disease. She enrolled in NB2012, a St. Jude clinical trial that combines standard cancer therapies—such as high-dose chemotherapy, surgery, radiation therapy and stem cell transplantation—with a secret weapon known as Hu14.18K322A. This experimental antibody, called a monoclonal antibody, is produced only at St. Jude.

The antibody used to treat Khushi's cancer is manufactured in the Children's GMP, LLC, an onsite facility that produces biologics and drugs under strict federal guidelines. Hu14.18K322A was engineered to decrease the pain and other side effects of antibodies used in studies elsewhere.

First, the scientists pinpointed the spot on the antibody that was causing the problems. Then they created a single point mutation designed to significantly decrease those negative side effects.

As part of the clinical trial, Khushi received the monoclonal antibody during every phase of treatment. The antibody itself does not attack the tumor cells. Instead, it alerts Khushi's immune system to attack the cancer.

The antibody works by recognizing and binding to a protein called GD2 that is present on the surface of almost every neuroblastoma cell. By binding to GD2, the antibody signals the immune system to attack and exterminate the cancer cell.

History of an antibody

St. Jude scientists and clinicians have been studying antibody therapy for more than a decade.

In the mid-2000s, they discovered that Hu14.18K322A showed promise in children with recurrent disease or with neuroblastoma that did not respond to traditional therapy. In a subsequent study, Federico and her colleague, Wayne Furman, MD, combined that antibody with chemotherapy. They found that patients tolerated the treatment well, and that the antibody was effective against neuroblastoma.

Because of those successes, the team designed NB2012, a clinical trial for children with high-risk neuroblastoma. This time, the researchers moved the antibody therapy to the beginning of treatment, as well as throughout the second and third phases of therapy.

"We really wanted to move the bar," Federico explains. "We didn't want to see a 5 percent improvement over national responses to neuroblastoma treatment. We wanted to see at least a 20 percent improvement."

After the first 20 patients completed two courses of chemotherapy and antibody therapy, Furman and Federico compared the results with those of a large national clinical trial. The St. Jude response was not 5 percent better. It wasn't even 20 percent better.

"The early disease response was double—more than 80 percent of children responded," Federico says. "That made us all very excited."

ANN-MARGARET HEDGES

IN EARLY RESULTS OF THEIR CLINICAL TRIAL, **SARA FEDERICO, MD,** AND HER COLLEAGUES HOPED TO SEE A 20 PERCENT IMPROVEMENT OVER NATIONAL RESPONSES TO NEUROBLASTOMA TREATMENT. "MORE THAN 80 PERCENT OF CHILDREN RESPONDED," SAYS FEDERICO, SHOWN HERE WITH **KHUSHI PATEL**.

"Out in the world, people may be fighting and killing each other, but at St. Jude people show such love. Sometimes it brings tears to my eyes when I see how the people here are willing to do everything for these kids."

–CHIRAG PATEL

Early promise

Furman recently shared the study's preliminary results at a national scientific meeting. In 80 percent of children in NB2012, the primary tumors were 47 to 96 percent smaller. In the remaining patients, the tumors had stopped growing. "The early response is very promising, among the best that we have seen against neuroblastoma," Furman says, "but we still have a long way to go."

Furman, Federico and their colleagues will closely follow the children in NB2012 to find out whether the early response translates into a long-term cure. "That's the $64 million question," Furman says. "Now we've got to wait for the kids to be off therapy for two or three years."

The first patient in the study recently passed the two-year mark, with no evidence of disease. Many other children, like Khushi, are still receiving treatment.

In the pink

Although the first cycle of high-dose chemotherapy made Khushi extremely sick, she responded well to the rest of her treatment.

"She's had an amazing response to therapy," Federico observes.

Federico and other hospital staff refer to Khushi as "Sparkle," because of her sunny personality and her affinity for brilliant pink clothing. Now 7 years old, Khushi spends her time painting, coloring, doing crafts, playing games and completing classwork through the St. Jude School Program.

"Math is my favorite thing in school," says Khushi, who wants to pursue a medical career when she grows up. "I'd like to be a physical therapist because I could help other kids," she explains.

Khushi's dad says the family's experience at St. Jude has renewed his faith in humanity.

"Out in the world, people may be fighting and killing each other, but at St. Jude people show such love," Chirag says. "Sometimes it brings tears to my eyes when I see how the people here are willing to do everything for these kids. Our family is fortunate that St. Jude is there for us."

As Khushi completes her last phase of treatment, her parents exude a renewed spirit of optimism and hope.

"She has come through a really rough time," Vaishali muses. "Now we want her to enjoy life. God is great; life is good. You don't know what is going to happen in the future, so we want her to enjoy life as much as she can.

"And we will never, ever forget what St. Jude has done for us." ■

"It makes perfect sense that we would try to unleash the immune system on cancer."

–SARA FEDERICO, MD

BARRY SHULKIN, MD (AT LEFT), NUCLEAR MEDICINE CHIEF, AND **SCOTT SNYDER, PhD,** OF DIAGNOSTIC IMAGING, HAVE DEVELOPED RADIOACTIVE TAGS TO PREDICT WHICH PATIENTS CAN BENEFIT FROM ANTIBODY THERAPY.

"Tag," That's It

Immunotherapy's success hinges on an antibody's ability to bind to an antigen on the surface of a cancer cell. An antigen called GD2 is present on almost all neuroblastoma and melanoma tumors. GD2 also appears on the surface of some osteosarcoma, Ewing sarcoma and small-cell lung cancer cells.

By binding to GD2, the antibody triggers the patient's own immune cells to spring into action.

But for some children, antibody therapy does not work well. A child's immune system may be so weak that it cannot muster the strength to fight the tumor. Or low levels of GD2 preclude a robust immune response.

How can scientists predict which patients have enough GD2 to benefit from antibody therapy?

Scott Snyder, PhD, of St. Jude Diagnostic Imaging and Barry Shulkin, MD, Nuclear Medicine chief, have developed radioactive tags to do just that.

"The idea is that we give the child a small dose of the antibody that has this little bit of a radioactive tag on it," Snyder explains. "Then we do a scan. If the antibody binds to the tumor, the tumor will light up on the scan. If it doesn't light up, then we know the tumor doesn't express GD2 and the antibody therapy isn't likely to help that child."

Besides creating radioactive tracers that determine GD2 expression, Snyder and his team are also developing a tag that can destroy the cancer.

"The long-term goal is to tag the antibody with a radioisotope that would actually kill the tumor cells by itself," he says. "You've got the immune system that's killing the tumors and you've got the radioactive tracer that's killing even more tumors. So it should be twice as effective."

Snyder predicts the new tracer will soon be approved for use in patients.

"It's really exciting that tracers we developed in our cyclotron radiochemistry lab will be helping patients within the next year," he says.

PETER BARTA

WAYNE FURMAN, MD, AND HIS COLLEAGUES WILL CLOSELY FOLLOW THE CHILDREN IN NB2012 TO FIND OUT WHETHER THE EARLY RESPONSE TRANSLATES INTO A LONG-TERM CURE.

Making the Right Connections

Connecting people who care with causes that matter: **How one gift can save many young lives.**

By Kerry Healy

Bernie Story's job is to connect people who care with causes that matter. As president and CEO of the Lehigh Valley Community Foundation in Allentown, Pennsylvania, Story helps philanthropists in his community use their charitable dollars to make a meaningful impact on the causes they care about most.

A gift to help fund proton therapy at St. Jude Children's Research Hospital is one example of how Story helped fulfill the legacy of the late George T. Walker.

Walker's advisers approached the Community Foundation, and Story says, "We were given to understand that he was a humble man of deep faith, who wanted to use his estate to improve lives in our region and across the country by increasing access to services."

Setting up an endowed designated fund with the assets from Walker's estate was ideal. When Walker prepared his estate plans, he requested annual evaluations of the charities his bequests would help fund. His advisers recommended making one large gift to the Lehigh Valley Community Foundation, creating The George T. Walker Charitable Fund. The foundation is uniquely positioned to facilitate such a gift.

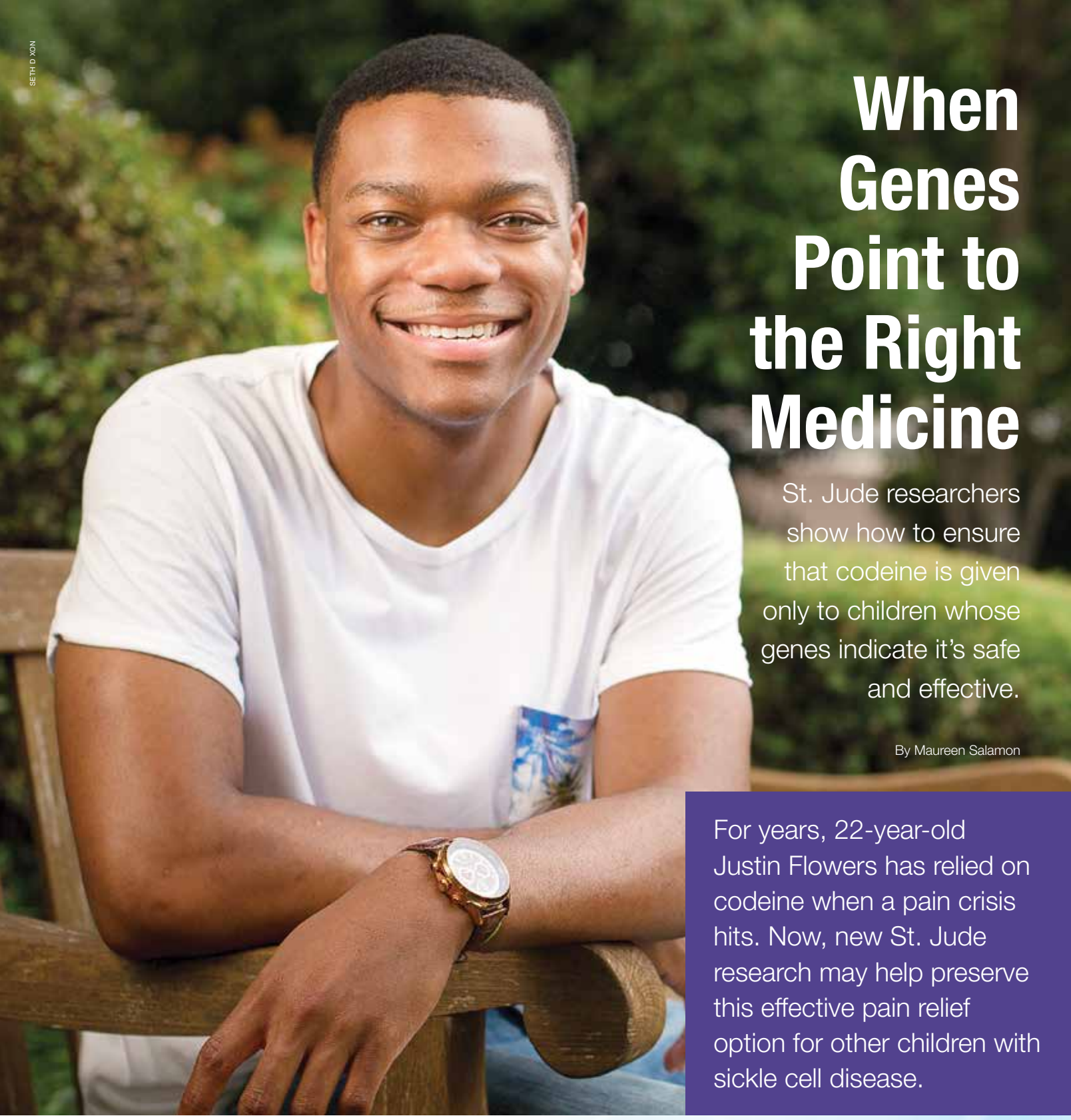
"As a result," Story says, "we have a large endowed fund of grantable dollars, and our staff works with the charities he designated to meet their needs and fulfill Mr. Walker's wishes."

About supporting proton therapy, Story says, "We really wanted to do something impactful for children with cancer, and we worked with our St. Jude representative to establish a multi-year grant plan. Because it is the very first proton therapy center solely dedicated to the treatment of children, it really resonated with the foundation from a human perspective."

Story attended the grand opening of the St. Jude Red Frog Events Proton Therapy Center and the unveiling ceremony for the plaque naming a proton therapy induction room in honor of the Walker Fund's support.

"It was absolutely wonderful," Story says, "seeing St. Jude families treated with such dignity and respect, and knowing that I represent the Community Foundation that is helping, in a small way, to make that possible.

"This is really the story of Mr. Walker's philanthropy, and his decision to improve people's lives across the country," Story adds. "It's been an amazing experience to partner with St. Jude and have the honor of fulfilling his charitable intent." ■



SETH D XON

When Genes Point to the Right Medicine

St. Jude researchers show how to ensure that codeine is given only to children whose genes indicate it's safe and effective.

By Maureen Salamon

For years, 22-year-old Justin Flowers has relied on codeine when a pain crisis hits. Now, new St. Jude research may help preserve this effective pain relief option for other children with sickle cell disease.

A fun afternoon playing basketball turned into a night of agony for Justin Flowers, who at age 12 woke up in excruciating pain. He didn't know it then, but Justin was having his first pain crisis related to sickle cell disease. Individuals with this disorder have sickle-shaped red blood cells that clog their circulation, triggering searing pain. This life-threatening disease affects about 100,000 Americans.

Emergency treatment halted Justin's pain, but the incident ushered him into a new era. Preventing recurrent sickle cell pain crises became a prime pursuit.

The drug codeine—at the center of a national controversy over its role in pediatric pain management—was crucial to that effort. For Justin, codeine became a regular tool to stave off full-blown pain crises. The medication

helped keep him on the court and field playing his favorite sports.

New research at St. Jude Children's Research Hospital may help preserve this inexpensive, effective pain relief option for children with sickle cell disease by determining how their DNA influences their drug response and making sure the information is readily available to health providers.

Known as pharmacogenetics, this form of precision medicine enables doctors to prescribe codeine only after genetic testing shows the medication will be safe and effective for that person.

"Having sickle cell and trying not to have a pain crisis is always on your mind, 24/7," says Justin, now 22. "When you do anything, the first thing you think is, 'Do I have my medicine with me?' More times than not, the codeine helped."

Personalized care

St. Jude has long been a leader in pharmacogenetics, the study of how a person's genes influence which medications and doses will work best or may cause dangerous complications. Research has shown that about half of all hospitalized patients each year may receive drugs that, because of the recipients' genetic makeup, could lead to serious side effects.

For more than two decades, pharmacogenetics has guided the use of chemotherapy in St. Jude patients treated for leukemia. The hospital is one of only a handful of institutions to offer pharmacogenetics testing to patients as standard care.

Since 2011, all new St. Jude patients have been screened for variations in 230 genes, including one called *CYP2D6*. This gene plays a pivotal role in how patients respond to codeine. The screening tests also determine responses to other drugs. These include certain chemotherapy agents as well as medications for nausea, depression and infections.

Codeine's widespread use in pediatric patients has been questioned in recent years. Nationwide, several children who received it for post-surgical pain relief died. These deaths were later linked to *CYP2D6* variations. After a warning by the U.S. Food and Drug Administration, some hospitals suggested ending all codeine use in children. Several pediatric hospitals removed the medication from their list of approved drugs.

But St. Jude is using personalized medicine to identify patients most likely to benefit from the drug, while avoiding codeine use in patients who are likely to experience side effects. Clinicians make sure codeine is given only to children whose genes indicate it will likely be safe and effective. About 12 percent of the general population carries *CYP2D6* variants that drastically alter how their bodies process codeine.

A model for others

Why is codeine such an important pain relief option?

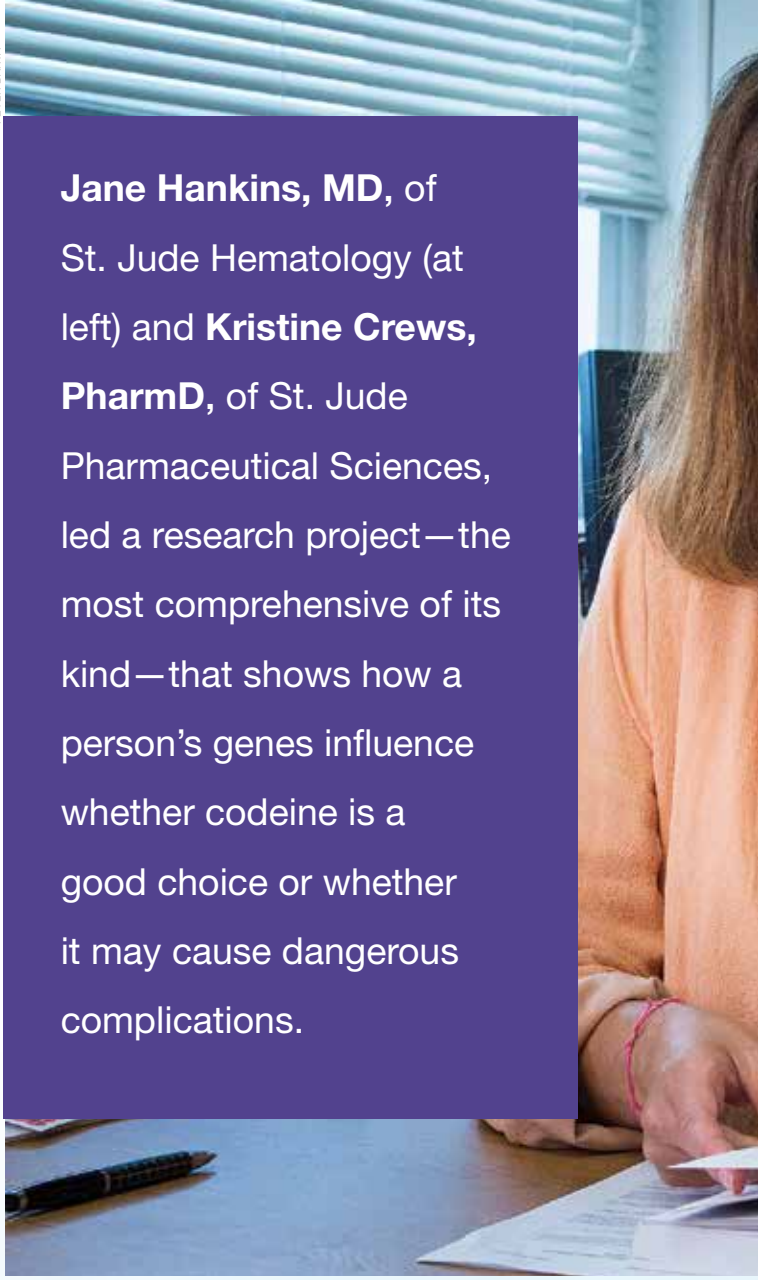
Over-the-counter ibuprofen is often not strong enough to alleviate sickle cell pain crises. Codeine alternatives include oxycodone, hydrocodone, fentanyl and morphine—expensive and tightly regulated drugs that doctors can't prescribe over the phone.

"There are a lot of really good and practical reasons to keep codeine around," explains Kristine Crews, PharmD, of St. Jude Pharmaceutical Sciences. "It's inexpensive. It's oral, so it doesn't require an IV.

"Our sickle cell doctors felt strongly that codeine should remain a choice because we have a lot of experience with it," she continues. "Access is greater because it can be called in to a pharmacy without necessarily a written prescription, and it works well in most patients. And with pharmacogenetic testing, we can know up front which patients should not receive codeine, keeping it an option for the majority of patients it is likely to help."

Crews joined Jane Hankins, MD, of St. Jude Hematology, to head a research project—the most comprehensive of its kind. Published in the journal *Pediatrics*, the study tested 621 St. Jude sickle cell patients to determine their *CYP2D6* status. About a third of the patients required significant pain relief during the study period.

Researchers found that in just over 7 percent of the patients, their bodies broke down codeine to such a great extent that even a small amount might result in a fatal overdose. Another


PETER BARTA

Jane Hankins, MD, of St. Jude Hematology (at left) and **Kristine Crews, PharmD,** of St. Jude Pharmaceutical Sciences, led a research project—the most comprehensive of its kind—that shows how a person's genes influence whether codeine is a good choice or whether it may cause dangerous complications.

1.4 percent had the reverse problem. These patients inherited no working *CYP2D6,* so codeine could not be processed at all. That meant the drug was unlikely to help.

Mutually fulfilling research

Medical alerts embedded into the St. Jude electronic medical record prevent any child with high-risk codeine status from receiving the drug. The model serves as a beacon to other health care systems on how pharmacogenetics can enhance drug therapy for any pediatric patient group coping with chronic pain.

"We wanted other people to realize they can safely get the drug to the patients who need it by using pharmacogenetics," Crews says.

The results will last a lifetime.

"Your genetics don't change," Crews notes. "We tell patients to share the information with their doctors and providers outside of our system when they outgrow St. Jude."

In related work, Kelly Caudle, PharmD, PhD, and James Hoffman, PharmD, of St. Jude Pharmaceutical Sciences, recently led a national panel working to establish a common vocabulary surrounding pharmacogenetics.

Published in *Genetics in Medicine,* the group agreed on standardized terminology to describe how gene variations affect function and clinical care. Their goal is for all institutions to use the same language to report test results. The aim is to expand the use of precision medicine.

Hankins and Crews feel gratified to help improve pain management in sickle cell patients, whose frequency of pain crises tends to increase as they get older.

"Pain crises are very difficult because they really interrupt the kids' lives," Hankins says. "They're at school and the pain comes unannounced and they have to go home. It stops everything.

"Knowing I'm doing research that's helping me treat them better is fulfilling to me and reassuring to them," she continues. "It makes me feel I'm having an impact in moving the field forward." ■

Hope FOR THE Holidays

JOHN ZACHER

Marlo Thomas celebrates St. Jude *Thanks and Giving* with patients (from left) Kenlie Jackson, Gunnar Charvat and Marley Harris.

Help children like Owen by taking part in this year's St. Jude *Thanks and Giving.*

By John Juettner

Owen Church is an active fifth-grader who loves soccer, basketball and running. He runs 5k races and kids' triathlons, enjoys animals and nature, and is constantly playing with his three siblings.

"He loves being outdoors," said his mother, Kelly. "We have one-and-a-half acres of land, so he's always exploring and playing with the other kids."

Owen is also four years removed from treatment for acute lymphoblastic leukemia at St. Jude Children's Research Hospital. During his two-and-a-half years of chemotherapy, Owen did not slow down one bit. He stayed active with his siblings and even played soccer.

He and his family also took part in St. Jude *Thanks and Giving*® in 2010. This campaign was created by Marlo, Terre and Tony Thomas, the children of St. Jude founder Danny Thomas, and has raised more than $693 million since it began in 2004. From Thanksgiving through December, the campaign unites celebrities, media, retail and corporate partners, encouraging consumers to donate to support St. Jude while they shop.

Giving back

While still receiving treatment, Owen joined Marlo Thomas in a video for St. Jude *Thanks and Giving*. He traveled with his family to New York to appear with her on NBC's *TODAY* show, which features St. Jude stories daily during Thanksgiving week.

In 2015, Owen and his family shared their story with one of the campaign's original corporate partners, Kay® Jewelers, part of the world's largest diamond jewelry retailer. They met with company employees during a St. Jude visit, and attended its annual leadership conference in Florida. Owen again visited the *TODAY* show, this time to help Kay Jewelers donate plush toys to the *TODAY* show's Holiday Toy Drive. These toys are sold annually in stores in support of the St. Jude *Thanks and Giving* campaign.

Kay Jewelers has been a partner in the lifesaving mission of St. Jude for the past 18 years. Through the dedication of team members at its stores and the tremendous generosity of its guests, Kay has raised nearly $53 million to support St. Jude since the partnership's launch.

Along with Kay Jewelers, more than 70 major brands are part of St. Jude *Thanks and Giving*, such as Kmart, Best Buy, Ann Taylor, HomeGoods, Domino's, Williams-Sonoma Inc., New York & Company, AutoZone, Dollar General, Brooks Brothers, Christopher & Banks, GNC, Claire's and many more. These companies help raise funds and awareness. They do this through social media, in-store and e-commerce programs, and sales of specialty items.

"We are truly grateful for the care and compassion our corporate partners, like Kay Jewelers, generous donors and celebrity friends have for the children of St. Jude," said Marlo Thomas, national outreach director for St. Jude Children's Research Hospital. "The amazing support we receive enables our doctors and scientists to continue to pursue lifesaving research and treatments while allowing us to keep my father's founding promise that no family ever pays St. Jude for anything —not for treatment, travel, housing or food."

Giving thanks

In addition to generous corporate partners, St. Jude *Thanks and Giving* features celebrity supporters who donate their time to support St. Jude. This year, Jennifer Aniston, Sofia Vergara, Michael Strahan, Jimmy Kimmel, Luis Fonsi and Marlo Thomas will appear alongside St. Jude patients in the ads. A movie trailer featuring these stars will also appear on theater screens nationwide at Regal Entertainment Group, AMC Theatres, Cinemark, Carmike Cinemas, Marcus Theatres and many more.

"Through the many years of helping raise awareness and funds, our team members continue to let us know that St. Jude Children's Research Hospital is the No. 1 company program about which they feel the most pride," said Tryna Kochanek, executive vice president of North America Stores for Signet Jewelers, the parent company of Kay Jewelers.

Owen's parents are grateful to St. Jude for helping to save their son's life.

"Owen has a good long-term prognosis," Kelly says. "Everything positive in Owen's life is because of the ground-breaking research done by St. Jude."

To help St. Jude create even more inspiring stories like Owen's, visit St. Jude *Thanks and Giving* partners, like Kay Jewelers, during November and December or visit *stjude.org.*■

3rd Floor: Nature's Orchestra

explori

5th Floor: Explore Space

4th Floor: Discover The Sea

new inpatient care floors at St. Jude

Quietly push aside palm fronds to encounter a slumbering cheetah. Taste the salt on your lips as you dive beneath the ocean and float among colorful seahorses. Pull on a space helmet and take flight, soaring to another galaxy.

Patients at St. Jude Children's Research Hospital no longer have to rely solely on their imaginations to visit such exotic locales. They need only stroll down the corridors of the Kay Research and Care Center.

In the fall of 2016, three inpatient units opened, each with a unique theme. Jungles, animals and lush plants greet children on the third floor. Undersea creatures large and small swim, paddle and float throughout the décor on the fourth floor. And kids blast off into space on the fifth floor. Ninety-foot-long interactive "journey walls" on each floor reflect the themes and offer opportunities for children to leave their hospital rooms for exercise, fellowship and mental stimulation.

St. Jude patient families served as embedded consultants for the facility's design and construction team. Together, they created a space that will provide healing and respite for years to come.

SEE MORE IMAGES of the new inpatient floors at *stjude.org/promise*.

Benjamin Krizhanovskiy (at left) and his brother, Joshua, marvel at the ocean creatures in a fourth-floor corridor.

In the Kay Research and Care Center, children can express themselves by controlling the color of lighting in their rooms. Other digital technologies within the rooms enable seamless delivery of health care as well as facilitate connections with friends and families.

Tyler Washington tries out the Imagine Room, a technological marvel with the ability to transport children into a virtual world and catapult them into another galaxy. A large, interactive screen covers one wall, curving into the ceiling. In addition to playing games, children can watch videos, talk with friends and family via webcam and enjoy interactive light displays.

Caleb Wells and Gracie Bain play a game with Gracie's mom, Jessica, on one of the interactive discovery walls. These kinds of activities are designed to entice children to leave their rooms and move around the unit—providing exercise, as well as interaction with staff and other patient families.

Designed with input from St. Jude patient families and nurses, each spacious suite features a sleeper sofa and full bath. An adjacent parent room also offers a full bath, as well as desk and storage areas. A glass wall between the rooms enables caregivers to have privacy while keeping a constant eye on their children.

FULL CIRCLE

PETER BARTA

"I always had a dream that I would return to St. Jude to work," says Andrew Elliott, MD.

By Elizabeth Jane Walker

The newest psychiatrist at St. Jude Children's Research Hospital dispenses a double-dose of empathy when his patients discuss their treatment challenges. But few of those patients know the true source of his insights.

The children and teens regard Andrew Elliott, MD, as an astute and compassionate physician. But he is much more than that. Elliott is a cancer survivor: a former St. Jude patient who now helps the next generation cope with their treatment experiences.

Elliott was only 14 when joint and knee pain, compounded by malaise, prompted a doctor's visit. "Am I going to lose my hair?" he mused, upon hearing the diagnosis of acute lymphoblastic leukemia. More than two years of chemotherapy followed, peppered with bouts of steroid-induced irritability and one excruciating encounter with pancreatitis. But there were also bright points: a close relationship with his St. Jude medical team; a recognition of his family's unswerving support; and the germination of career aspirations.

Although Elliott understands his patients' struggles, he doesn't want them to assume he has all the answers—or even most of them.

> "Anything we can do to lessen their pain or their struggle is what we want to do."
>
> — Andrew Elliott, MD

"My experience here taught me how to deal with huge stresses and think about how other people are dealing with theirs," he says. "But I don't usually share the details of what I've gone through, because my experience may not equate to theirs."

Elliott is part of a team dedicated to helping children achieve the best possible quality of life.

"Andrew can help patients who require medical treatment for symptoms of depression or anxiety," explains Sean Phipps, PhD, chair of St. Jude Psychology. "Our patients also receive a lot of medications that can cause reactions such as delirium. We collaborate to prevent or treat delirium early."

Elliott emphasizes that the children at St. Jude are normal kids faced with an abnormal situation. His job is to assist them as they navigate this unfamiliar terrain.

"When kids are at their most challenged, we can often help them work through it in a positive way, with medicines or therapy or a combination of the two," he says. "Then we can have a big impact—shaping their experience and giving it some meaning and purpose. Anything we can do to lessen their pain or their struggle is what we want to do."■

STREPTOCOCCUS PNEUMONIAE (PNEUMOCOCCUS) IMAGE COURTESY OF CDC/JAMES ARCHER

A BABY'S LEGACY

The untimely death of a little boy 30 years ago leads to a scientific victory that may help other children infected by dangerous bacteria.

By Maureen Salamon

She remembers him as Baby Branford.

Fresh from pediatric training and immersed in a research fellowship in infectious diseases, Elaine Tuomanen, MD, encountered a little boy with pneumococcal meningitis. This infection causes inflammation of the lining around the brain and spinal cord. Antibiotics killed the bacteria, but the treatment failed.

The 3-year-old died.

That wrenching experience three decades ago became a springboard for a pivotal new finding at St. Jude Children's Research Hospital. The discovery revolutionizes our understanding of how pneumococcus bacteria survive and flourish. This breakthrough also opens the door for sweeping changes to current vaccines and medicines to attack a worldwide killer of children.

Capsules hold the key

Pneumococcal infections cause mild illnesses such as ear infections and bronchitis as well as life-threatening meningitis, pneumonia and bloodstream infections known as sepsis. These infections claim about 1.6 million people globally each year. More than 800,000 of those deaths are among children, according to the World Health Organization.

"Baby Branford—with this information turned into a therapeutic—would never have died. It's a super victory from my perspective."

Elaine Tuomanen, MD

Tuomanen, chair of St. Jude Infectious Diseases; postdoctoral fellow Colin Kietzman, PhD; and their colleagues made a discovery about an enzyme called LytA. Long known to be the trigger by which antibiotics cause bacteria to explode and die, LytA has a much different function in the everyday life of bacteria growing in humans. In response to normal molecules made by the immune system to control microbes, the bacterium uses LytA to shed its outer layer, or capsule, promoting its survival.

The research also suggests bacteria can rapidly add or remove capsules as needed to avoid detection and destruction by the body's immune system.

"I decided if I could better understand the surface of the bacteria, I would use that medical paradigm to take apart how the disease happens and how I could fix it," Tuomanen says. "I didn't understand why, if we did everything right, Baby Branford didn't live. That was the beginning of a long and tortuous road to make his situation treatable, with more survivors."

PHOTOS BY PETER BARTA

Elaine Tuomanen, MD, St. Jude Infectious Diseases chair, and her colleagues shed new light on how pneumococcus bacteria survive and flourish. This breakthrough opens the door for sweeping changes to current vaccines and medicines to attack a worldwide killer of children.

Changing coats

Scientists have known for decades that a bacterium can change how thick a capsule is on its surface. After two years of research, St. Jude investigators built on that principle. They found that bacteria have an entire pathway devoted to shedding the capsule off the surface, and that LytA is responsible.

"It's like changing your winter coat to a summer coat," Tuomanen explains. "The bacteria have learned that a thick, heavy coat in the lung hinders the ability to invade into the bloodstream, so in response to signals in the lung, pneumococcus activates this enzyme for capsule shedding.

"Surprisingly, the shedding activity of LytA is completely independent of its role in antibiotic killing," she continues. "Shedding is so important to bacterial life in the host that the bacteria are forced to keep the *LytA* gene even though losing it would make it resistant to penicillin-induced death."

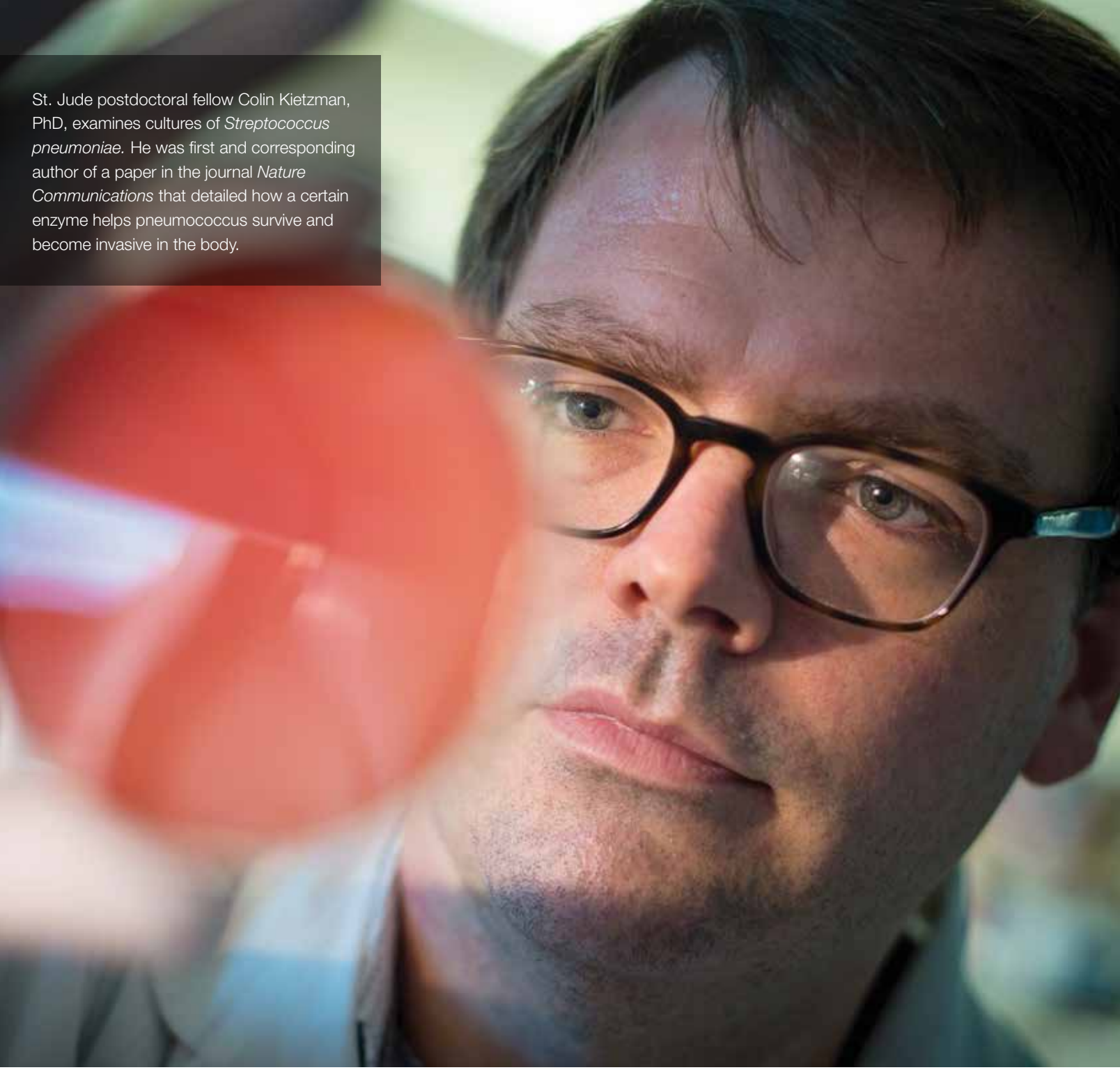
Capsule-shedding also sets the stage for dangerous infections. This process makes it easier for pneumococci to invade cells and move into the bloodstream. Once in the blood, the bacteria—also known as *Streptococcus pneumoniae*—again produce capsules to protect against the body's basic immune response.

"The bacteria hunker down and tightly adhere to lung surfaces, causing more serious disease," Kietzman says.

Patience, hard work and victories

These new details radically alter our understanding of pneumococcus. The findings may one day transform the arsenal of vaccines and drugs available to prevent and treat pneumococcal infections.

Most vaccines aimed at pneumococcus currently target its capsule to trigger a protective response. But this strategy won't work if the capsule is shed off the bacteria's surface. This explains



St. Jude postdoctoral fellow Colin Kietzman, PhD, examines cultures of *Streptococcus pneumoniae.* He was first and corresponding author of a paper in the journal *Nature Communications* that detailed how a certain enzyme helps pneumococcus survive and become invasive in the body.

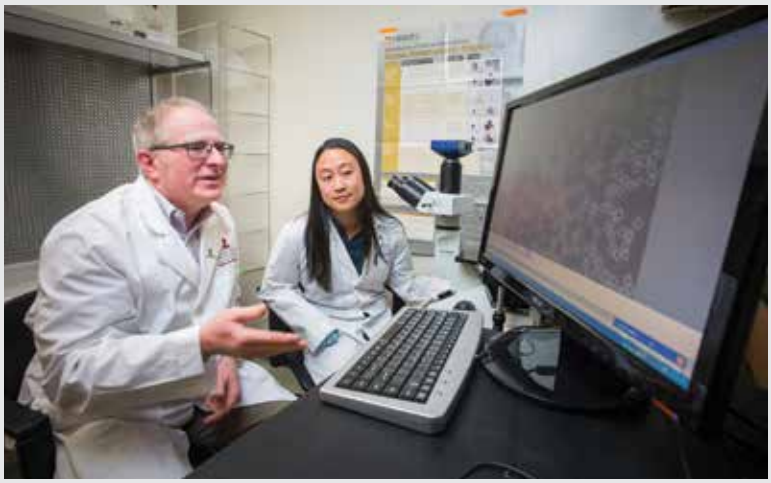
why current vaccines work well against bloodstream infections where the capsule is thick but are much less effective against pneumonia, where bacteria automatically shed the capsule. Instead, Tuomanen says, vaccines targeting pneumococcal surface proteins should be created. This is already occurring at the Children's GMP, LLC, on the St. Jude campus as well as by commercial drug manufacturers.

"It will take time for those in the field to understand that vaccines are now going to have to be built differently," Tuomanen says. "It will be a slow road for the big vaccine companies, and they have a lot to lose since they have established capsule-based vaccines they make billions of dollars on."

But if she's tempted toward impatience, Tuomanen need only think about Baby Branford and how far she and her St. Jude colleagues have come.

"Now everything is turned upside down, and we understand much more about what penicillin and other antibiotics can do, and what vaccines can and can't do," she says. "Baby Branford—with this information turned into a therapeutic—would never have died. It's a super victory from my perspective." ■

PHOTOS BY PETER BARTA



Mitchell Weiss, MD, PhD (at left), and Elizabeth Traxler

Editing sickle cell disease

Despite improved therapies, patients with sickle cell disease often face recurring pain, organ damage and early death. The only cure is a bone marrow transplant, which has its own risks.

What if there were another option that involved just a few snips of the DNA to give patients lifelong relief?

An international team of scientists used a technique called CRISPR gene editing to help fix the effects of sickle cell disease. The approach has yet to be tested in patients, but it may be getting closer to the clinic.

The St. Jude-led team made specific genetic changes in blood-forming cells from sickle cell patients. The changes were designed to mimic mutations found in a genetic condition called hereditary persistence of fetal hemoglobin (HPFH). This harmless condition eases symptoms in patients with sickle cell disease.

After editing, red blood cells with the HPFH-like changes were healthier and less likely to become misshapen or sickled.

"This work offers proof-of-principle for a possible approach to treat sickle cell and related disorders like beta-thalassemia," said Mitchell Weiss, MD, PhD, St. Jude Hematology chair.

The next challenge will be to pursue the safest and most effective option to deliver a cure.

The work was published in *Nature Medicine*.

Researchers identify master flu assassin

St. Jude scientists have identified a crucial protein trigger in the body's innate immune system that is the front line of the disease-fighting immune system. This "master assassin," called ZBP1, recognizes the influenza virus in infected cells and helps trigger their death.

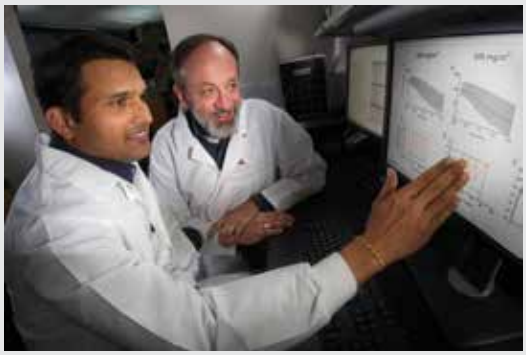
The team, led by Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology, set out to discover how the innate immune system is alerted to the presence of the flu virus in cells and causes infected cells to commit suicide. The team found that cells lacking ZBP1 could resist viral-induced cell death.

Teneema Kuriakose, PhD (at left), and Thirumala-Devi Kanneganti, PhD

When the innate immune system recognizes the flu virus, it activates an "emergency response" that causes infected cells to commit suicide. But sometimes the innate immune system overreacts, causing lung inflammation and cell damage. If a person has pneumonia—a dangerous complication of the flu—this overreaction of the innate immune system can make the pneumonia worse. Now that scientists understand the function of ZBP1, they may be able to develop drugs to protect against flu and pneumonia.

The findings appeared in the journal *Science Immunology*.

SETH DIXON



Yogesh Patel, PhD (at left), and Clinton Stewart, PharmD

Applied math and supercomputing help smooth transition from lab to clinic

Chemotherapy drugs proven to work against the brain tumor ependymoma are lacking. Current treatment is built on surgery and radiation. So, one report from St. Jude Children's Research Hospital was welcome news. Scientists found that a drug widely used against colon cancer may also be effective against ependymoma.

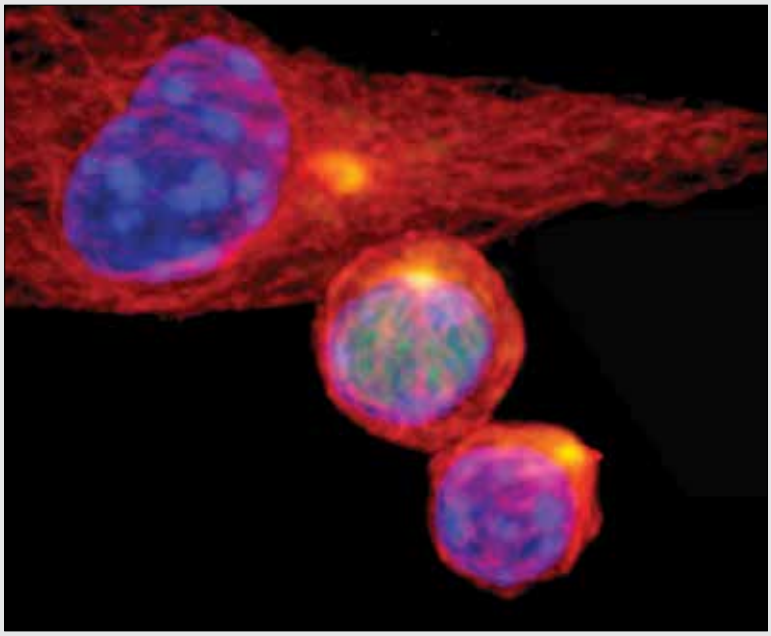
The drug is 5-fluorouracil. Working in laboratory models, researchers had shown that giving the drug rapidly in a single dose called a bolus, rather than infusing it slowly, magnified the drug's benefits. But more information was needed about how children would react and to determine the effective dose to kill brain tumors.

Researchers used applied math, supercomputing and other tools to analyze lab data to find the best starting bolus dose for children. That dose was well tolerated and had an anti-cancer effect when used in a phase I study of children and young adults whose brain tumors had returned.

"The modeling and simulation used in this study streamlined identification of the optimal bolus dose of 5-fluorouracil for young ependymoma patients," said Clinton Stewart, PharmD, of St. Jude Pharmaceutical Sciences. "The approach is a template for drug development, especially for rare diseases like ependymoma."

The research was published in the journal *CPT: Pharmacokinetics and Systems Pharmacology.*

KATHERINE VERBIST, PhD



The fate of daughter T cells in the immune system (lower cells in image) is decided at the first cell division and influenced by the expression level of c-Myc protein (in green).

Cancer immune therapy: A potential new avenue

T cells have been called the "watchdogs" of the immune system. They monitor the body for threats, and attack invading agents when needed.

A single activated T cell can divide into daughter cells with different jobs. One becomes a rapidly dividing attack cell — an effector T cell — and the other a long-term sentinel, called a memory T cell.

St. Jude scientists have discovered how this process works. The results may open new avenues into immune therapies that harness the immune system to fight disease.

The crux is a signaling protein called c-Myc. The scientists found that a dividing T cell prompts the production of more c-Myc in one of its daughter cells, which triggers attack dog properties, such as rapid proliferation. The other daughter cell makes less c-Myc and becomes a slow-dividing memory T cell.

"Our work suggests that it may be possible to manipulate the immune response by nudging production of c-Myc in one direction or the other," said Douglas Green, PhD, chair of St. Jude Immunology. "Potentially that could mean more effective vaccines or help to advance T-cell immune therapy for cancer treatment."

The work was published in *Nature*.

Targeted antibiotics may help protect bacterial good guys in the gut

The discovery and widespread access to broad-spectrum antibiotics is one of the chief medical feats of the past century. But antibiotics take a toll on the trillions of bacteria and other microbes—known as the gut microbiome—that live and work in our digestive tract.

PHOTOS BY SETH DIXON

Charles Rock, PhD (at left), and Jiangwei Yao, PhD

We depend on the gut microbiome for proper nutrition and immune protection. Broad-spectrum antibiotics act against many kinds of microbes. These drugs reduce the size and diversity of the gut microbiome. Frequent use of the medicines early in life has been linked to changes in the microbiome that increase the risk of problems like infections, obesity and celiac disease.

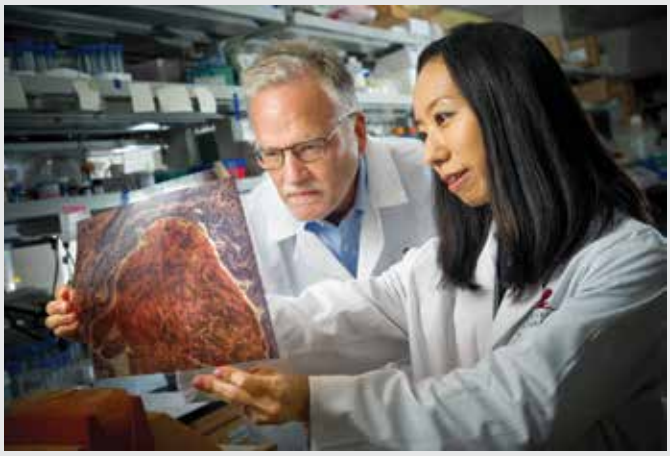
St. Jude scientists have shown that an experimental antibiotic designed against a specific microbe is easier on the gut microbiome.

Charles Rock, PhD, Jiangwei Yao, PhD, and their colleagues found that such a drug targeting staph infections caused fewer changes in the size and diversity of the gut microbiome than common broad-spectrum antibiotics. The microbiome also bounced back faster after treatment with the targeted antibiotic. By targeting staph specifically, the bacterial good guys in the gut microbiome stay to protect against new infections and other problems that pose a threat to patients.

The research was published in *Antimicrobial Agents and Chemotherapy.*

Rare genetic variations may solve porphyria mystery

An international research team led by St. Jude has found that variations in a cell membrane protein determine symptom severity in a disease called porphyria. This rare disorder may affect the skin, liver and nervous system.



John Schuetz, PhD (at left), and Yu Fukuda, PhD

Porphyria is usually caused by an inherited mutation in one of the eight enzymes involved in assembling heme. The heme molecule plays a critical role in oxygen transport, drug metabolism and other vital processes.

In this study, researchers discovered rare variations in the *ABCB6* gene, also called *Lan*. The changes were more common in patients with severe porphyria than in those with less severe symptoms.

One of the mysteries of this disease has been why some individuals with the same genetic defect have mild symptoms while others have severe symptoms and require hospitalization in the intensive care unit.

"The findings raise hopes for future therapies by restoring the supply of ABCB6 protein to more normal levels," said John Schuetz, PhD, of St. Jude Pharmaceutical Sciences.

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

Finding new ways to protect patients during chemo

Infections are one of the greatest threats to cancer patients during chemotherapy. The anti-cancer drugs lower the supply of disease-fighting immune cells that fight infections.

St. Jude scientists have discovered a potential way to solve this problem by remodeling white blood cells called macrophages. Macrophages are a type of white blood cell that resides in tissue.

Working in the lab, researchers found that vaccination led to production of a new form of macrophages in the lung. Scientists called the newly recognized cells vaccine-induced macrophages or ViMs.

ViMs are different from conventional lung macrophages. Their population remains stable during chemo. In the lab, they also offer more protection against infections.

The research suggested that ViMs are maintained in the lungs through cell division. ViMs also don't rely on immune cells in the bone marrow, which are wiped out during chemo. Work continues to find safer, easier ways to produce ViMs in cancer patients.

"I am an infectious diseases doctor and have witnessed how infections can disrupt cancer treatment and threaten patient survival," said Akinobu Kamei, MD, of Infectious Diseases. "This study suggests a possible framework for developing new ways to protect patients during chemotherapy."

The research appeared in *Proceedings of the National Academy of Sciences.*

Elaine Tuomanen, MD (at left); Akinobu Kamei, MD; and Peter Murray, PhD

Most teen survivors of childhood cancer are well adjusted

Here is another way that adolescent survivors of childhood cancer are like their peers who did not have cancer: Most are well adjusted.

"Of the almost 4,000 survivors in this study, the majority did not have elevated symptoms of behavioral, emotional or social problems. This is really good news," said Tara Brinkman, PhD, of St. Jude Epidemiology and Cancer Control.

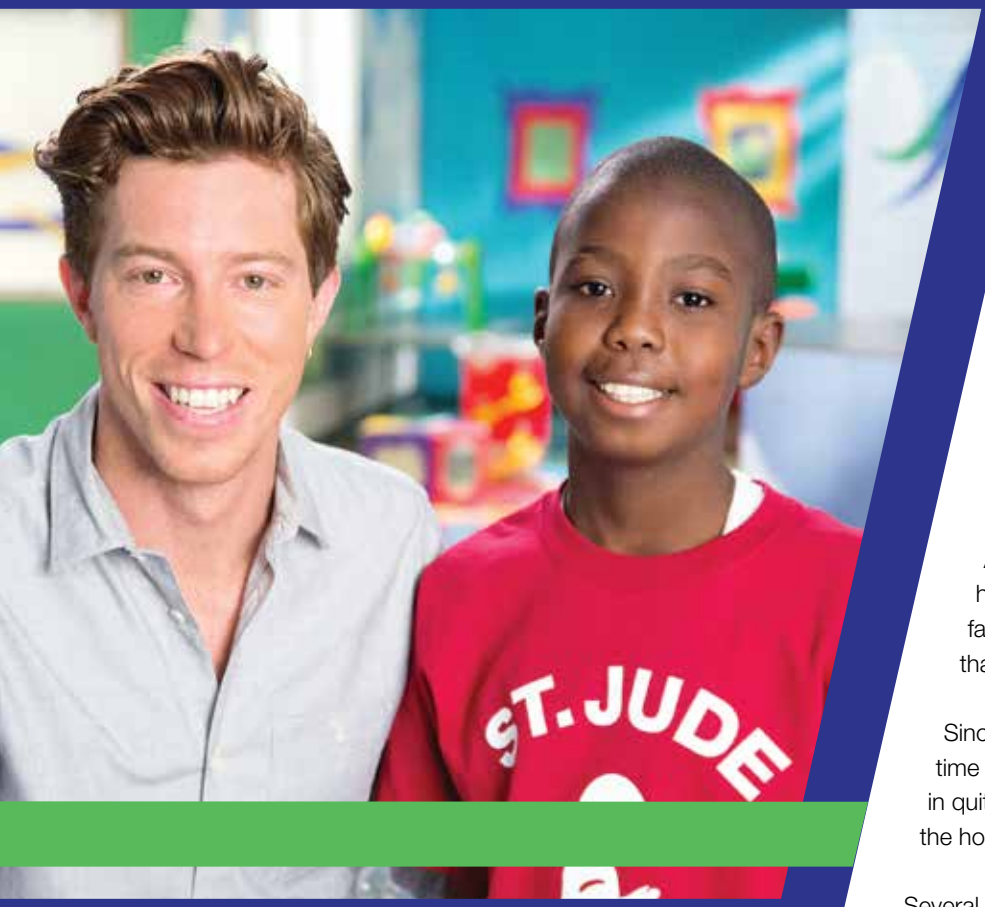
Data from the federally funded Childhood Cancer Survivor Study contained other lessons.

When psychological symptoms were reported, researchers found the patterns of symptoms were often the same among survivors who shared similar cancer treatments or the same late effects of treatment. For example, reports of depression, anxiety, social withdrawal and poor attention were more common among survivors treated with brain irradiation than among other survivors. In contrast, headstrong behavior and attention problems in combination were more evident in survivors who did not have brain irradiation.

Tara Brinkman, PhD

The findings also suggest that some teen survivors may benefit from more comprehensive mental health screening to find and address symptoms while they are still young. The research was published in the *Journal of Clinical Oncology*.

WHY I SUPPORT ST. JUDE



The first time I visited St. Jude Children's Research Hospital, I was 16 years old and had agreed to do a skateboard demo in the hospital's parking lot. At that age, I was involved in my own world. I didn't really think about much except my schoolwork, my parents and family, and whatever task was at hand. So, I was taken aback when I came to the hospital for the first time. I was blown away to see all the hope and love in the patients and families in spite of all they were going through.

That really struck a chord with me. You see, soon after I was born, I had to undergo two open heart surgeries, and my parents lived in the hospital with me. During that time, my sister also had some medical complications. It was a crazy time for my family. When I visited St. Jude years later, it gave me a glimpse into what my family had gone through.

As a teen meeting those St. Jude families, I realized how deeply an experience like this affects the whole family. I had not really understood that before.

Since that time, I've visited St. Jude often, spending time with the kids and their families. I've also taken part in quite a few events and other activities to support the hospital.

Several years ago, my brother and I helped redesign the living room area at Target House, the hospital's long-term housing facility. We remodeled the common area to be the coolest place, containing oversized lamps and a coffee table made of broken skateboards and a wall of pictures. I've gotten to see the kids enjoying themselves in that space. It means a lot to see that.

I've been going there long enough now that I've seen patients get better, leave the hospital and go on to live their lives. I really believe there are miracles taking place at St. Jude.

Because St. Jude relies on donations, they need our support to keep the doors open. It's an incredible feeling to be able to help make that possible for the families. And it's a powerful thing to be able to brighten up their day during a dark time. ■

"I'VE BEEN THERE LONG ENOUGH NOW THAT I'VE BEEN ABLE TO SEE PATIENTS GET BETTER, LEAVE THE HOSPITAL AND GO ON TO LIVE THEIR LIVES."

Professional snowboarder and skateboarder Shaun White is a two-time Olympic gold medalist who has won 14 gold medals in the X Games.

Give thanks.

Give to help him live.

St. Jude patient
Muhammad, age 4
cancerous tumor

Give thanks for the healthy kids in your life, and give to those who are not.

Muhammad is a smart, loving boy. After he complained of back pain, his mom was devastated to learn he had a rare cancerous tumor. He was referred to St. Jude for treatment, and now they have hope. Treatments invented at St. Jude have helped push the overall childhood cancer survival rate from 20% to more than 80% since it opened more than 50 years ago – and we won't stop until no child dies from cancer.

Give today at **stjude.org** or **800-4STJUDE**

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Thirteen-year-old Gloriuna Hamilton visits with her new canine friend, Bailey, during Doggy Daze at St. Jude. The hospital's Child Life staff members coordinate the activity, which allows children and caregivers to interact with specially trained dogs. Besides fostering sensory stimulation and a sense of normalcy, the program encourages mobility as kids meet their new furry friends.

JUSTIN VENEMAN

Finding cures. Saving children.