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Promise

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

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Promise

A publication of St. Jude Children's Research Hospital Winter 2014



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A test developed by St. Jude simplifies and improves the selection process for bone marrow transplants.

A natural killer (NK) cell destroys a cancer cell in this illustration. The risk of death following bone marrow transplantation can be reduced by about 60 percent using a St. Jude technique to identify bone marrow donors who make the most potent NK cells.





A simple blood test developed by St. Jude scientists helped identify the best possible transplant donor for Regan Peel, shown with her St. Jude teacher, Kaci Richardson.

hen 7-year-old Texas resident Regan Peel underwent treatment for acute myeloid leukemia (AML) several years ago, the chemotherapy made her violently ill. But that's all it did. Because of a genetic mutation, the AML, a cancer of the white blood cells, did not respond to treatment.

Regan's only hope was a bone marrow transplant. And she needed one quickly.

The Texas hospital had good news: They had identified an unrelated donor. But they also had bad news: The transplant would cost the family \$200,000, because the procedure was not covered by insurance.

Fortunately, the family obtained a referral to St. Jude Children's Research Hospital, which has the world's highest survival rates for high-risk leukemia patients undergoing haploidentical, or partially matched, transplants Not only would the family never receive a bill for Regan's treatment, but the little girl would benefit from new research that would help save her life.

Defeating cancer with NK cells

In addition to controlling infection, the immune system can sometimes help control tumor growth. But Regan's leukemia cells seemed invincible: They could resist chemotherapy as well as fend off an immune system attack. "We have been able to double the survival rate for patients who have bone marrow transplants for childhood leukemia." —Wing Leung, MD, PhD

A few years before Regan arrived at St. Jude, the hospital's researchers had made an exciting discovery about certain cancer-fighting immune cells, called natural killer (NK) cells. Scientists had learned that NK cells with a certain protein on their surface are adept at killing cancer cells.

The protein on those NK cells is a specialized product of the *KIR* gene. Everyone is born with *KIR* genes, but some people possess a more potent form of this particular gene and some have a weaker form. St. Jude scientists found that patients who received bone marrow from donors with the more potent form of *KIR* had dramatically better outcomes than children who received NK cells containing the weaker form.

An innovative blood test

Based on that research, the St. Jude transplant team developed a simple blood test to reveal whether a potential donor's NK cells contained the preferred KIR protein. The new test now occurs as part of the routine donor screening process at St. Jude.

"If we have 10 potential donors, for example, we are able to use this test to discern which donor has the strongest gene," explains Wing Leung, MD, PhD, St. Jude Bone Marrow Transplantation and Cellular Therapy chair. "The stronger NK cells control the leukemia; therefore, the risk of relapse after transplant is smaller and the outcome is better."

The new blood test, coupled with existing screening criteria, indicated that Regan's dad, Kelly, was the best match.

Thanks to the expert medical care Regan received at St. Jude, she was able to leave the hospital only 12 days after transplant, remaining in Memphis for an additional 118 days for follow-up care.

A perfect match

St. Jude investigators were the first to show that donor *KIR* typing is crucial in improving transplant outcomes. A recent study published in the *Journal of Clinical Oncology* confirmed the success of the new screening test.



The St. Jude blood test, coupled with existing screening criteria, indicated that Regan's dad was the best match for her bone marrow transplant. Today, Regan (pictured with her parents, Phyllis and Kelly Peel) is a high school student who aspires to a career in pediatric nursing.

"We have been able to double the survival rate for patients who have bone marrow transplants for childhood leukemia," Leung observes.

In transplants using the best donor identified by the new test, the risk of death was reduced by 60 percent and the risk of disease progression by 62 percent. The benefits occurred regardless of patients' age, condition, previous treatment, genetic match, or whether the donor was a relative or an unrelated donor.

In keeping with the hospital's commitment to share discoveries, St. Jude has licensed the test, which will soon be available to transplant centers worldwide. Thus far, St. Jude researchers have studied the *KIR* gene in connection with transplants, but Leung says that this gene family may also have applications for disorders such as diabetes, scleroderma, psoriatic arthritis, chronic hepatitis C or HIV infections.

"We don't yet know how this gene and this new lab

Bone Marrow Transplant

A transplant replaces damaged or diseased bone marrow with healthy marrow from a donor.

FINDING THE RIGHT DONOR

Ideal donor-patient pairs have matched tissue types.



MORE THAN JUST MATCHING

New research from St. Jude Children's Research Hospital shows patients do better with transplants from donors who have cancer-fighting immune cells with a specific genetic makeup.



A simple new test can identify these donors during normal screening.

Bari R. et al., J Clin Oncol. 2013

www.stjude.org

test will affect other diseases," he says. "More studies are needed."

Because donor NK cells can control leukemia well, total body radiation is no longer necessary, and most transplant patients can quickly resume their daily routines. Regan was no exception. After graduating from the eighth grade as valedictorian, she has continued to excel, maintaining her high academic standing. When she's not practicing the piano or guitar, serving as manager of a baseball team or hanging out with friends, Regan sings and leads worship with her church's youth band.

She also focuses on her career goals.

"The whole experience at St. Jude inspired me to go into nursing—maybe oncology; definitely pediatrics," she says.

Regan is convinced that it will be another perfect match.

The *KIR* gene family may also have applications for disorders such as diabetes, scleroderma, psoriatic arthritis, chronic hepatitis C or HIV infections.



"If we have 10 potential donors, we are able to use this test to discern which donor has the strongest gene," says Wing Leung, MD, PhD, St. Jude Bone Marrow Transplantation and Cellular Therapy chair. "The stronger NK cells will control the leukemia; therefore, the risk of relapse after transplant is smaller and the outcome is better."

Cancer survivor and nursing student Brooke Brown (at left) chats with Emily Browne, the nurse practitioner who inspired Brooke to enter the medical field. Landard Robert

From Patient to Practitioner

By Elizabeth Jane Walker

Inspired by their St. Jude caregivers, seven former patients help others by pursuing careers in health care.

hen 12-year-old Brooke Brown lost her beautiful, long tresses to chemotherapy treatments, the experience took a toll on her self-esteem. Recognizing Brooke's distress, St. Jude Children's Research Hospital Nurse Practitioner Emily Browne pulled out her secret weapon.

"Ms. Emily showed me a picture of herself when she was a teenager," Brooke says. "In the photo, she was standing by a Christmas tree, and she was bald. Ms. Emily said, 'See, this is me. I had cancer, and I got better. Now I'm going to help you get better.'

"I really took that to heart."

Not only did the experience provide the motivation Brooke needed to persevere through treatment for non-Hodgkin lymphoma, a cancer of the immune system, but it also provided the impetus for a career choice. "I realized the reason I went through this is so that I could come back as an adult and help other children," says Brooke, a nursing student who aspires to work at St. Jude. "As a nurse, I'll be able to say, 'Yes, you feel bad. I understand that, because I've been through it. But you have to get up; you have to be strong; you have to smile; you have to laugh. You can get through this, and you can not only be better physically, but also mentally and spiritually."

Brooke is one of many St. Jude patients who have transformed their experiences into the ultimate way to give back: helping others through careers in health care.

"I'm passionate about coming back to work at St. Jude," Brooke says. "Whenever I'm tired or don't feel like studying, I just think, 'Brooke, you have to do this to be able to reach your end goal; to see yourself in St. Jude scrubs, helping these kids.'

"That is my motivation, my drive."

Jason Schwartz, MD, PhD

n 1995, Jason Schwartz's life goal was to play professional football. But a leukemia diagnosis changed that scenario.

"Why me? How did this happen?" the seventh-grader asked himself. In

search of answers, Jason immersed himself in understanding more about his treatment. Taking ownership of the process, he learned all he could about cancer.

"As I went through treatment and looked at my lab results and talked to my doctors, my curiosity and interest in human physiology was strengthened," he recalls.

Dennis Medford, Jason's teacher at St. Jude, helped the boy keep up with his classmates back home. Jason's goal was to return to the hospital as a physician.

"The whole time, there was this light at the end of the tunnel that gave me a reason to be laser-focused," he says. During college, Jason was chosen to participate in the St. Jude Pediatric Oncology Education program, where he worked in the Department of Structural Biology.

"That cemented the fact that I really liked research in

addition to clinical aspects," he says.

Following in the footsteps of his St. Jude oncologist, Jeffrey Rubnitz, MD, PhD, Jason earned both MD and PhD degrees. During medical school, Jason had the opportunity to return to St. Jude and work with his mentor.

"It was really special to work on service with this physician who had been my primary doctor when I was there as a patient," Jason says. "It's something that I won't forget."

After completing medical school, Jason entered a pediatric residency program at Vanderbilt University, always keeping his eyes on St. Jude.

His hard work has paid off: Jason has been chosen as a Pediatric Hematology/Oncology fellow at St. Jude. In July of 2014, his journey will come full circle, as he cares for children at the hospital where he received cancer treatment.

Alex Niswonger

or many college students working in research labs, an experiment is an experiment. But for Alex Niswonger, each test she conducts is personal—as the former cancer patient conducts cancer research.

"It's nice to have that personal

connection—from having cancer to learning the science behind it," says Alex, who received treatment for non-Hodgkin lymphoma at St. Jude during her high school years.

Alex has worked in cancer research labs at both Mississippi College and The University of Memphis as part of preparation for medical school. She credits her St. Jude clinical team with inspiring her career path.

"My nurses were amazing, so I originally planned to go into nursing and actually attended nursing school for a couple of semesters," Alex says. "Then I realized I wanted to learn more of the science behind the care, so I switched to pre-med." Her St. Jude oncologist, Scott Howard, MD, supported her evolving career goals. Alex says she hopes future patients will benefit from her experiences as a patient as well as a support person.

"Before my diagnosis, I dated someone who had cancer, and so I had already gone through the process with him," she says. "I think it's a lot easier being the patient than it is watching someone you love go through it.

"As a doctor, I hope I can offer families the comfort of knowing that I have been through it from both sides," she continues. "That's something most doctors can't say. I've experienced it firsthand. I can tell them that, 'Yes, it's hard, but you can get through this,' and offer them that support."

Alex is considering pursuing both MD and PhD degrees so that she can conduct cancer research while providing patient care.



Ashley Rhodes

shley Rhodes doesn't miss a beat when asked why she decided to go into the medical field.

"I had a great relationship with my whole team—particularly my oncologist, Dr. Scott Howard; my radiologist, Dr. Matthew Krasin;

Nurse Practitioner Lauren Duffy; and Nursing Care Attendant Regina Simmons," Ashley says. "But my primary nurse, Beverly Dunlap, is absolutely the reason I went into nursing. She helped me throughout the entire journey."

Diagnosed with Hodgkin lymphoma at age 16, Ashley endured three weeks of radiation therapy, 12 grueling weeks of chemotherapy and the severe weight loss that accompanied relentless nausea.

"My close friends and family walked on eggshells around me during that time," she recalls, "but Beverly treated me like a perfectly normal teenager."

During college, Ashley helped raise money for the hospital through her sorority, Tri Delta. She also returned to St. Jude to complete an externship in the hospital's Intensive Care Unit (ICU), a place she had never visited before.

"I was fortunate," she recalls, "because I never even had to spend one night in the hospital during my treatment." MISSISSIPPI MEDICAL CENTER

Ashley says she gleaned all the wisdom she could from the ICU nurses, many of whom had worked at St. Jude for decades. "They had such a wealth of knowledge to share," she says.

"I really liked the structure and the fast pace and the criticalthinking aspects of the ICU," she adds. "I know there are a lot of the sickest kids in the world in the St. Jude ICU, but the nurses get to see most of those kids get better. It's really cool to see them go from being down at their lowest point to going home or back to the regular floor."

When she graduates from nursing school in May 2014, Ashley knows exactly what she wants to do.

"I'm going straight back to St. Jude," she says.

Jessie Houston

Because both of her parents are physicians, Jessie Houston grew up with a clinician's perspective of the medical field. But when she was 15 years old, Jessie also gained a patient's point of view. That's when she traveled to St. Jude for treatment of Hodgkin lymphoma.

Even though the chemotherapy made her violently ill and the steroids played havoc with her emotions, Jessie recognized St. Jude as a special place.

"Immediately, I noticed that St. Jude didn't necessarily feel like a hospital," she says. "I think that was really eye opening for me, because I was used to hospitals having white walls. Instead, there were fish tanks and color. Families were pulling their younger children around in red wagons. And the medical staff every single interaction I had was incredible. I noticed how hard everybody around me worked to put my needs before their own. I really took it to heart, and it made me want to do the same for other people."



Jessie says her St. Jude oncologist, Scott Howard, MD, encouraged her interests, which ranged from biology to Spanish.

"He knew I was a Spanish major, so he always took time to talk to me a bit in Spanish, and that was fun," she says.

The experience cemented her growing aspirations. While awaiting entry into medical school, Jessie is working at South Baldwin Regional Medical Center in Alabama.

"I believe my experiences at St. Jude have helped me have more empathy for the patients I work with," she says. "I've always felt pretty strongly about service—whether it's community service or just helping other people individually—but my cancer experiences have definitely reinforced that passion." s a little boy, Matt DiVeronica believed he was the child depicted in the St. Jude logo. Today, he chuckles at the memory.

"I always felt special and important when I was at St. Jude," says Matt, who is now in his final year of medical residency

at Oregon Health & Science University in Portland. "Everybody was excited to see me; the atmosphere was so positive. I think that's one of the reasons why I thought the logo was me."

St. Jude has been an integral part of Matt's life for years. At 14 months old, the native Floridian traveled to Memphis for treatment of neuroblastoma, a cancer of the nerve tissues. Throughout his childhood and young adulthood, he returned to Memphis for regular checkups, spending most of those years under the care of Melissa Hudson, MD, director of the hospital's Cancer Survivorship Division.

A propensity for science—paired with frequent interactions with doctors and other medical professionals—helped Matt realize that "being a doctor just felt right." As an adult, Matt enrolled in the St. Jude LIFE study, an initiative that brings childhood cancer survivors back to campus to study the long-term effects of their disease and its treatment. St. Jude is the world's first institution to embark on such a project, which provides a uniform clinical assessment for a large group of childhood cancer survivors.

Although he plans to practice internal medicine, the longterm survivor says he finds the field of cancer survivorship intriguing.

"I think the care of adult survivors of childhood cancer is going to be an ever-increasing field," he says. "They're a special population who need specialized care. That's one thing that I could potentially go into."

Kendra von der Embse, DO

hen Kendra von der Embse underwent treatment for an aggressive brain tumor in 2004, she never dreamed that one day she would work side by side with the oncologist who would save her life.

That partnership was made possible by a phone call Kendra's mom received from a radiologist in their hometown.

After removing a mass from the girl's brain, clinicians in Ohio had decided to wait a month before beginning treatment. That's when a concerned radiologist called Kendra's family. "The doctors here have never treated medulloblastoma before, and they're excited to be the ones to treat the first case," the physician said. "As a doctor and a mother, I'm advising you to take your daughter to St. Jude."

By the time Kendra arrived in Memphis, the tumor had wrapped around her brain and spine like cellophane. Although the subsequent treatment was grueling, it piqued Kendra's interest in the medical field. Her St. Jude oncologist, Amar Gajjar, MD, encouraged that interest, offering academic advice as well as medical care.

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During college, Kendra worked with David Solecki, PhD, of Developmental Neurobiology as part of the St. Jude Pediatric Oncology Education program.

"We looked at some of the genes and mutations that could possibly be precursors to medulloblastoma, which was kind of ironic," observes Kendra, who later returned to the hospital to work with Gajjar, her physician and mentor.

Now a resident at Firelands Regional Medical Center in Ohio, Kendra plans to practice family medicine and possibly complete a fellowship in hospice care.

"What I learned as a patient gives me quite a different perspective than any of my other classmates in medical school," she says. "I think I have more empathy for patients because I've been there myself; I know what they're going through." ■





A Gummy in My Tummy

By Summer Freeman

Chemo can make foods taste yucky. St. Jude staff have created special gummies that are delicious, fun and (don't tell the kids) nutritious.

B lending one part science, one part culinary skill and a dash of creativity, staff members at St. Jude Children's Research Hospital have solved a common problem for childhood cancer patients.

Chemotherapy, a mainstay of cancer treatment, wreaks havoc on appetite and taste buds. Nausea and painful mouth sores are common—and chemo drugs can cause a metallic aftertaste or may make sweet foods intolerable. With all of these issues surrounding food, patients are less likely to eat. That is unfortunate, because research shows that well-nourished children have a higher ability to withstand infection and tolerate therapy.

This was the conundrum faced by St. Jude dietitians Karen Smith and Kristy Gibbons: How do you entice justifiably picky eaters to eat and get the most nutritional wallop from a meal?

Three years ago, the Clinical Nutrition colleagues began to brainstorm to create the perfect treat—small in portion, fun in shape and color, tart in taste, and most importantly, loaded with nutritional value.

Their first idea was to use gummy worms as a base for the treat, but the gelatin in its original form is high in carbohydrates and resulted in a solid mass that was unappealing.

Smith and Hope Shackelford, one of the department's student employees, spent an entire semester creating a tart, gelling product infused with nutrients. Other students in Shackelford's Experimental Foods class at the University of Memphis helped with taste-testing. "It was a labor-intensive process," Smith says. "If we changed one ingredient just a tiny bit, the texture would change. It would fall apart or it would have the consistency of a rock. For four months, we tasted and tweaked over and over again."

St. Jude focus groups composed of patients, families and staff volunteered to taste-test the product. Based on that feedback, Smith and Shackleford finalized the gummy recipe and gave the product a name, Sour Gems.

St. Jude chefs streamlined a system for creating the treats, which were shaped like dragonflies, puppy paws, hearts, guitars and ladybugs. Patients could order their favorite shapes and flavors and have them sent to their bedside in less than an hour.

Sour Gems are packed with calories, protein and fat; a serving of five or six pieces easily provides 250 calories or more, the equivalent of one can of a commercially made liquid supplement.

The treats have been so successful that St. Jude staff members have begun working on a way to increase Sour Gems' shelf life so that patients can take them home between treatments. More than 100 St. Jude patients have given the new treats their stamp of approval.

St. Jude hopes to have the recipe patented and is now partnering with a company to make Sour Gems widely available.

"We are hoping that this new product will not just benefit our kids, but will eventually be used by people outside of St. Jude: children with cystic fibrosis; geriatric patients; people with dementia," Smith says. "Anyone who has problems getting enough nutrition would benefit." ■

Grateful Hearts

By Clay Meredith

"Our family owes everything to St. Jude. There is no doubt that if it weren't for St. Jude, we would have buried our kids by now. No doubt."



n 1996, my wife, Suzan, and I received a phone call that took our breath away.

"We've reviewed your children's medical records," the doctor told us, "and there's really nothing more that we can do. Just enjoy the time you have left with your kids."

How could this be happening? We were an average family, living paycheck to paycheck in middle-class America. But our infant son, Mitchell, had life-threatening breathing problems; our 6-year-old daughter, Alee, had partial paralysis as a result of a stroke.

There was no doubt in my mind that we were going to bury these two kids, and in short order. I don't think "panic" can even hold a candle to where we were in our thought process. We were living a nightmare.

I sat down at the desk of a family member who is a funeral director.

"I don't have the money right now," I told him, "But if you will allow me to bury these kids with dignity, I'll pay you every nickel I owe you."

A rough beginning

Shortly after my wife had given birth to our second child, things had begun to go terribly wrong. Almost overnight, we went from being a normal family to watching both of our children almost die. We had been in and out of hospitals for many months, and the children had been given a long list of diagnoses—from asthma to lactose intolerance to a rare genetic disorder. But no one, not even the best specialists, could tell us what was making our kids so sick.

We had two sick babies and really didn't have an answer about what was going on.

When Mitchell was 6 months old, we finally got

that answer: Our children had been born with the human immunodeficiency virus, or HIV. We were devastated. In 1996, my wife and I knew nothing about HIV—only that it was a death sentence.

Like most people who contract HIV, my wife had carried the virus for many years without knowing it. Ten years before, her fiancé had died. We now realized that he most likely had AIDS.

Alee and Mitchell were put on a regimen of medicines. Two weeks later, our daughter had a stroke. Mitchell had the worst case of HIV that our local medical community had ever encountered.

The doctors offered us no hope.

"You're telling us to watch these kids die?" I asked them. I was determined that we would not let that happen without first exploring every avenue.

So that started my quest. I got on the phone and started calling HIV clinics from Washington, D.C., to San Francisco. I don't know the exact number of phone calls I made, but it was in the hundreds. Time after time, people suggested that

We put our two little broken babies in the back seat of our ratty old Escort, and with a prayer and a few dollars in our pocket, we headed to Memphis. That was the beginning of new life, new hope.

we take our children to an institution in Tennessee, called St. Jude Children's Research Hospital.

"That's where I would go if I were in your shoes," said a doctor from Houston, Texas. "That's where I'd take my kids."

Memphis miracle

As soon as we got the referral to St. Jude, we put our two little broken babies in the back seat of our ratty old Escort, and with a prayer and a few dollars in our pocket, we headed to Memphis.

That was the beginning of new life, new hope.

From the moment we pulled into the gate, the staff at St. Jude started taking care of us. They answered our

questions. They knew instantly what the course of action should be for our children. Dr. Patricia Flynn and her staff got the kids started on their treatments, and then we loaded up our babies and headed back home.

I didn't know it then, but the miracle was in place and was starting to happen. All of the treatment we had received before coming to St. Jude had been a failure, so we didn't really know what to expect. But within a week or two, our kids' eyes were bright, their appetite had picked up, and things had begun to change.

Those changes began to instill hope, because we started seeing our children returning to us. A month later, a St. Jude checkup revealed that the treatment was working very well. At the following checkup, the news was even better.

As time went by, we felt blessed and wanted to give back by sponsoring a child who was HIV positive. One day, Suzan found the website of an orphanage for HIV-positive children. On that site was a video of a 3-year-old Ethiopian boy singing "If You're Happy and You Know It." Watching that video, we both began bawling like babies. Instead of sponsoring the little boy, we initiated the adoption process.

Thirteen months later, we brought Yonas home.

Here's to hope

Through the years, the St. Jude medical team has kept our family on the right track medically. And our social worker, Chris Sinnock, has helped guide Alee and Mitchell through issues of disclosure they faced as they entered their teen years.

Thanks to St. Jude, all three of our children are thriving. Alee recently graduated from college and will soon be teaching English and working on her master's degree. Mitchell is a high school senior who plans to become a pharmacist. Yonas is now in the sixth grade. Who knows what he will do?

Our family owes everything to St. Jude. There is no doubt that if it weren't for St. Jude, we would have buried our kids by now. No doubt.

If I could meet the people who donate to the hospital, I would say, "Thank you." And if those donors would form a line, I would hug each and every one of them. People who support St. Jude give hope to families who have no hope; they give a chance to children who have no chance. And due to that overwhelming generosity, parents like us get our kids back.

Treatment with the drug cisplatin helped save DJ Todd's life, but damaged his hearing. A recent discovery may one day help children avoid this side effect.

The Sound of Science By Carole Weaver, PhD

St. Jude researchers find clues to preventing hearing loss and other side effects of chemotherapy.

A free concert is underway in the waiting area of the Solid Tumor Clinic at St. Jude Children's Research Hospital. The music being played with great force on a tinny-sounding toy piano consists of only four notes. But to anyone who knows the performer, 13-month-old DJ Todd, it sounds beautiful.

That's because DJ is lucky to be able to hear the high notes. "When you see him playing, it looks like he hears and responds to everything," says DJ's father, Darrick Todd. "But the computer says he has hearing loss."

Diagnosed with aggressive neuroblastoma at 2 months old, DJ has spent most of his young life as a St. Jude patient, undergoing intensive treatments to destroy this cancer of the nerve tissues. Thanks to the treatments, which included chemotherapy with a drug called cisplatin, DJ's cancer has now virtually disappeared. However, although cisplatin is a powerful weapon against neuroblastoma and other cancers, it can also penetrate and kill healthy cells—in the inner ear, for example, as well as in nerves and kidneys.

Like DJ, most children treated with cisplatin experience some degree of hearing loss, particularly in the upper ranges. In some cases, the loss is irreversible. Nerve and kidney damage are other major side effects.

Still, cisplatin is likely here to stay—at least for now, says Alex Sparreboom, PhD, of St. Jude Pharmaceutical Sciences.

"Despite efforts throughout the world to come up with newer drugs, it's unlikely that we'll ever see the time when we won't use cisplatin anymore, because it is part of a curative treatment regimen," he says.

"It may seem like achieving a cure is worth the trade-

off of having these side effects, but the impact on quality of life is astonishing," he adds. "So it's important to try to do something about the problems this drug causes."

Discovery of a major key

The big challenge is finding ways to block the side effects of cisplatin without weakening its power to fight cancer. Attempts by researchers during the last decade have yielded disappointing results, both for cisplatin and related drugs in the platinum family.

But a hopeful note was struck recently, thanks to Sparreboom and other scientists. Their research has identified a key to the side effects caused by platinum drugs.

This key is a protein called OCT2.

OCT2, the research shows, transports cisplatin into vulnerable healthy cells. And cisplatin is not OCT2's only dangerous passenger. Recently, Sparreboom and his St. Jude colleagues discovered that oxaliplatin, a different platinum drug, relies on OCT2 to gain entry into nerve cells.

"Oxaliplatin, which is used to treat colorectal cancer, causes pretty harsh nervous system toxicity in patients," says postdoctoral fellow Jason Sprowl, PhD, who led the project with Sparreboom. "We were wondering why, and if there is a way to decrease the chances of it happening."

Building on their finding that OCT2 was involved, the scientists decided to ask a simple question in the lab: Would drugs that target OCT2 ease side effects by keeping oxaliplatin out of cells?

Sprowl and Sparreboom tested an FDA-approved drug,

Jason Sprowl, PhD (pictured), and his Pharmaceutical Sciences colleague Alex Sparreboom, PhD, led a project that may one day help protect children against hearing loss.

cimetidine, and the results were definitive: a single dose protected nerves from damage by oxaliplatin.

Variations on a theme

So, will a similar strategy one day protect children from cisplatin-related side effects?

The answer is likely yes, Sparreboom says, based on their findings and a growing body of research. "The interesting thing with cisplatin is that all three side effectsthe hearing loss, the kidney damage and the nerve damage -are connected to this same transporter, OCT2," he says.

Therefore, blocking OCT2 may prove to be the winning strategy to protect against many side effects at once.

"It looks interesting, very promising," Sparreboom says. His team is now conducting initial studies in patients, which are showing that cimetidine does not hamper the cancer-fighting ability of cisplatin. The researchers are also exploring the potential value of other drugs that block OCT2.

"The best outcome imaginable would be that we could get rid of specific cisplatin-related toxicities in the future," Sparreboom says.

This would be wonderful news for future patients like DJ, who may one day be spared the risk of lifelong challenges that may occur because of platinum drug treatments.

Coda: Next steps for DJ

DJ will likely be fitted with hearing aids soon, to help him catch the high-pitched sounds that are necessary for normal speech development.

"They're saying that he needs it for speech, so he won't miss any of the developmental stages he's coming up to," Darrick says. "We're just trying to cope with it right now, trying to deal with the fact that he's going to have to have two hearing aids."

"He's been through so much," adds Sandy Crenshaw, DJ's mother. But through it all, DJ has remained happy and active. "He has been a strong little baby," she says, smiling. "It shocks a lot of people."

DJ may be able to hear his parents' discussion, but he isn't listening. He's too busy being a typical 1-yearold. As the volume of the music from his piano peaks, he accompanies it with a crow of delight. And as abruptly as the concert started, it's over.

Time for the next big adventure. ■



High-risk Leukemia: Blocking the Shuffle By Mike O'Kelly

St. Jude scientists develop a new treatment strategy that offers hope to children and adults with a form of high-risk leukemia.

Someday, children like Reagan Kuehn may not have to undergo transplants for Ph-positive ALL, thanks to research conducted at St. Jude.

Like a deck of cards shuffled by a clumsy dealer, Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph-positive ALL) occurs when portions of two chromosomes swap places and begin a process that leads to the unchecked cell growth characteristic of cancer. This subtype of ALL is difficult to treat and causes more complications for patients than traditional ALL.

As leukemia cells form in the bone marrow and travel through the bloodstream to crowd out healthy cells, the body's chances of infection increase, which can cause other problems such as unexplained fevers. This was the case for Reagan Kuehn in October 2012. When the normally outgoing and lively toddler became sluggish and developed fevers, a visit to the pediatrician indicated that her liver and spleen were enlarged—a symptom of leukemia. Doctors referred her to St. Jude Children's Research Hospital, where Reagan began a two-year treatment plan for Ph-positive ALL. But clinicians quickly realized that Reagan's leukemic cells were resistant to chemotherapy.

"After the first round of chemotherapy, Reagan received a bone marrow biopsy, and it revealed that the drugs were not effective at all, so her doctors decided that a bone marrow transplant was the best option," says her mom, Jessica Kuehn.

Reagan had a successful transplant and is now back to being the rambunctious girl she was before her disease was diagnosed.

Although transplants are often an effective treatment for Ph-positive ALL, a new therapy developed in the lab of Joseph Opferman, PhD, of St. Jude Biochemistry, might

NN-MARGARET HEDGE

be even more effective in killing leukemia cells, possibly eliminating the need for transplants.

In the lab

The swapping or translocation of pieces of the *ABL1* and *BCR* genes—found respectively on the ninth and 22nd chromosomes—leads to production of a protein called BCR-ABL, which plays a key role in the development of Ph-positive ALL.

This environment paves the way for proteins to wreak havoc by blocking the process of programmed cell death known as apoptosis, which is how the body eliminates damaged, dangerous or unneeded cells. St. Jude researchers identified one of those proteins, MCL1, and discovered that it is essential for preventing leukemia apoptosis.

Using these findings, the scientists began combining drug therapies to find ways to reduce MCL1 levels and offer hope to children and adults with the disease.

The investigators combined drugs that reduce MCL1's levels in leukemia cells with a drug that targets a different protein that inhibits cell death. The result was an increase in apoptosis in leukemia cells.

"These findings suggest that disrupting the ability of leukemia cells to produce MCL1 renders those cells vulnerable to other drugs," Opferman says. "That's exciting because we already have drugs like imatinib and other inhibitors that reduce MCL1 production in tumor cells, leaving those cells vulnerable to being pushed into death via apoptosis by other drugs already in development."

Beyond leukemia

The research could also enhance the effectiveness of drugs used to treat other cancers in which MCL1 levels are elevated.

Opferman's study found that MCL1 was required for leukemia cells to survive throughout the Ph-positive ALL disease process, beginning when white blood cells known as B lymphocytes were transformed from normal to tumor cells. Scientists also showed that deleting MCL1 from leukemia cells blocks cancer's progression.

Completely deleting MCL1 might have a downside, though. Opferman's laboratory made earlier discoveries that revealed MCL1 also protects heart health by preventing loss of heart muscle cells through apoptosis.

"Together these findings suggest that MCL1 is a relevant



Brian Koss (foreground) and Joseph Opferman, PhD, of St. Jude Biochemistry, discuss research findings that hold promise for patients with a rare form of high-risk leukemia.

target for cancer treatment," said Brian Koss, a staff scientist in Opferman's laboratory, "but efforts should focus on diminishing the expression of MCL1, rather than completely eliminating its function."

What is Ph-positive ALL?

Philadelphia chromosome-positive acute lymphoblastic leukemia (also known as Ph-positive ALL) is a high-risk cancer that accounts for about 40 percent of ALL in adults and about 5 percent in children. Ph-positive ALL is a subtype of acute lymphoblastic leukemia. It received its name because it was discovered in 1960 by a team of scientists working in Philadelphia. The Philadelphia chromosome occurs when portions of chromosomes 9 and 22 translocate or change places.

The chromosomal rearrangement brings together pieces of the *BCR* and *ABL1* genes. The *ABL1* gene from chromosome 9 fuses to a portion of the *BCR* gene on chromosome 22 to create an elongated chromosome 9 and a smaller chromosome 22—the Philadelphia chromosome. This fusion leads to production of the BCR-ABL protein, which fuels the unchecked cell growth that is a hallmark of cancer.

St. Jude: Part of By Leigh Ann Roman My DNA

"Yes, we play country music. But we are a St. Jude radio station."

ooking back on 28 years as a successful on-air personality, Don Chase of WKML 95.7 FM in Fayetteville, North Carolina, can easily identify the high point of his career: his station's involvement with St. Jude Children's Research Hospital.

"When you can play a small part in saving the life of a child, it's a little piece of heaven," says Chase, who has been a part of *Country Cares for St. Jude Kids*[®] for most of the radiothon program's 25 years.

Chase recalls his first visit to St. Jude 24 years ago, when he met the parent of a St. Jude patient.

"I remember the profound impact it had on me to sit there and talk to this mom who was telling us her story," he says.

Chase's heart sank as he heard how her son, an excellent student and topnotch athlete, had become ill, and the doctors had diagnosed cancer. But then the woman's son—happy and healthy emerged from a back room.

"They were going home, and it was for free. That's all it took," Chase says. "How do you not jump behind the lifesaving miracle called St. Jude? It is the most incredible thing I ever have been or will be a part of."

Although he has visited St. Jude many times, Chase says, "That one-day trip did it for me. St. Jude is part of my DNA now."

Country Cares for St. Jude Kids was launched in 1989 after Randy Owen, lead singer of the legendary group ALABAMA, answered St. Jude founder Danny Thomas' request to support the hospital. Since then, more than 200 radio stations nationwide have helped raise more than \$480 million for the kids of St. Jude. Many country music artists, including Darius Rucker, Keith Urban, Faith Hill, Brad Paisley, Lady Antebellum, Chris Young and John Rich, have supported Country Cares through hospital visits, recorded appeals and event appearances.

Chase has been involved in Country

Cares since 1990, and his commitment to St. Jude carries special significance because cancer has touched several people in his life, including his father, grandmother and wife, as well as his mother, who is currently receiving cancer treatment.

He applauds his station's dedication to the St. Jude mission. "God has put it on the conscience of this radio station. It's what we do. We are fortunate to be able to do a number of events for St. Jude throughout the year," Chase says.

Mac Edwards, market manager for WKML, says, "The cause and the purpose of St. Jude speak to the heart of not only us as broadcast professionals but as family members and members of the community."

The station's entrance boasts a St. Jude "wall of fame" decorated with patient artwork and plaques recognizing WKML's years of dedication to the radiothon.

"Yes, we play country music," Chase says. "But we are a St. Jude radio station." ■

> "How do you not jump behind the lifesaving miracle called St. Jude?" asks Don Chase.

Caring for the Children

By Rachel Schwartzberg

Through their support of St. Jude, the Plooy family memorializes a gentle, caring man.

oAnne Plooy's late husband, Henry W. Plooy, was deeply committed to helping children who were battling serious illnesses, and she continues his legacy as a dedicated supporter of St. Jude Children's Research Hospital.

While undergoing treatment for mesothelioma in a Boston hospital, Henry saw children coming for their own cancer treatments. According to his wife, he was touched by their innocence and hated to see them suffering.

"My husband wanted to help the children," says JoAnne, who lives in Wisconsin. "He thought of St. Jude a lot when he was in the hospital, and I have carried on his wishes."

Sadly, Henry lost his battle with cancer in 2009 at age 70. As a tribute, JoAnne made a generous gift to dedicate the Activities of Daily Living Kitchen in the Department of Rehabilitation Services to his memory. This special kitchen is used by therapists to help children learn or relearn how to perform everyday activities, when illness or its treatment has affected normal functioning.

The tribute to Henry seemed especially fitting, as the Plooys' kitchen had always been the heart of their home and a gathering place for their six children and now 15 grandchildren.

JoAnne considers herself fortunate that many of her grandchildren live nearby. She enjoys helping with the children and especially going camping with them. She is proud that her husband's passion for caring for children has continued within



JoAnne Plooy (at left) dedicated the St. Jude Activities of Daily Living Kitchen to the memory of her husband, Henry. (Above) Occupational therapists Lexi Florian and Jessica Sugg help Tyler West cook goodies in that kitchen as part of his therapy.

their family: Two of the couple's teenage grandchildren have chosen each year to donate a portion of the proceeds from the 4-H sale of their animals to St. Jude.

Originally from California, the Plooys moved to Wisconsin 29 years ago, where they purchased a dairy farm. "My husband milked cows until he was 67 years old," JoAnne says proudly. Two of the couple's sons worked on the farm alongside their father.

The couple sold their large dairy farm nine years ago, but JoAnne says her husband was not quite ready to retire.

"After we sold the farm, Henry worked part-time delivering cattle, and I used to enjoy traveling with him, all over the state," she says. She returns to California to visit family every year.

Although she has not yet visited St. Jude, she shares her husband's commitment to helping the children.

"St. Jude is close to my heart," Joanne says. "I think it's a wonderful cause."

JoAnne finds it especially meaningful that St. Jude covers all the costs associated with a child's treatment—including travel, housing and meals. She recalls how much she had to spend on a hotel room and meals while she was in Boston with her husband during his treatment. "You don't think about how quickly the costs add up," JoAnne says.

"It's wonderful that St. Jude helps so many children," she adds. "And they are helping the families, too." ■

Research Highlights



Dr. Evans announces retirement plans

St. Jude patients pull out notepads and don their journalist hats to interview Dr. William E. Evans, St. Jude director and CEO, as he announces his plan to retire as the hospital's CEO in July 2014. Evans, who began his career at St. Jude in 1972 and became CEO in 2004, will continue to lead his research laboratory at St. Jude after retiring from the CEO position.

Can childhood cancer survivors lower heart risks?

Treatments that are excellent at fighting cancer can sometimes be hard on the heart. As a result, childhood cancer survivors are much more likely than others to experience serious cardiac problems as adults.

The good news is that survivors may be able to lower their risk of heart problems by taking specific action. New research led by St. Jude shows that cancer survivors may benefit from staying in a healthy range for blood pressure, weight, blood sugars and blood lipids like cholesterol.

The findings are based on data from more than 10,000 childhood cancer survivors and were published in the *Journal of Clinical Oncology*. "For doctors who are caring for survivors, the key message from this study is that aggressive management of hypertension is especially important for this population," said Greg Armstrong, MD, of St. Jude Epidemiology and Cancer Control.



Downing elected to Institute of Medicine

James Downing, MD, scientific director, deputy director and executive vice president, has been elected to the Institute of Medicine (IOM), a prestigious branch of the National Academy of Sciences.

"Dr. Downing's election to the Institute of Medicine is a great testament to his many scientific accomplishments and a great honor for St. Jude," said Dr. William E. Evans, St. Jude director and CEO.

Downing is internationally recognized for his seminal contributions to understanding the molecular pathology of acute leukemia and the application of this information to increase the number of children cured. In 2010, he was instrumental in launching the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project, the world's largest project devoted to understanding the genetic origins of childhood cancers.

St. Jude has one of the highest numbers of IOM members among U.S. children's hospitals. Other IOM members from St. Jude are Nobel Laureate Peter Doherty, PhD; Director and CEO Dr. William E. Evans; Arthur Nienhuis, MD, former St. Jude CEO; Charles Sherr, MD, PhD, Howard Hughes Medical Institute Investigator and Tumor Cell Biology chair; and Mary Relling, PharmD, Pharmaceutical Sciences chair.

Fight cancer, not yourself

The body's immune system does much more than fight off colds. It can also fight cancer. Immunotherapies seek to harness and enhance this power of the immune system to kill cancer cells. But care must be taken in developing the therapies, because misguided immune activity can attack healthy tissue.

St. Jude scientists have discovered a way to direct the immune system to shrink or eliminate tumors without causing autoimmune problems later. The work, published in the journal *Nature*, focused on white blood cells called regulatory T cells. These cells guard against autoimmune and inflammatory disease, but can also interfere with the immune system's cancer-fighting ability.

Dario Vignali, PhD, St. Jude Immunology vice chair, and his colleagues found a way to uncouple these two functions of regulatory T cells. "We may now have an opportunity to selectively target the activity of regulatory T cells for treatment of cancer without inducing autoimmune or inflammatory complications," he said.

Endless immune cells, created in a petri dish

Your immune system is exquisitely complex, made of many different types of cells with specific jobs. A major scientific challenge has been to figure out how each type of immune cell develops and carries out its job.

This challenge may have just gotten easier, thanks to a breakthrough from St. Jude scientists, reported in the journal *Nature Methods*. By adding two factors to bone marrow preparations, researchers found they could generate an unlimited supply of immune cells in the laboratory. This simple method, which can be used to create a variety of key immune cell types, opens a new avenue to pursue research on the immune system and immune-based therapies.

"This is a terrific system to answer many basic questions related to immune cell development and differentiation, or immune cell function," said Hans Haecker, MD, PhD, of St. Jude Infectious Diseases. "Although this is a preclinical system, we are already dreaming of the therapeutic applications."

Highlights

Putting the "ME" in social media

Morinsola Keshinro of St. Jude Child Life (right) works with Paishence Watkins during "All of Me Week" activities. This year's theme was social media, with each activity incorporating the world of technology. The week's events concluded in a show-and-tell reception that featured patients' finished products on display along with a video compilation.



Survivors may face early aging

Feeling exhausted? Having trouble getting off the couch? Many people might voice these complaints after a tough day at work. But for childhood cancer survivors, these symptoms may be signs of something more serious: premature aging.

A surprising number of young adult survivors showed signs of early aging, or frailty, in a recent study conducted at St. Jude. The study tested 1,922 survivors for strength, muscle mass, fatigue and other measures. In a comparison group of 341 adults who did not have cancer as children, no frailty was reported. Survivors should use these findings as motivation to take action, emphasized Kirsten Ness, PhD, of St. Jude Epidemiology and Cancer Control. "This is an opportunity for them to take control and start working with their health care providers on ways to improve their fitness," she said.

The research, published in the *Journal of Clinical Oncology*, underscores the importance of work now underway at St. Jude on the best methods to combat frailty in childhood cancer survivors.

Sickle cell drug cuts health costs for patients

A drug that is effective in treating sickle cell anemia led to reduced hospitalizations for affected infants and toddlers and cut their annual estimated medical costs by 21 percent, according to an analysis led by St. Jude. The report appeared in the journal *Pediatrics*.

The study is the largest ever to focus on the economic impact of the drug hydroxyurea in children with the inherited blood disorder. The result supports expanded use of the drug to extend the length and quality of life for sickle cell anemia patients of all ages, said Winfred Wang, MD, of St. Jude Hematology. Wang led the multicenter clinical trial known as BABY HUG.

"We estimate that hydroxyurea cut overall annual medical expenses by about \$3,000 for each patient by helping them avoid disease complications that require inpatient hospital care," Wang said. "We expect those savings will grow along with patients, whose symptoms often increase in severity and frequency as they age."



Counted blessings

St. Jude chaplains (from left) Kimberly Russell, Mark Brown, Brent Powell and Walter Spears bless the hands of employees and families during the annual Blessing of the Hands. The event is held each year in recognition of Spiritual Care Week.

Native American ancestry influences leukemia risk

How does ethnic background affect a child's risk of developing and surviving cancer?

Jun Yang, PhD, of St. Jude Pharmaceutical Sciences and his colleagues have linked an inherited gene variation to a nearly four-fold increased risk of developing a deadly subtype of pediatric acute lymphoblastic leukemia (ALL).

The subtype, Philadelphia chromosome-like ALL, accounts for as much as 15 percent of childhood ALL and is associated with a high risk of relapse and a poor outcome. The high-risk

Taking aim at Lou Gehrig disease

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig disease, is diagnosed in about 5,600 Americans each year. With no effective treatment, ALS causes progressive deterioration of nerve cells in the brain and spine and usually leads to death within five years of diagnosis.

St. Jude scientists and their collaborators have discovered an important clue to ALS that may provide new hope for developing treatments. Previous work from the St. Jude team found that mutations in a gene called *VCP* lead to ALS, but it was not clear why. The new work revealed that *VCP* mutations cause a toxic buildup of proteins and other materials inside nerve cells, potentially pointing to how these mutations trigger disease.

"The results go a long way toward explaining the process that links a variety of neurodegenerative diseases, including ALS, frontotemporal dementia and related diseases," said J. Paul Taylor, MD, PhD, of St. Jude Developmental Neurobiology.

The findings were published in the journal Cell.

variant was found in the GATA3 gene.

Hispanic Americans and others whose genetic profile suggested Native American ancestry were more likely to have the high-risk variant than those from other ethnic backgrounds. The study's findings highlight how inherited and tumor genetic variants may work together to influence a person's risk of developing and surviving cancer.

The findings were published in Nature Genetics.

A new look at an old drug: Improving AML survival

The quest to push cure rates for children with acute myeloid leukemia (AML) recently got a boost from a study led by St. Jude. The study, published in the journal *Cancer*, took a new look at an old drug.

The drug, trade named Mylotarg, was withdrawn from the market in 2010 due to concerns about its safety and effectiveness. But scientists found that the drug likely helped children with highrisk AML who received the medication while it was on the market. Mylotarg targets AML cells that carry a certain protein on their surface. St. Jude investigators are working to develop new treatments that target the same protein. The research may provide desperately needed new agents to help AML patients whose cancer returns or persists. "The results of this and earlier studies make a strong case that some patients benefit from this targeted therapy," said Jeffrey Rubnitz, MD, PhD, of St. Jude Oncology.

WHERE IS HE NOW?

By Elizabeth Jane Walker

In 1998, the inaugural issue of *Promise* magazine featured 7-year-old Carlos Rodriguez. What is he doing today?

arlos Rodriguez has one minor regret in life: He has never learned to use scissors.

"That was something I missed out on when I was little because I was busy fighting for my life," says Carlos, with a smile.

He and his family were living in El Salvador in 1996 when doctors diagnosed a high-risk form of acute lymphoblastic leukemia (ALL) and gave the 4-year-old boy a 20 percent chance of survival.

Carlos obtained a referral to St. Jude Children's Research Hospital, where the odds were higher: 60 to 65 percent at that time.

While learning English, entering kindergarten and undergoing treatment, Carlos missed a few milestones—such as learning to wield scissors.

"Honestly, I don't think I would have changed anything," he says. "Going through treatment was one of the hardest things in my life, but it taught me to be a better person. It taught me how to grow and to value every single thing that I have."



Back in 1998, confetti drifted onto Carlos' head, shoulders and bed as he celebrated his last chemotherapy treatment, surrounded by his family and ebullient medical staff. "The thing I like most about that picture is that my grandmother is in the corner with her hands together praying, giving thanks that we were able to make it through," Carlos says.



Today, Carlos and his family (including his grandmother, Rosa Muller; his mom, Maria Rodriguez; and his 7-year-old sister, Gaby Rodriguez) appreciate the opportunities St. Jude has provided. "It's all due to St. Jude that I am here," Carlos says.

Carlos participated in the hospital's Total XIII clinical trial for ALL, which helped lay the foundation for today's treatment regimen, with its 94 percent survival rate.

As an adult, he has participated in St. Jude LIFE, an unprecedented study aimed at understanding the long-term impact of childhood cancer and its treatment. Childhood cancer survivors worldwide are benefiting from results of the ongoing project.

Now 22 years old, Carlos is pursuing a college degree in management and working at ALSAC, the hospital's fundraising organization.

"St. Jude has been there for me every single step of the way," he says. "I plan to do whatever I can to help the hospital—it's my way of giving back." ■

"I could not think of anything more loving and rewarding than to know that my legacy can help to cure a child."

> - Ellie Noury Wagenti

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Kayla, medulloblastoma, at age 8





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Celebrating creativity

Imagination and creativity melded with self-expression as Nate Owens and other teen patients presented their artwork during the 11th annual Teen Art Show. Organized by St. Jude Child Life, the show included patients' representations of their journeys through painting, sketches, photos, music, poems and even a baked cake. Families and staff gathered to hear patients share the personal meaning behind their works. More than 50 pieces were unveiled at this year's show. The artwork will be displayed throughout the year in the hospital's Teen Art Gallery.



Finding cures. Saving children.