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In an effort to give back to the hospital that saved his life, a St. Jude patient raises an army of fundraisers working toward a single goal.

By Tom Charlier

Adam Cruthirds stepped onto a podium one sunny June day four years ago and made a pledge that might have sounded audacious, even outlandish, to anyone who hadn’t met the young cancer patient or gauged his determination. “Adam’s Army is about to go nationwide, or maybe international,” the then-17-year-old told a crowd assembled in front of the headquarters of ALSAC, the fundraising and awareness organization for St. Jude Children’s Research Hospital.

Adam’s Army, the alliterative moniker he gave to the group of family and friends raising money for St. Jude, indeed launched an offensive. Teams participating in the St. Jude Walk/Run and St. Jude Memphis Marathon races that first year collected some $140,000, far surpassing the initial goal of $100,000 Adam had announced.

Adam and his supporters — active across the U.S. and in other continents — continued their fundraising. Four years later, they are poised to attain an even more amazing goal: $1 million. With the achievement, St. Jude will name a place on campus in honor of Adam’s Army.

Now 21 and heading into his senior year of college, Adam plans to complete his first full marathon during the St. Jude Memphis Marathon Weekend this December, having already participated in a slate of races and events earlier in the year.

As big a challenge as a marathon might seem, Adam has overcome plenty of other difficult trials since he was diagnosed with acute lymphoblastic leukemia in 2014. Allergic to one of the main chemotherapy agents, he endured an especially difficult treatment regimen. The setbacks along the way included septic shock, temporary delirium and surgery to rebuild his hips after they were ravaged by treatment-induced avascular necrosis.

His treatment, which ended in 2017, cost more than $3 million, he says. But like all other St. Jude families, the Cruthirds never received a bill from the hospital.

“I know what I want to do in my life. I want to give back,” he says. Adam’s mom, Connie Cruthirds, remembers watching him complete his first half marathon in 2015, linked arm-in-arm with supporters, despite failing hips and the effects of the chemotherapy he had received only hours earlier.

“It was that same determination,” she says, “that got him through all of the treatment.”

To help Adam meet his fundraising goal, visit fundraising.stjude.org and search for Adam Cruthirds.
St. Jude sets the standard for quality, patient care and clinical improvement science for children with life-threatening diseases.

By Mike O’Kelly

When Elizabeth Day arrived at St. Jude Children’s Research Hospital three years ago with her son, Stone, she never dreamed she would help shape the hospital’s patient safety program.

As a parent adviser for the hospital’s Quality/Patient Safety efforts, she helped launch a program that allows parents and staff to monitor for signs of sepsis. This dangerous condition occurs when the body abnormally responds to an infection. Day also took part in a video used to educate staff and caregivers about sepsis.

“When I joined the St. Jude Patient Family Advisory Council, I was amazed to see the level of detail we were involved in – from clinical processes to safety procedures,” Day says. “It means everything to see the extra steps St. Jude takes to protect our children.”

St. Jude patients often have weak immune systems due to their diseases and treatments. That’s why patient safety policies and infection prevention are always top of mind.

Parent advisers offer crucial feedback to enhance patient safety. The hospital created a program called “Safe and Sound” to shine a light on these efforts.

Leading the way

“We provide outstanding care,” says Pat Flynn, MD, St. Jude deputy clinical director, “but there are always ways to improve. We want to partner with everyone who can help every child be safe and sound at St. Jude. We’re strengthening our quality and patient safety efforts through an organized approach.”

The plan seeks to get patients and families more involved in safety efforts. Not only does this improve patient safety overall, but it also helps St. Jude guide other hospitals in creating positive change.

Safety-focused research led by St. Jude is already making an impact.

James Hoffman, PharmD, St. Jude chief patient safety officer, recently published two studies in the journal Pediatrics. He figured out a way to reduce alert fatigue in medical records systems.

He also identified the patient safety research topics most important to hospital leaders and parents.
Alert accuracy
When a user of the electronic health records system inputs medicines that may not work well together, an alert appears. If incorrect alerts appear often, users tend to override them. The stream of warnings can cause staff to pay less attention to the alerts. This is called alert fatigue.
Hoffman and his colleagues looked at alerts and found ways to reduce the overrides by 40%. The research provides a guide other hospitals can use. Hoffman stresses the importance of vigilance.
“Persistence and monitoring are so important,” he says. “You can’t implement something and walk away. You must monitor and sustain, and then evaluate.
“St. Jude has always had a strong commitment to patient safety,” Hoffman continues, “but we want a higher level of rigor, accountability and structure.”

Parent partners
In another study, St. Jude researchers teamed with other children’s hospitals to outline the top 24 research topics that could improve patient care and safety. The team collected data from parents, clinicians and hospital leaders. Hospitals around the world can use these results to decide the best ways to improve patient safety and clinical outcomes.
Parents played an important part in the research process in that study. This kind of parent involvement is a growing trend in patient safety. It had early roots at St. Jude. The hospital has had at least one parent adviser on its patient safety committee for more than a decade.
“Including parents and families in the discussion makes a difference,” Day says. “The hospital truly cares about constantly improving processes to benefit the patients. That makes St. Jude even more special than it already is.”

Hoffman and his colleagues found ways to reduce medication-alert overrides by 40%. The research provides a guide other hospitals can use.
An integrative medicine program offers a new level of holistic care to St. Jude patients.

By Keith Crabtree, PhD

In 2017, oncologist Jennifer Cox, MD, of the the St. Jude Affiliate Clinic at Huntsville Hospital for Women and Children in Alabama made a potentially life-saving diagnosis: Fanconi anemia, a rare genetic disorder that affects the bone marrow.

Cox had treated patients with this disorder more than a decade ago as a fellow.

“Dr. Cox just looked at Maelin and at her labs, and she knew instantly,” recalls Megan Carlson, mother of Maelin-Kate “Mae” Carlson, age 4.

Adopted from China by Paul and Megan Carlson, Mae underwent a bone marrow transplant in March 2019. She has endured “a lot of poking and prodding,” Carlson says. But a non-traditional therapy, pediatric massage, has reduced Mae’s anxiety.

“We’re not taught a lot of these things in medical school,” says oncologist Holly Spraker-Perlman, MD, of the Quality of Life and Palliative Care program at St. Jude Children’s Research Hospital.

Spraker-Perlman specializes in integrative medicine. These therapies complement standard medical care by focusing holistically on the patient’s body, mind and spirit.

Pediatric massage

“Massage therapy is a perfect example of a low-risk, potentially high-benefit integrative intervention,” Spraker-Perlman says.

Although adult massage elicits images of massage
oils and spa equipment, pediatric massage uses storytelling and bedside instruction.

Pediatric massage therapy not only feels good, but also leads to symptom relief, explains Jennifer Smith, a St. Jude child life specialist. Research has shown that massage therapy may increase oxytocin (thought to be a happiness-inducing hormone) and decrease anxiety.

Carlson says massage therapy calms Mae. “She loves hand massages,” Carlson adds. “She’ll even put her hands out to express, ‘I need this now.’”

Can we talk?

Spraker-Perlman is busy laying the groundwork for a St. Jude Integrative Medicine Consultation Service. By 2020, this service will act as an information clearinghouse, answering families’ questions about herbals, supplements and other integrative medicine topics.

For now, Spraker-Perlman is the program’s unofficial on-call physician. “The goal isn’t to recommend X, Y or Z,” Spraker-Perlman says, “but to talk to patients and families about the things they read online and answer their questions.”

This is particularly important when a child has no further curative options and the family is trying to decide which path to take: a phase I clinical trial, an alternative therapy (which is not part of integrative medicine) or a combination of the two.

A growth mindset

The massage therapy, yoga and acupuncture programs at St. Jude are growing.

Thirty St. Jude health care providers have already received training in pediatric massage. The annual St. Jude Pediatric Palliative Oncology Symposium in September will also offer an interdisciplinary workshop on that topic for doctors, nurses and other health care providers.

In a current St. Jude study, nurses massage the hands and feet of leukemia patients for brief intervals to see whether the intervention brings significant symptom relief.

St. Jude investigators are also conducting a systematic review of pediatric oncology yoga to see if a popular program adopted by many public schools benefits children with life-threatening diseases.

Acupuncture, a technique sometimes used to alleviate pain as well as chemo-induced nausea and vomiting, will soon be available to St. Jude patients. Acupressure, in which therapists use thumbs or fingers to achieve a therapeutic effect, is already used at St. Jude for young children.

Mission possible

“I think we’re on the cusp of what integrative oncology is going to be,” Spraker-Perlman says.

Not long ago, she started the St. Jude Integrative Medicine Working Group: doctors, nurses, child life specialists and other health care providers who meet monthly to discuss how to build a world-class program.

More recently, Spraker-Perlman spearheaded the application for a pediatric integrative oncology special-interest group through the American Society of Pediatric Hematology-Oncology.

“Our goal is to meet families where they are,” she says, “to let them know that they can talk to us about anything, to put them on the path to safe and helpful therapies.”

For Mae, massage therapy is both.

“Mae is the most joyful person,” Carlson says. “She loves to play princess and wear her princess costume.

“She had a couple of complications during transplant, but we had fabulous doctors, who took great care of her, and now she’s doing amazing.”

Holistic therapies

Holly Spraker-Perlman, MD, of St. Jude Quality of Life and Palliative Care, specializes in integrative medicine, which includes massage therapy, yoga and acupuncture. These therapies focus holistically on the patient’s body, mind and spirit.
The rattle of oak leaves under an angry sky. The reassuring chirrup of crickets on a steamy summer night. The rhythmic squeak of a rocking chair in a darkened nursery. Many of us take these sounds for granted. But for a child recovering from a brain tumor, those noises can be muffled ... or silenced.

That’s what happened to Lucy Krull, who lost her hearing after treatment for medulloblastoma, the most common childhood brain tumor. As Lucy’s mom can attest, academics can be difficult for a child who has undergone surgery, chemotherapy and high-dose radiation to the brain. Add profound deafness into the mix, and the challenges increase exponentially.

“Lucy’s extremely intelligent,” Kate Krull says, “but when she suddenly lost her hearing, she had not yet learned to read. She had learned a little phonics in advanced preschool, and yet she had a lot of trouble pronouncing words. She couldn’t decode words or spell them because she couldn’t hear the sounds in those words.”

The sounds of silence

Scientists at St. Jude Children’s Research Hospital have found about 75% of children treated for medulloblastoma experience some degree of hearing loss. That damage might occur because the tumor affects the cranial nerve that transmits information to the inner ear. High-dose irradiation to the brain can also cause hearing loss. Most notably, cisplatin, a chemotherapy drug used to kill tumor cells, can damage hair cells in the cochlea, the main organ of hearing.
Despite receiving a drug designed to protect hearing, more than 30% of children in a recent study developed severe hearing loss.

As survival rates for childhood cancer have risen, scientists have redoubled their efforts to improve survivors’ quality of life. For Heather Conklin, PhD, chief of Neuropsychology at St. Jude, that means identifying the cognitive problems that accompany brain tumor treatment and developing ways to avert or eliminate those issues.

“We know these children are at cognitive risk, and we’re doing what we can to refine treatments to decrease that risk,” Conklin says. “Preventing or compensating for hearing loss is an exciting way to improve their functional skills and meaningfully impact their quality of life.”

**Back to basics**

Many childhood brain tumor survivors have problems reading, which contributes to poor school performance. Children like Lucy, who receive high-intensity treatment at an early age, are at highest risk. Although researchers assumed hearing loss contributed to those problems, no one had identified the specific cognitive skills that led to low reading levels. To find answers, Conklin, St. Jude postdoctoral fellow Traci Olivier, PsyD, and their colleagues studied 260 brain tumor survivors from the U.S., Australia and Canada. They wanted to target the specific language-based skills that contribute to poor reading levels.

“This is the first time anyone has drilled down to discover the key cognitive components leading to reading problems in these children,” Conklin explains.

Patients in the study agreed to be tested for five years after diagnosis. The annual assessment included a hearing evaluation, as well as three hours of cognitive testing that spanned reading, math, attention, memory and IQ. The scientists concentrated on phonemic skills — the ability to identify individual units of sound and use those units to decode (or “sound out”) words. This ability is a basic skill in learning to read.

The team learned that hearing loss typically occurs within the year following chemotherapy, but the learning problems are most severe two to five years after completion of treatment. The combination of slower processing speed and phonemic problems appears to affect a child’s reading comprehension.

**It’s a miracle, Momma**

Lucy was one of 64 children in the study who had severe hearing loss.

**International collaborators**

Scientists had assumed hearing loss contributed to reading problems and poor school performance. But, no one had pinpointed the specific cognitive skills that lead to low reading levels. Heather Conklin, PhD (at left), and Traci Olivier, PsyD, led an international study to do that.
“A kid with severe-to-profound hearing loss might not be able to hear a dog bark or a piano or a telephone, or even louder sounds, such as a motorcycle,” Olivier explains. “When you think of that in terms of what they might miss in the classroom, you can really see the impact.”

Lucy’s story began in 2011, when the little girl began vomiting and having balance problems. Immediately, her parents took her to the doctor.

“She had six brain tumors, as well as a sugar-coating of tumors all up and down her spine,” Kate recalls. Surgery, chemotherapy and high-dose radiation were required to save Lucy’s life. About a year after treatment, she began having hearing problems. Hearing aids helped for a while, until she suddenly entered a world of absolute silence.

St. Jude provided Lucy with two cochlear implants. Now she can once again hear the voices of her friends, her teachers and her family. She can hear the whinny of her favorite horse and the clop, clop of his hooves during horse therapy.

“The cochlear implants changed her life,” Kate says. “The doctors said her brain would have to relearn how to process sound, which might take up to six months. But about six weeks later, she nonchalantly announced, ‘I can hear.’ I began screaming with excitement. Her little brother looked up at me and said, ‘It’s a miracle, Momma.’”

Early diagnosis, early intervention

Although Lucy now has functional hearing, the sixth-grader still struggles with reading and writing. That is in keeping with results of the research by Conklin and Olivier, who found that children with severe hearing loss had more problems with phonemic skills, phonetic decoding, reading comprehension and processing speed than children with normal or mild-to-moderate hearing loss.

“The research into hearing and reading is all about quality of life. By helping kids regain cognitive function or protect it, St. Jude is providing a window to the world for their minds.” – Kate Krull

“Early diagnosis, early intervention is vital to helping kids with hearing loss succeed.”

“It’s particularly important for the younger kids, especially those who are under 7,” Olivier says. “From a cognitive perspective, your brain is primed to absorb language at a really young age. That’s why young kids can easily learn other languages when they’re young, but the older we get, the harder it is. So, while those skills are developing, it’s crucial that our cancer survivors have access to sound as soon as possible after hearing loss is detected.”

Personalized learning interventions are also vital. “The analyses we did — uncovering specific vulnerable reading processes — will help us better match interventions to children,” Conklin explains. “So, a child may need help with phonological decoding, or fluency or reading comprehension. We will be able to match the problem to the intervention because we now know the core processes involved. We can make recommendations to the child’s home school on how to intervene.”

A breath of fresh air

“I always tell my children that the window to the world is reading. If you can read, you can learn anything; the whole world is open to you,” Kate says.

Now 13, Lucy enjoys creating art, riding horses and reading with the help of assistive devices. In addition to providing the cochlear implants, St. Jude helped the family obtain the best learning resources for Lucy.

“We’ve seen such an improvement in her ability to process language and learn words,” Kate says. “That might seem odd, because it’s a skill she struggles with, but she enjoys it.”

“The research into hearing and reading is all about quality of life,” Kate continues. “By helping kids regain cognitive function or protect it, St. Jude is providing, again, a window to the world for their minds.”

WATCH VIDEO:
stjude.org/blog-hearing-loss-reading-problems
In the first study of its kind, Heather Conklin, PhD, Traci Olivier, PsyD, and their colleagues discovered the specific language-based skills that contribute to poor reading levels in brain tumor survivors.

Back in the saddle
Lucy Krull (shown with her horse therapy instructor) lost her hearing after treatment for medulloblastoma. St. Jude provided Lucy with two cochlear implants. Now she can once again hear the whinny of her favorite horse and the clop, clop of his hooves.
St. Jude sets a goal of having zero new HIV cases in Memphis by 2030.

By Maureen Salamon

With her glass-half-full outlook on life, Andrea Stubbs isn’t easily discouraged. This trait comes in handy for the manager of the Community HIV Program at St. Jude Children’s Research Hospital.

Two-thirds of Memphians diagnosed with HIV, the virus that causes AIDS, are ages 15–34. Memphis is among the nation’s top-10 cities with the highest HIV rates.

But these grave revelations don’t stop Stubbs in her tracks. Instead, they spur her to action.

For more than 10 years, she has led a local community coalition, Connect to Protect, or C2P. Its 25 members, including the local health department and county schools, work to improve HIV prevention and care for youth. Stubbs, Aditya Gaur, MD, clinical director in the St. Jude Infectious Diseases department, and C2P members are determined to eliminate new cases of HIV in Memphis by 2030. Their efforts are part of a global movement called Ending the Epidemic, or ETE.

One-stop shop

For years, St. Jude has been the only comprehensive care center for HIV treatment in children and youth in Memphis. That work had its genesis in 1987, when the hospital’s founder, Danny Thomas, declared AIDS a catastrophic disease of childhood and prioritized HIV/AIDS research.

Through the decades, the hospital’s research and treatment efforts have contributed to far lower rates of the virus passing from pregnant mothers to their babies. The focus now is to replicate such gains in youth. Stubbs and Gaur hope to keep these individuals healthy through aggressive HIV prevention strategies.

“Of course, we can treat them once they’re diagnosed,” Stubbs says, “but how can we get to them before they take part in risky activities? We have opportunities to think broadly and creatively – and we’re using the community to help us develop novel and innovative ways of education.”

Danny Thomas

A global movement

Andrea Stubbs and Aditya Gaur, MD, are determined to eliminate new cases of HIV in Memphis by 2030. Their efforts are part of a global movement called Ending the Epidemic.
A holistic approach

ETE aims to prevent new infections and provide medication for everyone who is HIV positive. This would maximize patients’ health. It would also lower the chances of passing the virus on to others.

But eliminating new HIV cases requires overcoming social factors. Southern states are particularly hard-hit by HIV. Stubbs says “certain conversations aren’t happening in homes” about prevention tactics.

Memphis’ high infection rate is also tied to poverty, underemployment, single-parent households and lower education levels.

“We have to consider all those factors,” Stubbs notes. The coalition’s tactics include boosting awareness, busting stigmas and changing laws so youth under 18 can consent to taking an HIV prevention drug.

“Our plan can’t focus only on the physical aspects of infection and transmission,” Stubbs says, “but also the social, spiritual and mental aspects that make up a total person.”

90-90-90

Between 30 and 50 new patients arrive at St. Jude each year for initial HIV treatment, with 250 to 300 receiving ongoing care. St. Jude is taking part in a clinical trial to test a long-acting HIV prevention drug in youth who are HIV-negative but at-risk.

“HIV has come a long way, but continues to be a disease that, if untreated, can be catastrophic,” Gaur says. “What we and this coalition do fits perfectly with the St. Jude mission.”

A major target of ETE is called 90-90-90.

Stubbs explains: “We know if we can get 90% of individuals who are HIV-infected but don’t know it to their first medical appointment, get 90% of those to take their medication, and then get 90% of those to have the virus suppressed in their system, we could achieve our goal of zero new infections by 2030.”

An added benefit is that quick testing and treatment, like that offered at St. Jude, often helps young HIV patients embrace the future instead of dreading it. Stubbs relishes putting the pieces in place for young people so they can successfully deal with something “so adult” as HIV.

“That’s why I do the work,” she says. “I always tell them, ‘Put me out of a job.’”
WHETHER HE’S DANCING TO HIS FAVORITE MUSIC or sprinting across a soccer field with his friends, Santiago Buther shows single-minded determination. On the playing field, he spares no effort to beat his buddies at their favorite game. As a dancer, the 8-year-old boy responds viscerally to the pounding beat.

So, it’s no surprise Santiago is facing his biggest foe head-on: a brainstem tumor known as DIPG, or diffuse intrinsic pontine glioma. Radiation treatment at St. Jude Children’s Research Hospital helped restore Santiago’s physical prowess — and his smooth dance moves — after effects of the rare tumor forced him to use a wheelchair.

He’s also part of a St. Jude clinical trial that aims to push DIPG treatment — which hasn’t significantly advanced in more than 50 years — a major step forward. The study, called SJPI3K, is testing a new chemotherapy drug. The drug targets a growth pathway that is overactive in most DIPGs and similar brain tumors. But unlike most other chemotherapies, this medication also crosses the blood-brain barrier, helping deliver its potent effects straight to malignant cells.

“For us, this drug seemed to give him the best everyday life along with the best fighting chance to go after the tumor,” says Santiago’s dad, Eric Buther.

New options

The trial will include about three dozen St. Jude patients who have newly diagnosed DIPG or similar tumors. About 250 children in the United States are found to have this disease...
each year. It has a dire prognosis: Patients survive only nine to 12 months on average, with fewer than 10% living longer than two years.

Typically, radiation treatment halts DIPG tumor growth and improves neurologic symptoms temporarily. Chemotherapy drugs don’t reliably work. And surgery isn’t an option on the brainstem, which controls vital functions such as breathing, swallowing and heart rate.

“New options are critical because there are simply no curative options,” explains Christopher Tinkle, MD, PhD, of St. Jude Radiation Oncology, who is leading the study with Amar Gajjar, MD, Pediatric Medicine chair.

“It’s an incurable disease that has remained resistant to all forms of therapy,” Tinkle adds. “It really flies in the face of what we proudly present as such dramatic improvements in pediatric cancer survival rates. It’s a desperate situation that really needs innovation and new ways of thinking.”

**Hope out of heartbreak**

Decades of research at St. Jude and elsewhere have unraveled DIPG’s mysterious biologic underpinnings. Genetic studies showed how the PI3K signaling pathway is commonly altered in children with DIPG and similar brain tumors. Suzanne Baker, PhD, director of the St. Jude Brain Tumor Research Division, and her colleagues recently discovered that a single mutation in a gene previously not linked to cancer changes the expression of other genes to drive DIPG’s development. The researchers zeroed in on this key mutation, which occurs in most cases of DIPG.

These discoveries were possible through the generosity of St. Jude families affected by DIPG. Many parents of affected children agreed to donate tumor tissue upon their children’s deaths — wrenching gifts fueling hope against a monster disease.

“For decades, these tumors really had remained a black box,” Tinkle says. “But to make progress, we needed insight on a molecular level of the mutations that drive this tumor and what cells they originate from. These kinds of studies can’t be done unless we study the tumor itself, so this was a way to think outside the box.”

**First steps**

The new St. Jude clinical trial is testing a drug known as GDC-0084. Scientists want to find out how well it is tolerated in children and the effects it may have on DIPG and related brain tumors. Like Santiago, patients will first undergo radiation therapy and then take GDC-0084 capsules daily. The drug does what most chemotherapies can’t. It crosses the blood-brain barrier — a natural barrier to keep toxins out — to deliver its potent effects straight to malignant cells.

**Smooth moves**

Between medical appointments, 8-year-old Santiago Buther immerses himself in the latest tunes — displaying finesse, power and dexterity far beyond his years.
Taking aim at DIPG

Amar Gajjar, MD, Pediatric Medicine chair, and his colleagues are leading a study that features a new chemotherapy drug. This drug targets a growth pathway that is overactive in most DIPGs and similar brain tumors.

“"In these walls, it feels like they only care about the children and a cure."”
— Eric Buther

the PI3K pathway in glioma cells. By finding its way to the tumor cells and inhibiting this critical growth pathway, the targeted therapy may act as a double-whammy to DIPG cells, preventing cell growth and promoting cell death. In adults who have experienced disease progression with a similar brain tumor, the chemotherapy has been well tolerated. The drug has prevented further tumor growth in several of those patients.

Tinkle describes the clinical trial of GDC-0084 as a “very tough, but necessary first step” on what is likely a long path toward DIPG treatment gains. As with many other cancers, a strategic blend of therapies will probably be required to improve survival rates.

“This is unlikely to be a disease that any one intervention will significantly impact,” Tinkle says. “The direction we’ll be moving is coming up with combinations that cripple the ability of a tumor cell to continue its growth and/or prevent its death.”

I’m gonna dance

Santiago is back to his energetic self after treatment paired with physical and occupational therapy. His tumor appears stable. Feeling more confident and independent again, he spends much of his time perfecting dance moves. Today, he sways to one of his mom’s favorite songs, “Vivir mi vida.”

“I’m gonna laugh; I’m gonna dance. Live, always keep moving forward,” Marc Anthony sings, as Santiago weaves and twirls, displaying elaborate footwork.

Santiago’s optimism and joy of life rub off on everyone around him.

“We’re all fighting, we’re all seeing wins, and we make sure we find ways to win every day,” Eric says. “In these walls, it feels like they only care about the children and a cure. Without question, this is my heaven.”

The path to progress

Christopher Tinkle, MD, PhD, shown with St. Jude patient Jessica Waltrip, says he hopes the SJPI3K clinical trial will be the first step in a path toward DIPG treatment gains. As with many other cancers, a strategic blend of therapies will probably be required to improve survival rates.
Generosity MAKES AN IMPACT

After researching St. Jude, one businessman supports the hospital’s work to find cures, save children and share knowledge worldwide.

By Zack McMillin

While growing his company over the past 25 years, Chickballapur “Manju” Manjunath became an admirer of something he noticed about many of the most successful people he encountered.

“One thing I have learned,” he says, “is that Americans are very generous people.”

An engineer who immigrated from India to his current home in New Jersey in the 1980s, Manjunath became aware of St. Jude Children’s Research Hospital through its affiliation with the PGA TOUR. An avid golfer, he researched St. Jude and has been a generous supporter ever since.

“I saw this fantastic organization, and that money donated goes to treatment and investments in research,” he says. “I said to myself, ‘If I can do something good, let me donate to someone making very good use of the funds.’”

A few years ago, Manjunath visited St. Jude, along with employees of his company, Benaka, Inc., a defense contractor.

“Seeing the children and the families makes you feel humbled and grounded,” Manjunath says. “You feel so fortunate for your own children’s health. At the end of the day, you feel part of something amazing. It makes your heart glad.”

That visit included a stop at the hospital’s Computational Biology Department to take a photo of a plaque commemorating one of the major gifts Manjunath and Benaka have made to St. Jude. The plaque offers a tribute to Supriya, daughter of one of Manjunath’s close friends from India.

Supriya had cancer as a teenager in college and, sadly, did not survive.

“When I sent the photo of the plaque to my friends,” Manjunath says, “it meant so much to them to see it.”

Jinghui Zhang, PhD, Computational Biology chair, provided an overview of the department’s work investigating the human genome for clues to the cause of cancer in young people like Supriya — and knowledge that may lead to cures. Zhang emphasized that St. Jude freely shares the discoveries it makes with the world.

“It was an honor,” Manjunath says, “to meet someone trying to better the human race and find cures for these deadly diseases. And to know you are helping.”

To learn more about ways to support the work of St. Jude, call 1-800-910-3188 or email giftplanning@stjude.org.
Success tastes like a tray of cookies fresh from the oven. Just ask 14-year-old Grace Ogle, a childhood cancer survivor who loves to bake in her free time. When she was a toddler, doctors in Virginia predicted she would die from a brain tumor called ependymoma. Today, she’s flourishing—making and sharing homemade treats with her family and friends.

Watching Grace thrive may be the sweetest reward of all for her care team at St. Jude Children’s Research Hospital. Her doctor, Thomas Merchant, DO, PhD, St. Jude Radiation Oncology chair, uses radiation to treat children with cancer. For the past 25 years, he has been working to increase survival rates for children with ependymoma, the third most common pediatric brain tumor.

Grace, who can often be found in the kitchen making cookies, is proof that radiation can play a role in long-term survival.

**Terrifying prospects**

In 2006, Julianne and Nathan Ogle were living in Chesapeake, Virginia, with their four children. Grace, the youngest, was 2 years old at the time.

“We were at the doctor for a well-visit,” remembers Julianne. “They noticed her head wasn’t in the normal size range, and she had some trouble walking.”

A scan revealed Grace had ependymoma. Doctors told the family her condition was terminal. Fortunately, a friend led the Ogles to Merchant and St. Jude, which offered a clinical trial for young children with the disease.

“Before Grace was diagnosed, we knew nothing about clinical trials,” Nathan says, “but there were no options for her in Virginia. So, as daunting as it was, we knew we had to get her a referral to St. Jude.”

**Hope for Grace**

Grace was a candidate for a clinical trial led by Merchant. It was the first cooperative group study to give radiation immediately after surgery to children under age 3 with ependymoma. Historically, infants and toddlers with that disease have a worse prognosis than older children.

“Part of being a doctor and researcher is refusing to accept the status quo,” Merchant says. “We are always striving for better treatments and more options to improve outcomes for our patients.”

The clinical trial explored whether radiation immediately after surgery could improve outcomes for all children, regardless of age. Open at more than 100 locations, the study enrolled nearly 400 patients.

“Knowing there is no other option for your child is scary,” Julianne says. “This trial gave us the first bit of hope that we could actually save her life.”

**With more than a decade of follow-up, results from a newly published clinical trial show that radiation after surgery triples survival for kids with ependymoma.**

By Erin Podolak
Improving outcomes

Thomas Merchant, DO, PhD, St. Jude Radiation Oncology chair, strolls a hospital corridor with former ependymoma patient Anna Dennis. For the past 25 years, Merchant has been working to increase survival rates for children with ependymoma, the third most common pediatric brain tumor. He led the first cooperative group study to give radiation immediately after surgery to children under age 3 with ependymoma.

Astounding results

Although the clinical trial closed in 2007, the study didn’t end. Long-term follow-up of participants showed that radiation after surgery nearly tripled the survival rate for childhood ependymoma.

The treatment helped achieve an overall survival rate of 85%. More than 75% of patients had progression-free survival. Recently published in the Journal of Clinical Oncology, the findings show that radiation can improve outcomes despite age and ependymoma subtype.

“Part of being a doctor and researcher is refusing to accept the status quo. We are always striving for better treatments and more options to improve outcomes for our patients.”

– Thomas Merchant, DO, PhD
Serious fun

Addison Dunavent eagerly anticipates her checkups with Alberto Pappo, MD, who blends medical care with play and laughter.

St. Jude researchers find a new melanoma mutation in kids and adults.

By Jane Langille
Six-year-old Addison Dunavent has a best friend whose birthdate is one day after her own. They call themselves “eternal twins.” They certainly look like they could be sisters, but the truth is hidden in their genes.

From a young age, Addison had a growth on her left arm that looked like a hemangioma — a benign lump made of blood vessels that usually goes away on its own. But as she got bigger, the growth did too. When she was 4 years old, a dermatologist near her hometown removed it and sent it away for testing.

“We were shocked to learn it was spitzoid melanoma,” says Jesica Dunavent, Addison’s mom. “The second test confirmed the diagnosis, so our doctor contacted St. Jude Children’s Research Hospital right away. We were in Memphis within days.”

Thanks to St. Jude research, the discovery of a new gene mutation in spitzoid melanoma is helping kids like Addison receive the best treatment approach. The finding also represents an exciting new target for developing precision medicines to treat adult melanomas in the future.

Hiding in plain sight

In 2019, an estimated 96,480 new cases of melanoma will be diagnosed in the United States. A small fraction, less than 1%, will occur in children and adolescents.

Spitzoid melanoma, the most common pediatric melanoma, can range from slow growing to quite aggressive, but it is usually less aggressive than adult melanoma.

“The standard treatment is surgery followed by close observation,” says Alberto Pappo, MD, director of the Solid Tumor Division and co-leader of the Developmental Biology and Solid Tumor Program at St. Jude. “Most pediatric patients, 99%, are disease-free five years later.”

But here’s the catch: Spitzoid melanoma is difficult to spot. A spitzoid tumor doesn’t look like a mole from the outside. It must be examined under a microscope to be diagnosed accurately.

“Spitzoid melanoma is also genomically different from other melanomas,” says Armita Bahrami, MD, of St. Jude Pathology. Changes in six genes called ALK, RET, NTRK1/3, MET, ROS1 and BRAF are known to play a role in about half of spitzoid tumors, but for the other half, any other driver mutation has been unknown — until now.

An exceptional case

Pappo and Bahrami recently collaborated with Scott Newman, PhD, and Jinghui Zhang, PhD, of Computational Biology, on an unusually aggressive case of spitzoid melanoma in an 11-year-old boy. Their research was published in the journal *Nature Medicine*.

The child’s spitzoid melanoma started as a red growth on his ankle, but it grew and spread, even after treatments with surgeries and immunotherapies. He enrolled in the St. Jude Genomes for Kids study and scientists performed comprehensive clinical genome sequencing, including whole genome, exome and transcriptome sequencing on a sample of his tumor.

Whole genome sequencing identifies the exact order of all 3 billion building blocks that make up human DNA, the molecule that carries the master instructions for everything that happens in the body. Whole exome sequencing examines the small subset of DNA that holds the instructions for making proteins. Transcriptome sequencing pinpoints how genes are read to make proteins.

For the boy, the sequencing results revealed that a gene...
called MAP3K8 was fused to another gene. Since fusion genes are associated with several cancers, Newman reviewed published studies to understand what this fusion gene might be doing. He learned that it could activate a gene called MEK, known for fueling melanoma growth in adults. Further lab testing confirmed that the MEK gene was indeed activated in the boy’s tumor.

That insight meant the mutation was potentially treatable with a precision medicine. The patient was treated with anti-MEK and anti ERK drugs, and the cancer partially responded. This critical response indicated more secrets were hidden in the genomic data.

**Fortune favors the prepared**

Several months later, another MAP3K8 mutation turned up in a second patient with spitzoid melanoma. To learn how common it was, the St. Jude researchers expanded their search to screen tumors from 49 patients in the database.

“We were extremely surprised to discover MAP3K8 fusions in one-third of patients, and that they were the most common gene rearrangements,” Newman says. “We thought everything common would have been discovered already.”

Popular commercial screening tests use gene panels of the most commonly known genes associated with cancer.

“Without the whole genome and transcriptome sequencing through the St. Jude Genomes for Kids program, we would not have been able to make this discovery,” Newman continues. “Commercially available assays can only screen for the gene mutations they’ve been designed to identify. Mining a complete dataset is the gold standard for finding actionable insights.”

Commercial screening tests do not yet include mutations in MAP3K8, but some may soon, given this new finding.

Next, to determine the prevalence of MAP3K8 fusions in adult melanoma, the St. Jude researchers hunted for the rearrangements in data from the Cancer Genome Atlas project, an open cancer genomics database founded by the National Cancer Institute and the National Human Genome Research Institute.

“We found MAP3K8 rearrangements in seven cases, representing 1.5% of the total,” Newman says. “That sounds small, but given the large number of children and adults around the world who develop melanoma, that translates to many people who may be helped with precision medicines in the future.”

**In good hands**

St. Jude surgeons carefully removed Addison’s spitzoid tumor in August 2017. Since then, she has returned every three to six months to St. Jude where Pappo and the clinical melanoma team have kept a close eye on her progress.

Jesica measures Addison’s moles at home too. A second spot popped up and grew quickly, and it was also removed at St. Jude. It looked different from the first tumor but turned out to be another spitzoid melanoma.

Caleb Dunavent says his daughter has maintained a sweet relationship with Dr. Pappo throughout all her treatment.

“He sits down and plays Barbies with her,” Caleb says. “They talk like they’ve known each other forever. There’s nowhere in the world like St. Jude. We couldn’t ask for better care.”

“Without the whole genome and transcriptome sequencing through the Genomes for Kids program, we would not have been able to make this discovery.”

– Scott Newman, PhD
Martine Roussel, PhD, of St. Jude Tumor Cell Biology has been elected to the National Academy of Sciences. Roussel was recognized for her distinguished and continuing achievements in original research. The organization is committed to furthering science in the U.S., and its members include nearly 500 Nobel Prize winners.

“This is a richly deserved honor for Dr. Roussel,” said James R. Downing, MD, St. Jude president and CEO. “She has made lasting contributions to our understanding of the molecular underpinnings of pediatric brain tumors. With that information, doctors are uncovering new avenues of treatments, and importantly, developing therapies that maximize cures and minimize long-term side effects.”

Roussel joins Nobel Laureate Peter Doherty, PhD; Robert Webster, PhD; Charles Sherr, MD, PhD; and Brenda Schulman, PhD, as St. Jude faculty who are members of the National Academy of Sciences. In addition, this marks the eleventh appointment of a St. Jude faculty member to the collective National Academies. Doherty; Sherr; William E. Evans, PharmD; Downing; Mary Relling, PharmD; and Arthur Nienhuis, MD, are members of the National Academy of Medicine.

Researchers reveal key process that regulates cell division

Like a baseball player itching to steal second base, cell division advances in part thanks to the fluctuations of a key regulatory protein. Researchers in Memphis and Europe used the latest technologies to capture the critical motions. The results provide clues about how proteins do their jobs. The findings also offer insight into uncontrolled cell division, which is a hallmark of cancer.

Researchers focused on the protein p27. Most proteins fold into a set shape, but p27 does not. The protein remains flexible and disordered. That lets p27 rapidly change its shape and function as the cells’ needs change.

In one shape, p27 prevents cell division. When cells need to divide, p27 must change again. Researchers showed that the flexibility and fluctuations of key segments of p27 make that change possible.

“The key insight in this study is that even though p27 appeared to be locked into a rigid shape that prevents cell division, there are regions of the protein that fluctuate enough to get the process started,” said Richard Kriwacki, PhD, of St. Jude Structural Biology.

*Nature Communications* published a report on this work.
Schedule changes improve ALL treatment

St. Jude scientists have shown that allowing more time between rounds of certain chemotherapy drugs limits their side effects and boosts their ability to kill leukemia cells.

The team used laboratory models to mirror acute lymphoblastic leukemia (ALL) therapy. Researchers tested the drug asparaginase with a discontinuous schedule of dexamethasone.

These drugs are more effective together but have been linked to bone damage. A discontinuous schedule of dexamethasone helps reduce bone damage.

The schedule change limited bone damage when the two drugs were given together. The treatment was also more effective.

“This regimen is part of the backbone of ALL treatment,” said corresponding author Seth Karol, MD, of St. Jude Oncology. “These results show that we’re on the right track clinically.”

A report on this work appeared in PLoS One.

How do we get more out of vaccine protection?

Vaccines help protect against serious infections caused by pneumococcal bacteria. Streptococcus pneumoniae is the most common cause of middle ear infections, pneumonia, meningitis and sepsis in young children.

But the vaccines do not stop the germ from spreading.

St. Jude scientists found about 70 proteins the bacteria need to spread and set up shop (colonize) on someone new.

Several of these proteins are on the bacteria’s surface. Scientists used the proteins to develop a vaccine that stopped the germ from spreading.

“The results suggest that developing combination vaccines may be an effective strategy for blocking the spread of this bacteria and preventing serious infections,” said Jason Rosch, PhD, of St. Jude Infectious Diseases.

Cell Host & Microbe published a report on this work.
Different immune cell implicated in lupus-related kidney disease

St. Jude led a study to identify cells responsible for kidney inflammation in patients with lupus, a chronic autoimmune disease that affects children and adults.

It was thought that B cells are the primary culprit in lupus. This work shows for the first time that a type of immune cell called a patrolling monocyte plays a critical role in lupus-related kidney disease.

The results suggest that treatments for kidney inflammation in patients with lupus should address the patrolling monocytes. The team is looking at the immune signaling pathways and the genetic regulation of patrolling monocytes to identify new therapies.

“Now we know that lupus complications are not all caused by the same thing,” said Hans Haecker, MD, PhD, Infectious Diseases. “In the kidney, patrolling monocytes appear to play a dominant role in disease, possibly independent of B cells.”

The Journal of Clinical Investigation published a report on this work.

First St. Jude director and CEO honored as Giant of Cancer Care

Former St. Jude CEO and director Donald Pinkel, MD, has been inducted into the OncLive 2019 Class of Giants of Cancer Care. Pinkel was recognized for his contributions to pediatric oncology, which include propelling multi-drug therapy for the treatment of acute lymphoblastic leukemia.

“Donald Pinkel introduced the word ‘cure’ to cancer,” said James R. Downing, MD, St. Jude president and CEO. “It was his bravery and unflinching commitment to move forward that changed everything.”
St. Jude physician-scientist receives AACR award

The American Association for Cancer Research has presented Esther Obeng, MD, PhD, of St. Jude Oncology with the 2019 Gertrude B. Elion Cancer Research Award. The award supports researchers early in their careers to support basic, translational or clinical research focused on the cause, diagnosis, treatment or prevention of cancer. Obeng’s research focuses on myelodysplastic syndrome (MDS), a disorder of blood stem cells with limited treatment options and a high risk of developing into leukemia. She is studying how mutations associated with MDS transform normal cells into cancer cells. Her goal is to develop new treatments that are better tolerated.

Mechanism revealed that dooms patients with Lou Gehrig disease

Sometimes oil and water work best apart. Consider the nucleolus. It is a compartment inside the nucleus where the cell’s protein factories are assembled. The nucleolus lacks a membrane. Instead, to maintain its shape and function, the nucleolus relies on the same process that causes oil to form droplets in water.

St. Jude researchers have discovered that the most common genetic cause of Lou Gehrig disease, also known as ALS, disrupts that process. The findings help settle the mystery of how the mutation leads to the death of cells in patients with the disorder.

“We have identified a protein in cells whose function is changed by the mutation,” said Richard Kriwacki, PhD, of Structural Biology. “The finding solves the mystery of how the mutation leads to cell death.

“The work may also lead to new diagnostic tests or new treatments for this deadly disease.”

A report on this work appeared in the journal Molecular Cell.

Biological machinery of cell’s “executioner” yields secrets of its control

Researchers led by St. Jude structural biologists have discovered how the cell switches on an executioner mechanism called necroptosis that induces damaged or infected cells to commit suicide to protect the body.

Abnormal function of necroptosis also plays a role in the pathology of a broad array of diseases. Cancer cells avoid destruction by inhibiting necroptosis; and abnormal activation of necroptosis is linked to the damage from multiple sclerosis, Parkinson’s disease and tissue injury from blood flow loss. Thus, the researchers’ basic findings opens the pathways for drugs to treat those disorders by controlling necroptosis.

Led by structural biologist Tudor Moldoveanu, PhD, an assistant member of St. Jude Department of Structural Biology, the team included scientists from St. Jude, and the Stanford University and Vanderbilt University Schools of Medicine. The research was published today in the scientific journal Cell Chemical Biology.

Their research revealed how a set of molecules called inositol phosphates acts as an activating code, like the combination to a safe, to unleash the cell-killing mechanism of a molecule called MLKL. The activation triggers an “executioner domain” of the MLKL molecule to break down the integrity of the cell membrane and kill the cell.
Tracking the source of bone cancer mutations

Cure rates for the childhood bone cancer osteosarcoma are 60–70% and have been static for 30 years. Most deaths occur when the cancer spreads to the lungs.

Treatment involves surgery and chemotherapy with the drug cisplatin. It’s widely known that chemo can cause mutations and second cancers. But cisplatin’s effect on osteosarcoma mutations has been unclear.

Recent research showed cisplatin treatment may double the number of mutations in the tumor. The changes include ones that may drive tumor growth.

The study involved whole-genome and targeted deep sequencing of two primary tumors and of 14 tumors that had spread to other areas. The tumors were from four patients.

“The findings show the value of figuring out the mutations associated with every DNA-damaging chemotherapy agent,” said Jinghui Zhang, PhD, chair of the St. Jude Department of Computational Biology. “The information would help us understand how the genetic changes might affect the patients’ risk of second cancers and drug resistance.”

The study was part of the St. Jude–Washington University Pediatric Cancer Genome Project. What scientists learned from this study may help them develop better treatments.

*Molecular Cancer Research* published a report on the study.

Genetic secrets yield treatment clues

Curing cancer is tough, especially when the diagnosis is uncertain. For nearly 100 years, specialists have tried to figure out how to define acute erythroid leukemia (AEL). There are no clear treatment guidelines for this disease. Sadly, there are few survivors.

St. Jude scientists recently led the largest and most complete effort yet to find the genetic basis of AEL in children and adults. Researchers from around the world joined the effort. The scientists found five age-related subgroups of AEL. Each has distinct genetic alterations and patterns of gene expression. The work also revealed promising treatments and mutations to target.

“These results mark a new era in understanding this aggressive leukemia,” said Charles Mullighan, MBBS, MD, of St. Jude Pathology.

A report on this work appeared in *Nature Genetics*.

Flu and strep team up to cause respiratory woes

St. Jude scientists found that flu virus and strep bacteria stick together, literally. The union likely helps them both.

*Streptococcus pneumoniae* causes pneumonia and other infections. It is one of the most common and lethal complications of flu. In the U.S., flu and pneumonia are a leading cause of death. Cancer patients have a high risk of death from these diseases.

Researchers found that flu sticks to strep and other common respiratory bacteria. This may help both germs adhere to cells that line the airways. That makes it easier for the germs to spread and cause illness.

The findings offer clues for designing better vaccines.

“The virus and bacteria both likely benefit from the interaction, possibly by hitching a ride to spread the infection when someone who is infected fails to cover their cough or sneeze,” said Jason Rosch, PhD, of St. Jude Infectious Diseases.

*Nature Microbiology* published a report on this work.
When I became a patient at St. Jude Children’s Research Hospital, I knew I’d receive excellent medical care, but I never dreamed I’d discover my life’s calling.

St. Jude was a godsend when I found out I was HIV positive. I was blessed to be able to receive my diagnosis and walk out the same day with medication. During all my appointments and follow-up care, the staff treated me as if I were the most important person in the world.

I built strong relationships with everyone in the clinic, especially with my nurse practitioner Carla London. Carla was invested in making sure I was OK and guided me in efforts to take control of my own health. When I transitioned to adult care, she and her colleagues followed me closely for a year, ensuring I got my medications and kept my appointments.

After graduating from college, I accepted a position with a Memphis organization that works to prevent the spread of HIV and empower those affected by HIV/AIDS.

I educate clients, health care providers, students, health fair participants and others about pre-exposure prophylaxis, PrEP, which is a pill that helps prevent HIV infection. I also help my clients find medical providers, assist with insurance and prescription access, and even accompany them to medical appointments.

It’s a challenging and rewarding job, but I love it when people tell me, “I appreciate you for helping me and for taking the time to get me checked out and taken care of.”

My undergraduate degree was in journalism. I’ve decided that if I pair my communication skills with a nursing degree, I can do more. That’s why I’m planning to return to school and become a family nurse practitioner like Carla. Eventually, I’ll either work in a specialty clinic or have my own — a safe place where people can get testing and holistic treatment without fear or judgment.

Rather than taking clients to the provider, I will be the provider.

Where I am now is another stepping stone — leading me toward an even greater capacity to help others.
Your legacy can make a lasting impact

St. Jude patient Devon, neuroblastoma, with his doctor

Invest in the future of kids like Devon with a gift from your donor advised fund.

Treatments invented at St. Jude have helped push the overall childhood cancer survival rate from 20 percent since we opened in 1962 to more than 80 percent today. We won’t stop until no child dies from cancer, but we can’t do it without you.

Explore DAF giving today.
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Glamour and glitz

Sierra Shuck-Sparer (left) and her friend Josie walk the red carpet during the 2019 Teen Formal at St. Jude. The teenagers spent the afternoon being pampered with salon treatments before donning glamorous dresses and riding in a limousine to an evening of dancing, food and fun.

“Walking the red carpet was the best part, Sierra said. “It made me feel kind of famous. Everybody was cheering. It made all my insecurities — about not wearing a wig while wearing a fancy dress — go away. Everybody was super supportive.”

The St. Jude Child Life Department hosts Teen Formal and other events to provide patients with a sense of normalcy during their treatment.