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reatment and care for childhood cancer and other life-threatening diseases is a journey, and at St. Jude Children's Research Hospital, we celebrate each milestone along the way.

In this issue of St. Jude Inspire, we welcome you to join the celebration.

Come along with us to Tina's quinceañera, a day made even more special for her parents because it was never guaranteed after a diagnosis of medulloblastoma, a devastating brain tumor, when their daughter was only 10.

"For me it was important to see her dance, to see her smile, to see her enjoy herself," her mom said. "And that is something that one longs for when one asks and prays to see her well, to see her healthy."

For two young men from South America, this is the time for high school graduation and making plans for college and careers.

Jean Pierre, from Costa Rica, was treated at St. Jude for a brain tumor at 3 years old. Now, he's on his way to Penn State University to study computer engineering.

Juan Sebastián left Colombia to be treated for acute lymphoblastic leukemia, the most common form of

childhood cancer, when he was 10. Today, he's looking forward to classes at the Universidad de los Andes in Bogotá. He dreams of becoming a doctor and working at St. Jude someday.

At St. Jude, we celebrate moments big and small because, really, there are no small advances in the fight against childhood cancer. From birthdays to drivers' licenses, quinceañeras to graduation and No More Chemo parties, we're inspired and moved to do all we can for kids here and around the world.

We thank you, our supporters, for making these special moments possible. Because of all you do, more kids will have a second chance at life, and moms and dads will get to see their smiles for a lifetime.

Richard C. Shadyac Jr. President and Chief Executive Officer, ALSAC

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# **05**Inspired by excellence

Alberto Pappo, MD, is sure there's no other place like St. Jude Children's Research Hospital—that's why he came back.



# 06 College bound

Juan Sebastián, who left Colombia to be treated for acute lymphoblastic leukemia, hopes to one day return to St. Jude as a doctor.



# **08**After high school

Jean Pierre, from Costa Rica, was treated at St. Jude for a brain tumor at 3 years old. Now, he's headed to college.



# Study Finds Genetic Ancestry Impacts Treatment, Survival for Kids with ALL

ву Ruma Kumar - ALSAC

hildren's genetic ancestry plays a significant role in how they respond to treatment for acute lymphoblastic leukemia (ALL), a study by scientists at St. Jude Children's Research Hospital has found.

The study bolsters work at St. Jude to improve the outcomes for children with cancer across the world. Recognizing differences based on their genetic ancestry can help doctors individually tailor therapy for the children they're treating in diverse, global populations.

The study showed racial disparities exist in both the incidence and treatment outcomes for ALL, the most common type of pediatric cancer in the world.

Analysis of more than 2,400 kids and teens with ALL treated in clinical trials in North America, Southeast Asia and Latin America showed Black and Latino children do not fare as well because their ancestry makes them prone to more high-risk subtypes of the cancer, and because their bodies respond to and metabolize commonly used chemotherapy drugs differently. Children of East Asian descent had survival rates similar to those of white children, but their ancestry revealed that some have genetic variations that make some medicines highly toxic for them.

Until now, widely used treatment protocols were developed based on studies conducted in the U.S. and Europe, involving mostly white children. The regimens did not consider the way treatment would affect children of African, Asian or Latin American descent, for instance.

"We need to stop assuming we can develop therapies focusing on white children and then they can just be extrapolated to others," said Jun J. Yang, PhD, a pharmacogenomics expert and corresponding author of the study. "The world is becoming increasingly diverse, and so are children with cancer. As we look to the next generation of therapies for ALL, it's going to be essential we consider the diversity of this cancer on a global scale."

The study's first author, Shawn Lee, MD, saw first-hand the impact of genetic differences on children with ALL in his clinic in Singapore. Patients seemed to tolerate much lower doses of an important medication called

thiopurines compared to patients in the U.S. and Europe, and no one seemed to know exactly why. The answer finally emerged in 2015 when Yang discovered that mutations in an important gene in thiopurine metabolism—NUDT15—were more common in Asians than in other ethnicities. Since then, extensive research on this gene has been performed, and even prompted the U.S. Food and Drug Administration to issue a warning in 2017 and spurred doctors treating those populations of kids to adjust the dosage of the medicine based on this gene.

In 2020, Lee joined Yang's lab as a research fellow, where he started working on genomics of racial disparities in ALL. What Lee discovered, with Yang's guidance, is that there are at least 8 (of 21) molecular subtypes of ALL which were heavily impacted by a child's genetic ancestry. A child's ancestry determined important factors like their overall survival, the risk of relapse, how much and what types of medicines they could tolerate, and potentially how their immune system responded to the treatment.

The findings have important implications for a plan at St. Jude to create a bank of quality cancer medicines for low-to-middle-income countries who have difficulty sourcing the life saving drugs necessary to treat children with cancer.

In conjunction with the World Health Organization, St. Jude will invest an estimated \$200 million over six years to provide medications at no cost to 50 countries by the end of 2027.

With this study's findings, both Lee and Yang said, St. Jude is uniquely positioned not only to improve access to lifesaving drugs, but also to equip low-to-middle-income countries with the knowledge of how best to dose and combine the medicines to improve survival for kids with cancer in their local populations.

"There's a large gap in outcomes across various countries and children of different race and ethnicities, so even though the cure rates in the west are pretty good, our job isn't finished until we can close those racial gaps," Lee said. "We aim to do more studies and to dig into the underlying biology so we can close these racial gaps in survival."



# GLORIA DE DIOS: BUILDING A 'MINI ST. JUDE' IN GUATEMALA

When Gloria de Dios started out, she was one woman crying over a laptop, wondering if cancer in children could even be cured. In her native Guatemala, children were being treated with adult doses of chemotherapy, kept away from their parents and loved ones during treatment. Worse yet, many of the children suffering from cancer would never even be diagnosed.

She knew something had to change. "It's not fair that we lose a child for lack of resources," she said. "It's all about dignity, because they deserve a second chance in life."

Since 1998, de Dios has been involved in a fundraising foundation called AYUVI, a St. Jude and ALSAC partner in the mountains of Guatemala that treats children with cancer. Under her leadership, fundraising has skyrocketed from \$3 million to \$11 million since 2007. and the survival rate at her clinic-which she calls a "mini St. Jude"-has risen from 20 percent to almost 70 percent.

"Having St. Jude Children's Research Hospital by my side makes me feel safe. Its international outreach program has helped us in so many ways, but if I must choose one, it is how the staff gave us the recipe on how to raise funds to save children's lives."



ALBERTO PAPPO, MD: INSPIRED BY A CULTURE OF EXCELLENCE

Alberto Pappo, MD, is sure there is no other place like St. Jude Children's Research Hospital.

He came to work in the Department of Hematology-Oncology at St. Jude in 1991 after graduating from medical school in Mexico City and completing a residency and fellowship in Texas.

Pappo left St. Jude in 2001, taking up other posts, but returned in 2010.

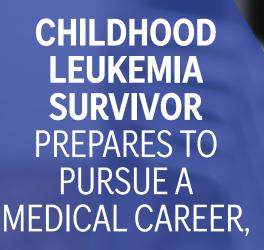
"St. Jude was always in my heart," he said, "and it called me back."

Pappo heads the Solid Tumor Division at St. Jude, developing and testing novel therapeutic interventions, particularly for those solid pediatric tumors that are most difficult to treat.

"What is happening here at St. Jude, it's just very, very rare," he said. The ground-breaking research. The support for patients and families. The dedicated staff united in their mission: to save children's lives.

"It's an inspiring place," Pappo said.

"I go to bed thinking about how I can do things better, and I wake up in the morning saying, 'I'm going to do things better today.' It's just a culture of excellence like no other place I've ever been at."



# WANTS TO GIVE BACK

ву Monsy Alvarado - ALSAC

uan Sebastián stood before his computer during a video conference call to the United States and enthusiastically showed his black school jacket given to final-year students at his high school in Colombia. The year 2022 is stitched in one arm.

Months before he graduated high school in July, the 18-year-old was preparing for graduation and the start of college. He was looking forward to the final months of high school when he would go to Cancun with his classmates for a final school trip. A few days before his graduation ceremony, he attended a formal dinner celebration with his parents and close friend to commemorate the big milestone.



The activities were a culmination of years of long hours of studying, but also a reminder of the hurdles Juan Sebastián has overcome. The teenager battled leukemia for years as a child, forcing him to miss nearly a year of school. When he had a relapse, he was treated in the U.S. at St. Jude Children's Research Hospital and missed nearly a year of school as well as birthday parties, soccer games and a school trip to Canada.

"It's quite incredible to think there was a point in my life when I didn't know if I was going to get to graduate," he said. "Now a new stage of my life begins. There are so many stories, so many times when I couldn't go to school, so many moments that I could not go to class because I was in the hospital. But now I'm moving forward, that's all behind me. And that's something very beautiful and special."

Juan Sebastián, who ranks third in his graduating class, has been accepted to the Universidad de los Andes in Bogotá, where he will study medicine. His dream is to become a doctor and one day work at St. Jude.

"St. Jude is hope, it's light and everything to me," he said. "They saved my life. I don't know how to explain what St. Jude means to me, but it's just hope to be alive and to continue to grow."

Juan Sebastián was 10 years old when he was diagnosed with acute lymphoblastic leukemia, the most common type of childhood cancer. He received grueling chemotherapy in Bogotá, which often left him weak and tired. At times, his parents didn't think he was well enough to go to school, but a dedicated student, Juan Sebastián did not like to be absent.

On some tough days, his father, Luis, recalled, his son would mix water with baking soda and lemon juice in a container that he would carry with him in school to help him through headaches and bouts of nausea.

Juan Sebastián was in remission for a few weeks before an analysis on his bone marrow showed that his leukemia had returned. Doctors in Colombia began a new round of treatment, but his prognosis was poor, his parents said. While Juan Sebastián organized a fundraising concert to help other children with cancer, friends urged his family to look elsewhere and to seek help at St. Jude because of its work with childhood cancers. Eventually, he was referred to the research hospital and traveled to Memphis.

When they arrived, it was cold and gloomy, Juan Sebastián recalled. But as soon as they entered the hospital with its bright lights and colorful wall art, they felt a sense of ease and hope that he would get better.

"They welcome you with a smile," he recalled. "My dad told us that here at St. Jude they were going to save his son's life."

He received a bone marrow transplant as well as chemotherapy and radiation therapy. While at St. Jude, Juan Sebastián missed nearly a year of school in Colombia. The relapse, though, didn't stop him from learning, so he took extra classes while away. He also continued his piano lessons in Memphis, an activity which he started earlier to help reduce the neuropathy in his hands caused by earlier chemotherapy. When he returned to South America, he studied extra hours to fill in

learning gaps and remain in the same grade as his friends.

"Despite all the difficulties of his illness, he managed to get excellent grades," Luis said. "He is very excited about his academic achievements, but the biggest emotion for us is to have him with us."

Earlier this year, Juan Sebastián and his mother, Maria Clara, went to a tattoo artist and got matching tattoos on their left arms. The tattoos are of the St. Jude logo, which features the silhouette of a praying child. Juan Sebastián said the tattoo is his constant reminder to not get too hung up on little things.

"There are times in life when one forgets a bit of what happened and everything they suffered and the really hard moments they lived through, and one begins to worry about things that are not worth it," he said. "It's also a reminder of that goal that I want to reach of trying to help and give other people opportunity, like St. Jude gave me the opportunity of life."



You can help ensure families never receive a bill from St. Jude for treatment, travel, housing or food. **stjude.org/donate** 



# PIERRE heads to COLLEGE

ву Monsy Alvarado - alsac

ean Pierre made a request of his parents months after COVID-19 caused worldwide shutdowns.

He wanted to leave the Costa Rican coastal town they live in and move more than four hours away to the capital of San Jose to finish his high school education. He wanted more intense studies at an international bilingual school that would offer more science courses and prepare him better for college.

"I didn't feel I was reaching my full potential, so I convinced my parents to let me go to San Jose," he said. "At the new school, I get to take physics and chemistry."

The teen, the oldest of four boys, and his father, Manfred, credit his independence to his fight against a brain tumor which

he was diagnosed with as a 3-year-old. He was treated at St. Jude Children's Research Hospital.

"Ever since I was a child, I have to remember to take my medicines, at what time and how much of it," he said. "I think it just made me more responsible."

Jean Pierre was taught early on about the medications he was taking, their purpose and what he needed to do to keep healthy, including what he should eat and what sort of physical activity he needed to do. So even though it is hard to let children move away from home, Manfred said he thought his son was ready.

"Those things made him mature, and he always wants to improve himself," Manfred said. "He is also a person who always wants to help because of all he has received from St. Jude."

Jean Pierre was born in Louisiana. His parents were about to relocate to their native country of Costa Rica when doctors discovered the brain tumor after their son experienced regular headaches and was always fatigued. He had a hard time communicating and had a growing thirst that could not be quenched.

He was diagnosed with craniopharyngioma, a brain tumor that grows slowly but can cause serious illness. Jean Pierre's tumor was found in the pituitary gland, a tiny but important part of the brain that produces hormones which help you grow.

The family first
went to a local
hospital where Jean
Pierre underwent
surgery, but after finding

surgery, but after finding out about St. Jude, they were referred to the research hospital in Memphis. There, Jean Pierre received radiation therapy every day for three months, his father said. He later received speech and physical therapy.

"Until we got to St. Jude, that is when we really understood what was happening, where the tumor was and how dangerous it was," Manfred said.

Jean Pierre graduated from high school this year, and started classes at Penn State University where he wants to pursue a degree in computer engineering. His love of building and design, he said, was sparked at St. Jude.

When he was a boy, he often played with colorful plastic building blocks

as he waited for a doctor's appointment or his radiation treatment to begin at the hospital. Manfred remembers hospital staff bringing his son building blocks when the waiting took longer than expected.

A few years later, Jean Pierre participated in the first Lego League event, an annual competition where participants research, problem-solve and then build and program a robot.

Through the years, Jean Pierre estimates he has built hundreds of Lego® building kits, many of which he purchased on annual trips to Memphis. His favorites are of Star Wars.

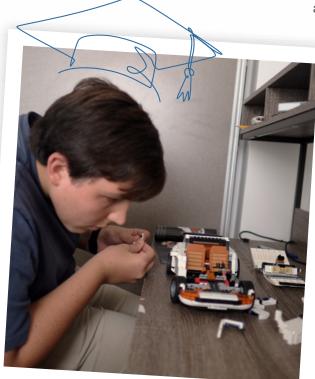
As he prepared to move out of the country for college, he said he was well prepared for the challenges ahead.

"St. Jude gave me a second chance and it's something I should take advantage of and not waste it." he said.

"It's also showed me to be more positive about life and do everything to the maximum."

His father said even though he was excited to have celebrated his son's high school graduation, the biggest milestone of Jean Pierre's life this year is that he no longer has to return to St. Jude annually for checkups. He had his last regular checkup earlier this year.

"Graduation from high school is pretty good we know, but graduation from St. Jude is amazing," Manfred said.





# IIICS OUINCEANERA:

A tradition of a lifetime

After overcoming a cancer diagnosis at age 10, this St. Jude patient and her family celebrated her 15th birthday in style.

ву Monsy Alvarado - ALSAC

Background artwork by Jana, sibling of St. Jude patient **Nasri** 



"We are celebrating Tina's life, faith and the love that we have for her, and that is why we are here so happy and euphoric," said family friend Maria Alejandra, who attended the celebration with her husband, Carlos.

# **Unexpected diagnosis**

Tina had always been a healthy girl. But when she was 10 years old, she started having a lot of headaches and vomiting. Afterward, she lost her balance easily; she tripped and fell. In class, the teachers noticed she was no longer writing straight.

Her parents took her to the hospital and after several tests she was diagnosed with medulloblastoma, a rapidly growing brain tumor of the cerebellum.

"At that moment our life was gone," Marina said. "You just can't believe it ... it was very painful."

Tina didn't know very much about what the diagnosis meant, but had heard about cancer before at school.

"Normally, it's associated with something very sad, people normally associate it with death," she said.

Tina underwent surgery to remove the tumor at a local hospital in Florida, but Carlos and Maria Alejandra urged them to look at St. Jude. They had read about the work the research hospital did with childhood cancers. Marina had previously donated to St. Jude, but hadn't thought of the hospital as a possibility for her daughter.

Days later, after several calls and conversations, they were referred to St. Jude.

"We felt that God sent us to this hospital and the people there

took our pain and turned it into hope," Marina said.

Tina received treatment for eight months, which included chemotherapy and proton radiation, before going into remission. Her parents never received a bill from St. Jude for treatment, travel, housing or food.

"At first, I couldn't believe that Tina had cancer," Vicente recalled. "And to know that there are people who support St. Jude to help families like ours, it's the best thing."

Today, Tina returns to St. Jude regularly for checkups.

"I always think that without St. Jude the story might have been different," Marina said.

# Tina's celebration

In Venezuela, as well as in other Latin American countries, the quinceañera symbolizes the transition of a girl into womanhood. Besides the traditional dance of the waltz, the birthday girl, la Quinceañera, dances with her brothers and other male relatives. The celebration includes a meal and speeches as well. Many of the festivities end with La Hora Loca -The Crazy Hourwhere guests dance with props such as party hats and glowing lights to inspire others to join in

the fun.

The venue was bustling with activity hours before the celebration was set to begin. Marina had chosen the site because of its lush gardens, which she thought would be perfect for an outdoor celebration and pictures.

Aura Molinares, one of the event planners, was busy decorating

tables throughout. She placed a pink book on a table near the entrance, which guests would be asked to sign. She then set up tables for the cocktail hour and for dinner. Pink balloons and pink-and-white rose petals could be seen strewn throughout the outdoors, complementing the natural red, pink and yellow flowers in the gardens.

Aura had heard of Tina's cancer battle when her parents hired her for her services a few weeks prior. She and her partner had been supporters of St. Jude and felt an immediate connection to Tina and her story.



On this day, she hung a special custom-made sign with Tina's name in lights on the balcony as a surprise gift for the teenager.

"This is a special day for her and we wanted to make it extra special," Aura said.

Several feet away, indoors, Tina sat happily on a wooden chair as a stylist brushed and curled her hair. Her long, dark tresses were soon styled into a half-up do, something simple so she could dance.

Her mother was nearby, taking in the moment. Years ago, Tina had lost her hair due to chemotherapy. Marina remembered how sad Tina had been when she saw her hair falling out little by little. The only thing she and her husband could do at the time, Marina recalled, was to shave their heads.

"We wanted her to see that people, that human beings, are more than hair, and that we were there by her side," Marina said.

But today, Tina's hair was long and healthy, and it looked beautiful. The hair stylist finished her hair by placing the tiara on her head.

# Tina's debut

A few moments later, once her hair and makeup were complete, all eyes were on Tina. Her strapless dress with flowers fit, just as she had hoped. Photographers, videographers and some family and friends watched as she posed for a photo shoot before she made her appearance on the balcony.

She knew the importance of the day.

"Not so long ago, I was in a hospital and I had cancer and it shows I won that battle," Tina said. »



We felt that God sent us to this hospital and the people there took our pain and turned it into hope. • Marina













She laughed and she danced. Merengue and salsa and some bachata were on the playlist.

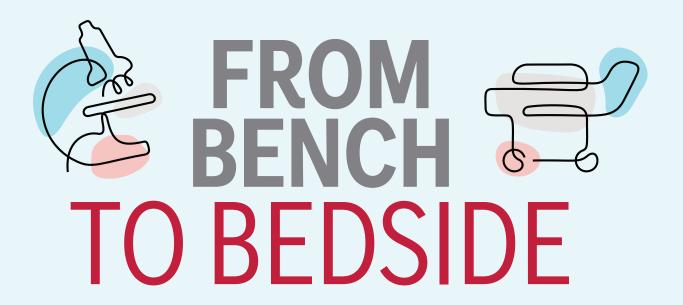
"I like to dance," she said. "I don't know how to dance very much, but whatever comes out will make me happy. I am having a good time."

Among the highlights of Tina's quinceañera for Marina and Vicente was seeing their daughter enjoy herself like any other teenager.

"Seeing her with that look in her eye that illuminates her entire face makes me very happy, especially because we were able to get here," Marina said.







Working together, doctors and researchers at St. Jude Children's Research Hospital develop new treatments and improve outcomes for patients.

ву Ruma Kumar - ALSAC

n the campus of St. Jude Children's Research Hospital in Memphis, where buildings with labs stand alongside buildings with clinics, Giles Robinson, MD, shares samples of tumor cells from his patients with Paul Northcott, PhD. who leads a lab that studies how those tumor cells behave at a molecular level and how patients respond to different therapies.

What Northcott finds about the differences within medulloblastoma helps inform how doctors like Robinson treat their patients. Their close collaboration has spawned new, more effective treatments for medulloblastoma, the most common malignant brain tumor in children.

It's an example of what's known at St. Jude as the "bench-to-bedside" model: how discoveries at a lab

bench translate to better care for patients in beds.

Over the last decade, Northcott and Robinson have identified 13 subgroups of medulloblastoma, some that require less radiation and chemotherapy, while others more. Until these recent discoveries. doctors treating medulloblastoma had thought it was one disease requiring uniform treatment for the more than 400 children diagnosed with it each year in the United States.

"It turned a light on for me," Robinson said. "On one hand it's overwhelming, and on the other hand it's fantastic because we can come up with multiple different treatments that suit these categories of medulloblastoma."

Robinson and Northcott shared their discoveries and the benefits of collaboration at the St. Jude

Partner Summit event, which hosted representatives of corporations that support St. Jude. The partners had a chance to listen to the doctors and also tour labs to learn more about the research that happens at the hospital.

Visitors explored parts of the recently constructed Inspiration4 Advanced Research Center, a 625,000-square-foot facility that features state-of-the-art equipment and technology in laboratories for the research of Developmental Neurobiology, Immunology and Cellular and Molecular Biology.

"I saw the tailored uniqueness that labs have in the tools and equipment they use for researchers to study and categorize these cancer cells to not only understand them, but to take steps to help eradicate childhood cancer forever." said Ben Ahern, Charity Account Manager for AmazonSmile, which has donated more than \$14.2 million to St. Jude since the partnership began in 2014.

Scientists showed visitors how small dishes that fit in the palms of hands contained tumor cells for various cancers to be studied for their features, strengths and vulnerabilities to devise treatment and cures.

In one dish, cells of a cancer that affects the muscles and soft tissue, called rhabdomyosarcoma, float like harmless specks of dust. When allowed to flourish over a week in conditions similar to the human muscle, images from the microscope show the cells grow, no longer spheres but a dense mesh spreading and filling the plate. The solid tumor lab is focused on learning how these cancers grow and spread and what it takes to stop them.

The lab also tracks elusive cancer cells that survive treatment in some patients. These rogue cells, few in number, remain hidden sometimes for years but then unexpectedly mount a resurgence causing difficult-to-treat relapses.

St. Jude scientists are working with doctors to improve survival rates for recurrent cases—rates that have been largely stagnant for more than two decades.

"Having first-hand visibility into the labs was eye-opening to understand the amount of time, technology and resources needed to detect and understand the impact of one genetic cell in a billion that can impact a child's life," said Carmen Murillo, Senior Director of Marketing for Melting Pot Restaurants, which has raised over \$13.9 million for



Paul Northcott, PhD, (left) and Giles Robinson, MD, converse while walking through Northcott's research lab in the Inspiration4 Advanced Research Center.

St. Jude since its partnership began in 2003. "As tedious as the research may be, it is the most important, groundbreaking work."

The work in his brain tumor lab is "very challenging," Northcott admitted, and the answers he and his fellow scientists seek lead to more dead ends than discoveries.

ST. JUDE DOES
EVERYTHING POSSIBLE
TO MAKE SURE THAT
CHILDREN HAVE THE MOST
SUCCESSFUL OUTCOMES
AND THAT FAMILIES
ARE COMFORTED AND
ALLEVIATED OF AS MUCH
STRESS AS POSSIBLE.

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Jill Maness, Manager, Community Relations for AutoZone "It's a 90 percent failure rate, maybe 95 percent," Northcott said. "But I'm driven by the fascination and curiosity and possibility for discovery. That's what gets me up in the morning."

Jill Maness, Manager, Community Relations for AutoZone, which has raised more than \$51 million since its partnership with St. Jude began in 2006, called the work the doctors, researchers and entire staff do every day at St. Jude "nothing short of remarkable."

"I can't imagine the gambit of emotional strain parents face upon learning that their child has been diagnosed with cancer or any lifethreatening disease," Maness said. "St. Jude does everything possible to make sure that children have the most successful outcomes and that families are comforted and alleviated of as much stress as possible."



Research at St. Jude is possible because of generous supporters like you. **stjude.org/donate**