St. Jude promise

stjude.org/promise summer2017

New **hope** for children with **leukemia** and **lymphoma** *pg. 20*

St. Jude speeds toward **global goals** *pg. 8*

St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder

promise

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

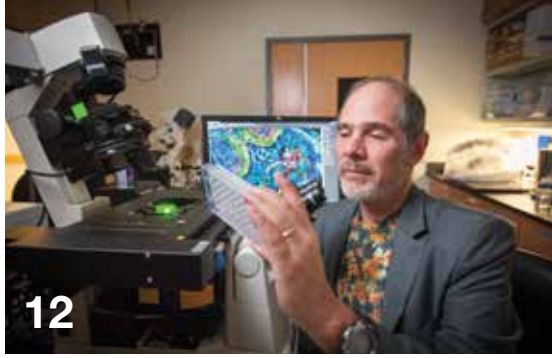
8

Cover story

Features

Contact us: *promisemagazine@stjude.org* (901) 595-2125
Subscribe online: *stjude.org/promise*
Public Information: 1-866-278-5833, ext. 3306
Donations: 1-800-822-6344

Social media:
Follow our science and medicine: *@stjuderesearch*
Follow our fundraising and awareness: *@stjude*



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

On the cover:
Brooke Brantner and Hiroto Inaba, MD, PhD
Photo by Seth Dixon

Discrimination is Against the Law

St. Jude Children's Research Hospital complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. St. Jude Children's Research Hospital does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

St. Jude Children's Research Hospital:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Patient Relations Coordinator at 901-585-8383 or the operator at 901-595-3300.

If you believe that St. Jude Children's Research Hospital has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with: Patient Relations Coordinator, St. Jude Children's Research Hospital, 1-901-5958383; 1-866-278-5833, 1-901-595-1040, Fax # 1-901-595-8600 or at *PatientRelationsCoordinator@stjude.org*. You can file a grievance in person or by mail, email or fax. If you need help filing a grievance, Jim Mobley, Patient Relations Coordinator, is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 1-800-368-1019, 800-537-7697 (TDD) Complaint forms are available at *http://www.hhs.gov/ocr/filing-with-ocr/index.html*.

ATTENTION: If you speak another language, assistance services, free of charge, are available to you. Call 1-866-278-5833 (TTY: 1-901-595-1040).

Amharic:
ማስታወሻ: የሚናገሩት ቋንቋ አማርኛ ከሆነ የትርጉም እርዳታ ድርጅቶች፣ በነጻ ሊያግዝዎት ተዘጋጀተዋል።ወደ ሚከተለው ቁጥር ይደውሉ 1-866-278-5833 (መስማትለተሳናቸው: 1-901-595-1040).**Arabic:**تنبيه: إذا كنت تتحدث بلغة أخرى، فيمكنك الاستعانة بخدمات المساعدة اللغوية المتوفرة لك بالمجان. يرجى الاتصال بالرقم 1-866-278-5833 (الهاتف النصي: 1-901-595-1040).

Chinese:
注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 1-866-278-5833 (TTY：1-901-595-1040)

French:
ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-866-278-5833 (ATS : 1-901-595-1040).

German:
ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-866-278-5833 (TTY: 1-901-595-1040).

Gujarati:
સૂચના: તમે ગુજરાતી બોલતા હો તો નિ:શુલ્ક ભાષા સહાય સેવા તમારા માટે ઉપલબ્ધ છે. ફોન કરો: 1-866-278-5833 (TTY: 1-901-595-1040).

Hindi:
ध्यान दें: यदआिप हदिी बोलते हैं, तो आपके लिए मुफ्त में भाषा सहायता सेवाएं उपलब्ध हैं। 1-866-278-5833 (TTY: 1-901-595-1040) पर कॉल करें।

Japanese:
注意事項：日本語を話される場合、無料の言語支援をご利用いただけます。1-866-278-5833 (TTY: 1-901-595-1040) まで、お電話にてご連絡ください。

Korean:
주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1-866-278-5833(TTY: 1-901-595-1040)번으로 전화해 주십시오.

Laotian:
ໂປດຊາບ: ຖ ້າທ ່ານເວ ົ ້າພາສາອ ື ່ນ, ການບ ໍ ລ ິການຊ ່ວຍເຫ ຼ ືອດ ້ານພາສາໂດຍບ ໍ ່ເສ ຍ ຄ ່າແມ ່ນ ມ ີໃຫ ້ແກ ່ ທ ່ານ. ໂທ 1-866-278-5833 (TTY: 1-901-595-1040).

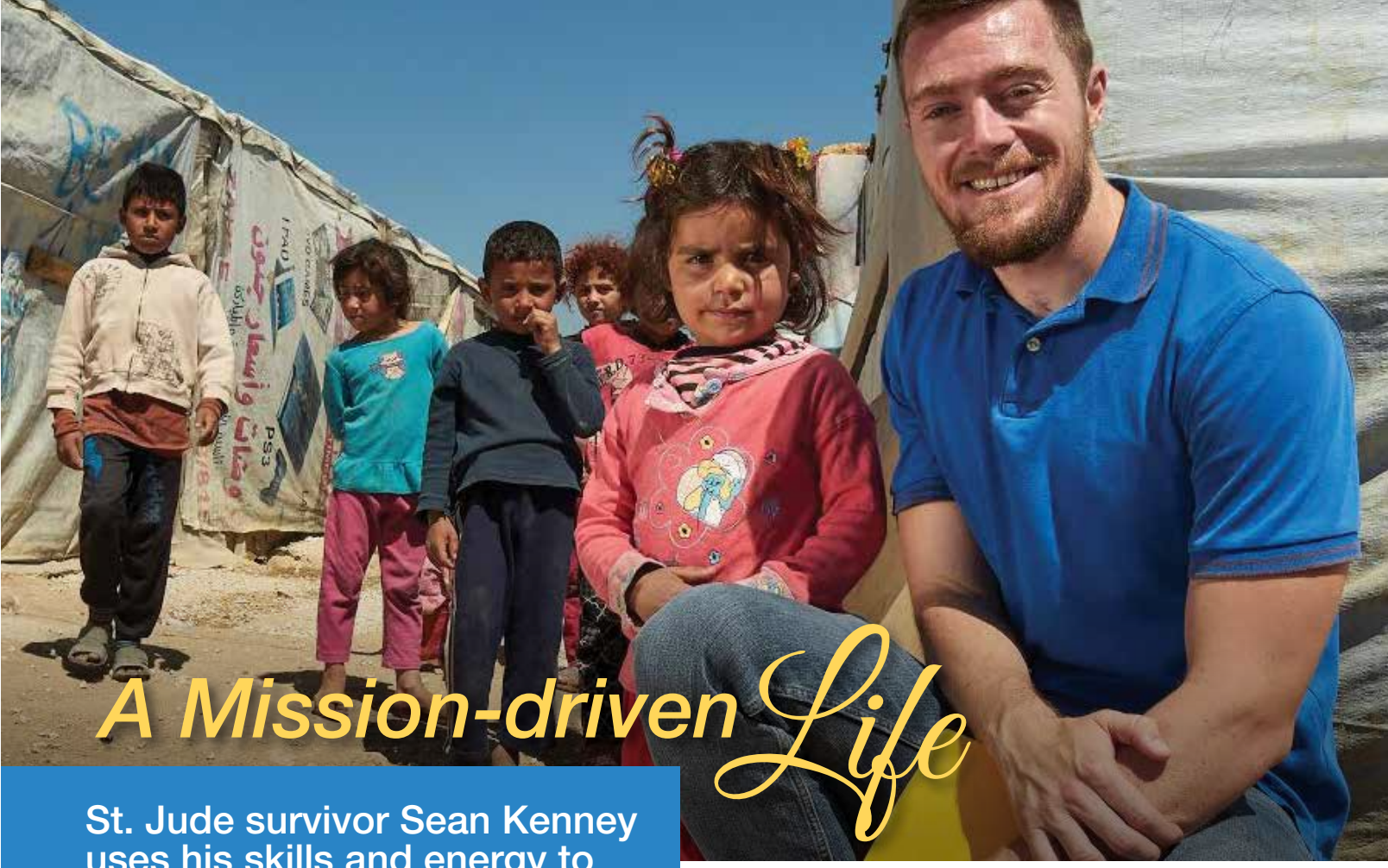
Persian:
اگر به فارسی گفتگو می‌کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می‌باشد. با ۱-۸۶۶-۲۷۸-۵۸۳۳ (TTY: ۱-۹۰۱-۵۹۵-۱۰۴۰) تماس بگیرید.

Russian:
ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-866-278-5833 (телетайп: 1-901-595-1040).

Spanish:
ATENCIÓN: Si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-1866-278-5833 (TTY: 1-901-595-1040).

Tagalog:
PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-866-278-5833 (TTY: 1-901-595-1040).

Vietnamese:
CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-866-278-5833 (TTY: 1-901-595-1040).



A Mission-driven Life

St. Jude survivor Sean Kenney uses his skills and energy to help others.

By Elizabeth Jane Walker

Sean Kenney owes his existence to a hospital founded by a man of Lebanese descent. Today, this childhood cancer survivor provides succor to refugees living in that same region of the globe.

Through his work with Catholic Relief Services in Beirut, Sean assists the nearly 2 million Syrian refugees who are straining Lebanon's fragile infrastructure.

How can one young man make a dent in an overwhelming situation that confounds the rest of the world?

Like Danny Thomas, who established St. Jude Children's Research Hospital, Sean is accustomed to beating the odds. When he was only 3 years old, Sean underwent treatment at St. Jude for a rare brain tumor called juvenile pilocytic astrocytoma.

For several years, all was well. Then the tumor returned with a vengeance. The surgery required to save the sixth-grader's life caused severe complications. Sean spent two-and-a-half years relearning how to swallow and speak.

"I feel fortunate to have made a recovery," says Sean, who participates in St. Jude LIFE, a study that evaluates the health of long-term survivors to help improve cancer treatment for current and future patients.

During college, Sean developed an interest in social justice issues, which led him to study and volunteer in El Salvador, the Dominican Republic and Ecuador.

When he was 3 years old, Sean Kenney underwent treatment for his first brain tumor. Today, he helps children who also face overwhelming challenges.

"As someone who had a hard time speaking for a long time, I felt grateful that people could understand me in another language," says Sean, who also speaks Spanish, French and Swahili and is learning Arabic.

After completing a two-year teaching stint in Tanzania, he earned a graduate degree and worked in Uganda and Jordan. Through his current post in Lebanon, Sean helps local organizations manage programs to support refugees.

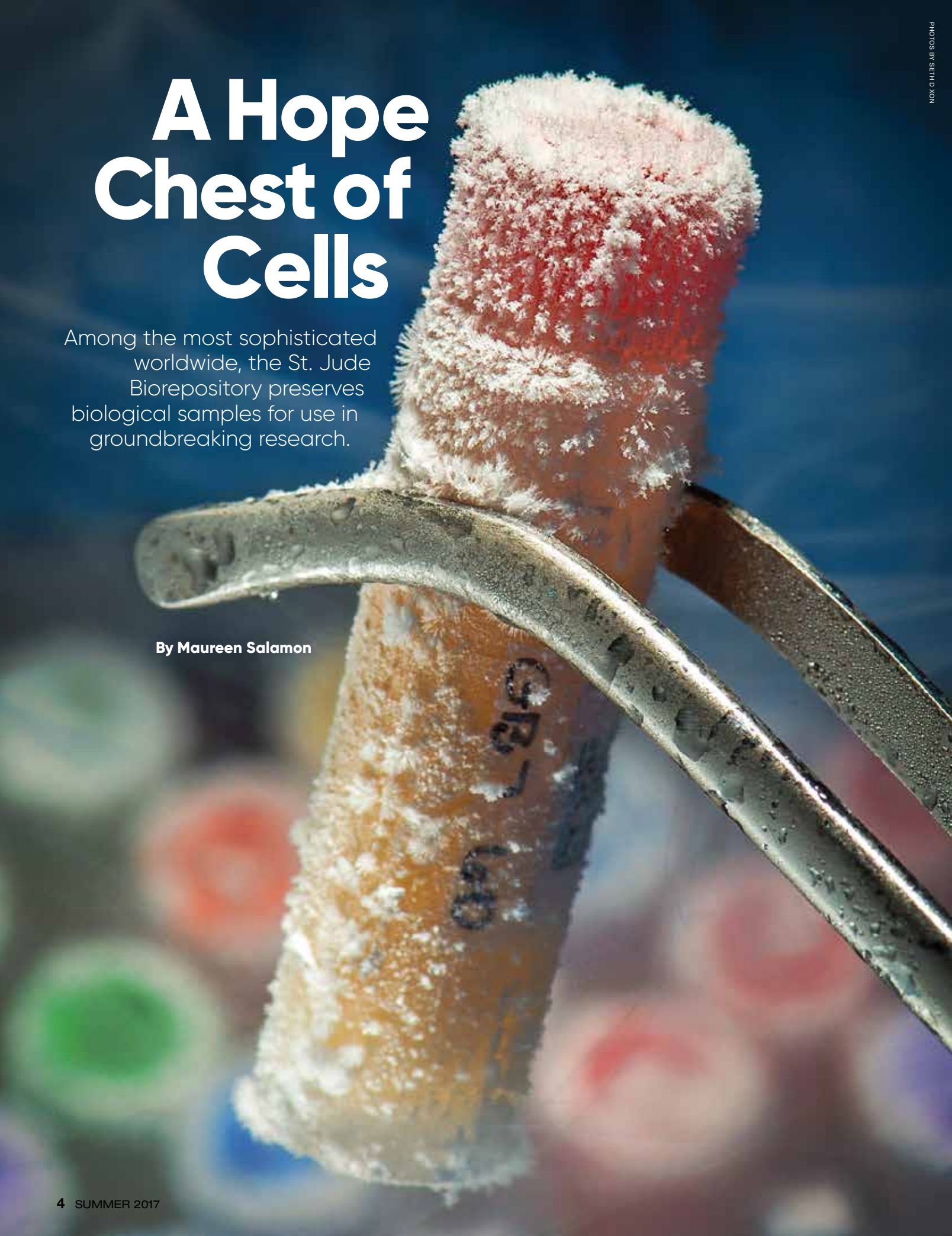
"It's amazing being here in Beirut with the St. Jude connection of Danny Thomas," Sean says. "When I reflect upon being a St. Jude patient and on the origins of St. Jude, whose founder came from this part of the world, I know I have a unique opportunity to serve here.

"It has all been possible because of the recovery St. Jude allowed me to make," he continues. "I feel very fortunate and grateful." ■

A Hope Chest of Cells

Among the most sophisticated worldwide, the St. Jude Biorepository preserves biological samples for use in groundbreaking research.

By Maureen Salamon



PHOTOS BY SETH D XON

In the week that Carlos Sepulveda describes as "the craziest of my life," the college student was diagnosed with a rare form of cancer, underwent three surgeries and embarked on a treatment plan entailing 35 sessions of radiation therapy at St. Jude Children's Research Hospital.

Four years later, one event from that whirlwind week still stands out to Carlos. He recalls giving consent for samples of his tumor to be collected and stored for research. Even while grappling with a jolting diagnosis and a flood of related details, the young man understood that capturing cells from his tumor—a cancer called liposarcoma—might someday benefit others.

Carlos agreed to contribute both tumor and healthy cells to the St. Jude Biorepository, one of the most sophisticated resources of its kind in the world. Also known as a tissue bank, the facility houses samples dating back more than 40 years.

The Biorepository fuels research into cancer and other diseases. Like a hope chest, this collection of cells is safely tucked away as research techniques increasingly "come of age" to unlock their secrets.

"When I first learned how rare my cancer was, I understood why it was a good research opportunity for St. Jude," says Carlos, now 25. "It was essentially a no-brainer for me to agree to participate and help other patients."

A BIOLOGICAL TREASURE TROVE

Launched informally in the mid-1970s with blood and bone marrow samples from childhood leukemia patients, the St. Jude Biorepository became one of the first five nationwide to be accredited by the College of American Pathologists. The collection now contains more than 500,000 specimens donated by current patients, long-term survivors, participants in St. Jude clinical trials worldwide, and children with non-malignant blood disorders such as sickle cell disease and bone marrow failure syndromes.

Growing at a rate of about 20 percent each year, the bank includes leukemia, brain and solid tumor samples, samples from patients with non-cancer conditions, serum, plasma, DNA, RNA and urine. St. Jude often collects both normal and diseased cells from the same patient, enabling scientists to compare the characteristics, such as genetic features, of each. All research samples are de-identified to ensure patient privacy.

"We collect about 5,000 specimens a month," says Matt Lear, the Biorepository's technical director. "That's fairly significant, given that St. Jude admits between 500 and 600 new patients per year. But most hospitals only see patients a few times in the course of their lifetime, whereas we see fewer patients but see them more often."

TIME IS OF THE ESSENCE

Although a cancer diagnosis is a fraught time for patients and families, it's also a pivotal point for collecting tissue samples, according to Charles Mullighan, MBBS, MD, medical director of the Biorepository. That's because researchers need to be able to contrast untreated tissue—taken before therapy begins—with cellular changes occurring after treatment.

More than 95 percent of St. Jude families agree to contribute.

"Many patients want to enable research that will try to understand the condition better and improve things for themselves or future patients," Mullighan says. "The culture at St. Jude is geared toward research, and most patients want to participate in that."

REVOLUTIONARY INSIGHTS

Which research using Biorepository samples has proven most compelling so far?

"That's like asking to choose between your children," Mullighan quips. But there are undeniable standouts, he adds, including many discoveries from the Pediatric Cancer Genome Project and the St. Jude LIFE clinical trial.

The St. Jude LIFE study brings long-term childhood cancer survivors back to campus for regular health screenings throughout adulthood. Scientists recently reported on next-generation gene sequencing conducted on tissue donated by 3,000 such survivors. About 25 percent of survivors who developed second cancers had inherited gene mutations predisposing them to cancer.

MAKING DISCOVERIES POSSIBLE

Meanwhile, the Pediatric Cancer Genome Project, the world's most ambitious effort to discover the origins of childhood cancer, teamed St. Jude with Washington University in St. Louis. Researchers compared the complete genomes from both cancerous and normal cells in more than 800 patients. This project identified unexpected genetic changes in many of the most clinically challenging pediatric tumors, such as high-risk acute lymphoblastic leukemia and brain tumors.

Sequencing of matched non-tumor samples from children with cancer also revealed that more than 8 percent of children with cancer have genetic predispositions.

"The Genome Project has been revolutionary," Mullighan says. "It has provided new tools to analyze cancer genomes, fundamental new understandings of how tumors develop and grow, new diagnostic tests and new therapeutic approaches. A number of these have been rapidly pushed into the clinic."

Matt Lear (at left) and Charles Mullighan, MBBS, MD, retrieve a tissue sample from the St. Jude Biorepository.

FROZEN IN TIME

The logistics of running the Biorepository are immensely complex, from coordinating the efforts of an expanding team to the technical demands of preserving and rationing samples for multiple types of research.

In the last nine years, the Biorepository's roster of lab technicians has doubled to six, while a trio of bioinformatics staff members have been hired to maintain a sophisticated database allowing sample searches according to exacting criteria. Lear and a lab supervisor have also come on board to manage the repository's day-to-day operations.

Likewise updated is the cluster of more than two dozen freezers in which tissue samples are stored, many of which suspend cells in sub-Arctic temperatures as low as minus 196 degrees Celsius. The samples remain in this "vapor phase" until St. Jude technicians pull them out of their frosty confines months or years later to propel scientists' research efforts.

Although some specimens remain stable for up to 48 hours after collection, others begin deteriorating within 15 minutes. Either way, time is of the essence.

"The sooner we can cryopreserve the tissue—we snap-freeze it in liquid nitrogen—the better data we're going to be able to generate when we sequence that sample," Lear says.

Tissues are preserved in their "native" state, with no specific components—such as genetic material—extracted or analyzed until researchers pinpoint exactly which cell type or fraction they need for a study.

SCIENTIFIC STEWARDSHIP

Obtaining a sample from the Biorepository is a bit like borrowing a library book, in that St. Jude typically requires the sample be returned to allow it to be used again in the future. Researchers at St. Jude and around the globe request these highly sought cells, with a dedicated Tissue Resources Committee meticulously reviewing each application. Samples from St. Jude patients processed by the Biorepository currently support more than 100 clinical trials nationally and internationally. Many of the studies test drugs that target specific molecules in the samples in hopes of creating or improving treatments.

The prospect of allowing a researcher to deplete any tissue sample is contemplated with extreme care, with sustainability a key philosophy.

"We have specimens going back 40 years, and 40

Like most St. Jude patients, Carlos Sepulveda agreed to have samples of his tumor collected and stored for research. Today, Carlos says he is gratified to know those samples may someday help other patients.

years from now somebody else should be telling you how we have samples that go back 80 years," Lear says. "We must continue to care for these samples so their ability to yield clues about particular diseases will be enhanced as time goes on."

LEAP OF FAITH

Like Carlos, most St. Jude patients who contribute to the Biorepository recognize the gesture is a leap of faith, because they likely won't ever benefit personally.

"But if I can help make the experience easier mentally or physically—or maybe help alter treatments in the future for someone who's diagnosed with the same thing—that's really gratifying," Carlos says.

For his part, Mullighan can't forget patients he treated as a new physician who were struggling with leukemia, many of whom died.

"You can get very bogged down in the day-to-day details and mundane aspects of running a lab," he says. "But we often have very touching stories from patients or relatives who say, 'We just received a diagnosis of a particular tumor type, and we'd really like you to have that sample in the bank.'" ■

ST. JUDE BIOREPOSITORY

Contains more than **500,000 specimens** donated over more than **40 years** by nearly **21,000 patients** enrolled in St. Jude clinical trials.

About **5,000 specimens** are donated each month.

27 freezers and refrigerators suspend cells in temperatures as low as **minus 196 degrees** Celsius.

One of the first **5 banks** to be accredited by the College of American Pathologists.

About **2,400 samples** from the bank were sequenced as part of the **Pediatric Cancer Genome Project**—the world's most ambitious effort to discover the origins of childhood cancer.

Specimens in the bank currently support more than **100 clinical trials worldwide.**

PETER BARTA

Six years? Who would dream of transforming the global landscape for childhood diseases in such a short time? St. Jude would… And look at the progress that has occurred thus far.

Accelerating Progress

By Elizabeth Jane Walker

The stakes are high, and time is of the essence. Every day, children worldwide are dying of cancer and other life-threatening diseases. Who has the intellect, the drive and the know-how to save them? The problem is too great for governments or international philanthropic organizations to handle alone. So two years ago, St. Jude Children's Research Hospital stepped into the gap.

The hospital's president and chief executive officer, James R. Downing, MD, announced a six-year, $7 billion strategy to accelerate progress toward curing childhood cancer.

Eager to accept that challenge, the hospital's faculty and staff embraced the task. As they can attest, progress comes quickly at St. Jude.

Race against time

The first task Downing faced was recruiting visionary leaders in areas such as financial operations, clinical efforts, strategic planning, information services, global outreach and the Comprehensive Cancer Center.

"It's important to have people who understand the culture of St. Jude, who know our history and recognize that special magic that makes St. Jude what it is," he explains. "We've been able to recruit seasoned leaders who bring new energy, offer new perspectives, and pose new ways of solving problems. We're able to draw incredible people to this institution. That's because of who we are—our workforce and our mission. People want to be a part of that."

The leadership team immediately set to work, creating new programs and ensuring that employees know their roles in accomplishing the hospital's mission. That dynamic has enabled Downing to begin checking tasks off the plan's to-do list. Because, after all, there's no time to lose.

Phenomenal precision

One of the earliest accomplishments involved establishing the world's first proton therapy center designed solely for children. The St. Jude Red Frog Events Proton Therapy Center enables scientists to define the best way to use this treatment, which propels sub-atomic particles into tumors while sparing healthy tissue. More than 150 children have undergone proton therapy at St. Jude thus far.

The hospital has also launched new precision medicine efforts, many of which have their genesis in the St. Jude – Washington University Pediatric Cancer Genome Project, which compared the genetic blueprint of cancerous and normal cells from more than 800 children. That project revealed important details about a host of childhood cancers.

During the past couple of years, the hospital has begun moving whole-genome

SETH DIXON

In the world's first proton therapy center designed solely for children, scientists such as Weiguang Yao, PhD, are defining the best way to harness this life-saving technology.

sequencing to the clinic. A study called Genomes for Kids evaluated the feasibility, acceptance and impact of using genomic sequencing for children with cancer.

St. Jude created a Cancer Predisposition Program to work with families whose children may have genetic lesions in their normal tissues that significantly increase their risk of developing cancer.

The hospital's clinical genomics service incorporates specialists from across the institution, all dedicated to using precision medicine to save lives. This service is already being used in front-line therapy through the hospital's newest clinical trial for leukemia and lymphoma *(see related article, page 20).*

Another precision medicine effort includes a project to sequence the genes of 3,000 survivors as part of St. Jude LIFE, a long-term follow-up study. Accomplished in 18 months, the sequencing effort uncovered germline mutations in cancer predisposition genes in long-term survivors of cancer. The study also shed light on the risk for second malignancies in that population.

A similar initiative involved sequencing the genes of 800 patients with sickle cell disease. By evaluating results of that study, scientists hope to learn why some patients live long lives while others die early or suffer from severe complications. Discoveries will provide new targets for potential cures.

Patients first

St. Jude staff are always on the lookout for new ways to reduce the stress experienced by patient families. Last year, the hospital completed construction of state-of-the-art inpatient units designed to entice patients to leave their hospital rooms for exercise, fellowship and mental stimulation.

"Those amazing facilities are providing a level of inpatient care and experience that are unparalleled in the United States," Downing says.

Outpatients now have enhanced housing options, with an upgrade of Tri Delta Place for short-term stays.

The new Patient Experience Office is also creating a host of additional perks for families, including a babysitting service, Zipcars and a town-square concept that simulates a small-town environment.

"When you think about a town square, you envision an area that may have a school and a church nearby, as well as a little store where you can get cookies and coffee and ice cream," Downing says. "We're going to convert the second floor of our Patient Care Center into a town square for such amenities as the School Program, chapel, concierge desk, post office and bank. It will all be in one concentrated area for our families."

Training tomorrow's scientists today

This fall, St. Jude welcomes the inaugural class of the St. Jude Graduate School of Biomedical Sciences. The PhD-granting program will reflect the hospital's mission and will provide a distinct educational experience for young scientists. Graduate students will inject energy and new ideas into clinics and labs across campus.

"It fills a niche we think we can fill better than anybody," Downing says. "In an institution where translational medicine has been at the core since Day One, these individuals will get a unique training experience that will develop a cohort of scientists who will go out and influence how science is done."

Uniting the world's top minds

St. Jude already collaborates on projects with institutions around the world. These studies generate discoveries that save untold lives worldwide. But time is of the essence. Cures must be accelerated. What if the hospital brought together the world's top minds to create new, St. Jude–funded

clinical trials and research projects to help find such cures?

The hospital is developing a clinical research consortium to generate clinical trials for pediatric cancers, non-malignant hematological diseases and other life-threatening disorders. Some of the planet's top pediatric programs are being invited to join this effort.

"These new clinical trials will not replace the collaborative protocols we develop and run," Downing says. "We will continue to run our own protocols. But someone at another institution may have an idea that no one's ever considered. The group will design the study, and it will be funded through this effort."

Similarly, a St. Jude research collaborative will identify the best talent around the globe to work as part of an international team dedicated to answering previously unanswered scientific questions. The first project in that program is already underway. World-renowned scientists gathered in May 2017 to explore how cells organize specific contents into functional compartments called liquid organelles. By better understanding the biology of liquid organelles, scientists can make progress in eradicating diseases such as cancer, immune dysfunction and neurodegeneration.

Mobilizing the world

Perhaps the most striking accomplishment thus far is the establishment of St. Jude Global, a major initiative to restructure and expand the hospital's reach. The goal of St. Jude Global is to create a network of interactive programs and institutions worldwide so that every child with cancer has access to quality care.

"In the past, our international outreach efforts were humanitarian in nature, but it wasn't a strategic, goal-oriented effort," Downing explains.

"This is really a change in focus. It's about building a workforce. It's about establishing consortia of institutions, and then teaching them how to do clinical research so they can continually advance the level of care they provide to children within those regions. And then it's about working across those regions around the globe so that we all learn from each other."

This massive effort is moving quickly and generating excitement. For the first time ever, the Association of Pediatric Hematologists and Oncologists of Central America held its annual meeting in the U.S.—at St. Jude.

The St. Jude Global Academy also held its first course for clinicians who deal with pediatric cancer. The eight-week training course for infectious disease specialists from Latin America culminated in an intensive workshop held on the hospital's campus.

Progress expedited

More dramatic advances should occur during the next few years, as the plan continues to unfold. New buildings and programs will be added to support the research and clinical care necessary to reach the hospital's goals.

Downing says St. Jude donors should take pride in the part they have already played in saving the lives of children around the globe. Continued support is needed to share the hospital's life-saving mission worldwide.

"We owe a debt of gratitude to our dedicated donors who believe in our ambitious plan to eradicate cancer and other devastating diseases of childhood," he says.

"Who's going to step up and accelerate progress? Who's going to mobilize the world and get them to work together? We think St. Jude—with the support of our donors—can do it better than anybody."

So the plan proceeds apace—because time is of the essence. ■

PHOTOS BY SETH DIXON

The hospital's new inpatient units entice patients such as Mabry Landstreet to leave their hospital rooms for exercise and exploration.

Miguela Caniza, MD, of Global Pediatric Medicine, works with Brennan Bergeron, one of the first students in the St. Jude Graduate School of Biomedical Sciences.

As part of the hospital's new research collaborative, J. Paul Taylor, MD, PhD (left), St. Jude Cell and Molecular Biology chair, confers with Cliff Brangwynne, PhD, of Princeton University and Rohit Pappu, PhD, of Washington University in St. Louis.

FINDING THE Magic IN CELL DEATH

By Maureen Salamon

PHOTOS BY PETER BARTA

MILLIONS OF CELLS IN OUR BODIES DIE EACH DAY. BY UNVEILING THE MYSTERIES OF CELL DEATH, SCIENTISTS OFFER OPTIONS FOR PATIENTS OF ALL AGES.

Clad in a shirt emblazoned with apoptotic cells, Doug Green, PhD, seamlessly combines his passion for science and magic. As the chair of Immunology at St. Jude, Green is world renowned for his research on the mechanisms of cell death.

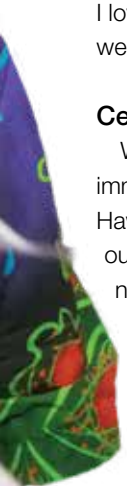
Leave it to Doug Green, PhD, to explain how science and magic are two sides of the same coin.

A practitioner and master of both, the Immunology chair at St. Jude Children's Research Hospital is also quick to point out how the two phenomena are at odds. Magic, of course, is based on illusion, while science is based on fact. But it's no sleight of hand that Green's pioneering exploration into the ways cells die and stay alive is reaping revolutionary insights.

Hooked on magic since grade school, when his father pulled nickels from his ears and bought him a $3 bag of tricks, Green has long been similarly passionate about how cells communicate. His latest discovery, a set of "rescue proteins" that can thwart cell suicide, could lead to sweeping health benefits in kidney transplantation, cancer, neurodegenerative diseases and infections. The next big trick—developing drugs to control this process—would pull the proverbial rabbit out of a hat, potentially transforming treatment for millions worldwide.

"Why do we even do science? It's because we want to improve the world and our lives, but also because it's a human endeavor; it changes the way we look at reality. In some ways, magic does the same thing," says Green, who came to St. Jude in 2005. "Good magic gives you a little moment where your reality is altered. How many times in a day do we actually experience wonder?

I love that I actually have two things in my life that, if I do them well, can do that."



Cell death: a Goldilocks dilemma

With his ready laugh, the guitar-playing, theater-hopping immunologist is neither a one-note nor a one-hit wonder. Donning Hawaiian and tie-dyed shirts at scientific conferences to stand out to peers—on the advice of a long-ago mentor—Green could never merely blend in. Three decades ago, during his earliest probes into the mechanisms of cell death, many scientists agreed with him that this phenomenon might carry wide-ranging health implications. But Green was one of only a handful at the time who decided to actually figure out how.

At its core, cell death, which occurs through processes known as apoptosis or necroptosis, is basic to human life. Millions of cells in our bodies die each day. Most die because they're worn out, damaged, infected or otherwise unneeded. These cells are quickly replaced by new ones. But sometimes it's not desirable for them to die, such as when the cells of a transplanted kidney are stressed due to lack of oxygen, triggering inflammation after re-oxygenation that can threaten the new organ's success. Other times, killing cells rapidly is the goal, such as in cancer treatment.

> "Why do we even do science? It's because we want to improve the world and our lives, but also because it's a human endeavor; it changes the way we look at reality. In some ways, magic does the same thing."
>
> *— Doug Green, PhD*
> *Immunology chair*

"Cell death is a Goldilocks situation: Too much is a bad thing, and not having enough is a bad thing. You want it to be just right," Green explains. "I'd say that's the case for every tissue in the body."

Proteins grant cells stay of execution

But life and death, even in cellular terms, isn't a fairy tale to the prolific writer. Green has authored more than 500 research papers, along with numerous books and scientific reviews, including one with the sinister title "Ten Minutes to Dead." His latest article, published in the journal *Cell*, revealed a set of proteins that can rescue a damaged cell from its death sentence.

Green led a team of St. Jude immunologists to discover how these proteins, called ESCRT-III, can delay or prevent the "executioner" machinery that kills damaged or infected cells in necroptosis. The list of far-reaching health advantages of controlling cell death by activating these proteins is spellbinding. They range from stopping cancer's spread through blood vessels eroded by necroptosis; to protecting otherwise doomed brain cells

"In discovery research, we don't know where the next breakthrough is going to come from," says Doug Green, PhD. "We're encouraged here to explore things that may, on the surface, appear to have no important implications for treating catastrophic diseases in children. But you never know … and breakthroughs are breakthroughs.

from dying in neurodegenerative disorders such as Lou Gehrig's disease; to extending the lives of cells infected by viruses such as influenza, granting them more time to mount an immune response.

But as charmed as the findings may seem, Green's research didn't involve wizardry. Instead, he and his team methodically manipulated isolated cells in the lab to trigger the last phase of necroptosis, performing a plodding, time-course analysis to examine what happened at each step.

"It had generally been accepted that once you activate the final step in necroptosis, the cells die. That's what everybody noticed," he says. "But our data now says that you can actually activate this ESCRT pathway to make the cell survive."

No hocus-pocus in drug discovery

Green hopes one day to develop a mind-reading trick known as mentalism that would make audiences believe he'd plucked a thought straight from their brains. "It's impossible," he acknowledges. "But we can create an illusion of that."

More than hocus-pocus will be needed, however, to develop drugs to control the cellular rescue mechanism at will, dictating a cell's life or death according to medical needs. And Green holds no fantasies about how long this process may stretch. It's a process that will potentially incorporate St. Jude chemical biologists, as well as pharmaceutical companies and even existing drugs repurposed for this new use.

"There's a slow pace to science. It basically takes a generation to go from a fundamental discovery to an actual treatment," he says. "The treatments developed at St. Jude that actually cure patients were completely unfeasible 50 years ago. They were crazy. Now they're routine."

With findings of this magnitude, Green is well aware his efforts could help patients of all ages, not just children. He tips his hat to the leadership at St. Jude, which emboldens faculty members to pursue research revelations without a crystal ball to predict exactly who will benefit in the end.

"In discovery research, we don't know where the next breakthrough is going to come from. We're encouraged here to explore things that may, on the surface, appear to have no important implications for treating catastrophic diseases in children," he says. "But you never know … and breakthroughs are breakthroughs. Of course, the clinical translation of research we do here is always going to be in children." ■

VOLUNTEERS FIND TIME TO SHINE

St. Jude Walk/Run chair finds volunteers through teamwork.

By Richard J. Alley

When Emily Savage was asked last summer to chair the volunteer committee for the 2017 St. Jude Walk/Run to End Childhood Cancer in St. Louis, she considered it. After all, her parents had always donated to St. Jude Children's Research Hospital when she was a child. She had chaired the philanthropic committee as a student at the University of Missouri. And she and her husband, Stephen, donate food to local charity events through their restaurants, Wheelhouse and Start Bar.

Then she witnessed firsthand the passion and mission of the Walk/Run as a participant in the September 2016 Childhood Cancer Awareness Month event.

This September, take part in the St. Jude Walk/Run to End Childhood Cancer:
stjude.org/together

"I thought it was awesome," Savage says. "Getting involved was something I was really excited about because I knew we could grow this if we had the help."

That help would come from an army of volunteers recruited through networking and social media. Savage and her team have recruited 36 volunteers to head subcommittees for the 2017 event.

Once Savage makes a connection, she tells her story. Then she moves on to the hospital's mission.

"I'm proud to be just a tiny part of that goal," she says, "and I look for people who want to share in that with me."

The key to success, she says, is to give volunteers ownership of their position.

"We're trying to find people's passions," she explains. "One of the volunteers, Katie, is our logistics chair. She was an event planner, so we put her on logistics because it seeps into everything she's always done. We brought her out to look at the location and talk about race starting and layout. She came the next day with an overview map and position settings. So filling in a strength we didn't have—that is the best thing about finding volunteers who can really shine."

Emily Savage participates in the 2016 St. Jude Walk/Run to End Childhood Cancer.

The 2017 St. Jude Walk/Run to End Childhood Cancer needs volunteers as well as participants. Visit *stjude.org/together* for details.

Teamwork is a tenet at St. Jude. That same reliance on teamwork carries over into the volunteer community.

"The importance of the volunteers in our committee has been unreal," Savage says. "With the growth we've had, you get all these new touchpoints in the community. Just getting the mission out has been amazing. It was incredible last year, but I knew there was much more we could do this year." ■

St. Jude Garden of Eatin'

By Elizabeth Jane Walker

PHOTOS BY JERE PATROBEK

The St. Jude Garden provides nutrient-packed food for patients and a delicious respite for volunteers and visitors.

It's not the tender green lettuce, the long pink radishes or even the purple tomatoes that capture the interest of 5-year-old Olivia Fontaine during her tour of the vegetable garden at St. Jude Children's Research Hospital. As the little girl from Canada peers over the edge of a metal bin, she stares in horrified fascination at shiny red worms wriggling in the rich, black compost. "*Les vers*," she whispers, squinching her delicate nose in distaste.

Olivia and her father have come to the garden as an afternoon diversion while Olivia's brother, Caleb, recovers from a bone marrow transplant for acute myeloid leukemia. On this humid but windy afternoon, Olivia and her dad join other patient families in exploring the wonders of the St. Jude Garden.

Berries, bushes and beehives

St. Jude was one of the first hospitals in the United States to create a garden dedicated to growing vegetables and herbs for consumption by patients, families, staff and visitors. Originally, hospital employees transformed a vacant lot across from the main campus into a small vegetable plot. Today, that space contains meandering footpaths, an orchard and 74 verdant beds bursting with color and fragrance. Heirloom tomatoes, spiky asparagus fronds, tomatillos and purple hull peas sway in the breeze, which swirls with the aromas of rosemary, mint, lavender and the pungent scent of garlic.

Most of the vegetables growing in the garden are destined for the hospital's cafeteria, Kay Kafe. Kevin Krueger, procurement and sustainability manager for St. Jude Food Services, estimates that volunteers will harvest more than 3,000 pounds of produce from the garden this year and about 5,000 pounds next year. That bounty will be supplemented by figs and cherries produced by mature trees tucked away in another corner of the campus. New landscaping near the hospital's data center will feature functional plantings such as berry bushes and fruit trees. And beehives will be added to the garden later this year, offering the sweet promise of rich, golden honey.

"Fresh produce is the most nutrient-dense form you can get," Krueger explains. "Growing vegetables in our garden encourages our chefs to incorporate seasonal items into their menus. If they know we're going to have a couple hundred pounds of a really nice varietal or an interesting type of produce coming out of the garden, they can write a menu for it. We can then roll it out in Kay Kafe."

Lettuce work together

In the past year, St. Jude has partnered with Memphis Tilth, a nonprofit organization that helps manage the garden and serve as a source of local food. Memphis Tilth also helps coordinate the St. Jude Farmers Market, a weekly on-campus resource for employees and patient families. Krueger and the team from Memphis Tilth focus on making the garden an exciting and

Facing page: Mary Carnes of Memphis Tilth explores the garden with Olivia Fontaine and her dad. *Above:* Carnes confers with Kevin Krueger, St. Jude procurement and sustainability manager.

attractive space for use by patients, families, staff and visitors. New paths have been constructed, shade trees have been planted and plans are in place to provide shade structures, picnic tables and additional landscaping on the garden's periphery. Recently, hundreds of St. Jude employees streamed into the garden one Friday afternoon to enjoy tours, live music and camaraderie. Another event later that month catered specifically to patient families.

All of those activities require willing workers. The hospital relies on volunteers to plant, maintain and harvest the garden's produce.

"When it's 100 degrees in the middle of summer, it probably takes about 40 hours a week just to keep the garden watered," Krueger says. "Then we need help with regular maintenance—weeding, helping with seed starts and other tasks that free up our garden team to conduct educational activities and plan new projects."

About 50 hospital employees recently signed up to volunteer in the garden after work and on their lunch breaks. Individuals in the community participate through the hospital's Volunteer Services Department. And university and corporate groups often provide sweat equity through organized work days.

All that romaines

As little Olivia now knows, there's more to growing veggies than just planting, watering and waiting. Sometimes you need the assistance of a hard-working worm.

"We can take material from this bin and add it to the soil, which helps the plants grow," Mary Carnes of Memphis Tilth explains to Olivia.

Even though Olivia's dad translates Carnes' explanation into French, the little girl is not convinced. But regardless of whether she fully understands the worms' purpose, Olivia will certainly remember her visit to the St. Jude Garden.

"We want our garden to be more than a place that simply provides food for the hospital's kitchen," Krueger says. "Healing gardens are becoming more popular in hospitals throughout the country. We want ours to be both—a functional garden as well as an energizing and restorative space." ■

To volunteer in the St. Jude Garden, visit stjude.org/vol-garden.

A Bountiful HARVEST

This year's yield from the St. Jude Garden is expected to include approximately:

Lettuce 650 pounds	Radishes 265 pounds
Arugula 250 pounds	Tomatoes 250 pounds
Beets 200 pounds	Greens 120 pounds
Turnips 100 pounds	Carrots 90 pounds
Herbs 45-50 pounds	

CELEBRATION OF A LEGACY

By Elizabeth Jane Walker

St. Jude pays homage to its first director by dedicating the Donald P. Pinkel, MD, Research Tower.

Donald Pinkel, MD (left), discusses the hospital's progress with current president and chief executive officer, James R. Downing, MD.

When Donald Pinkel was a youngster, he provoked more than his fair share of sleepless nights and parental concern.

What, his parents wondered, would become of their little boy with the shining blue eyes and the incandescent intellect?

"My mother and father had seven children, but I was their problem," recalls Pinkel, decades later.

Every Friday night, his parents took him to St. Michael's church in downtown Buffalo, New York, where they said a novena to St. Jude, the patron saint of hopeless causes.

"They prayed for me to turn out as a real person, and not just a problem," Pinkel explains, with a wry smile.

Ironically, this brilliant young man would one day help found a hospital named after that saint. As the first director of St. Jude Children's Research Hospital, Pinkel would set a scientific trajectory for curing a disease once considered universally fatal. In the process, this one-time "problem child" would save the lives of countless children around the world.

A soaring testament to greatness

On a mild March day in 2017, the St. Jude Board of Governors and the hospital's administration named the campus' tallest building in honor of Pinkel. As the 90-year-old honoree watched the event online from his home in California, people from across the nation gathered in Memphis to celebrate his legacy.

The Donald P. Pinkel, MD, Research Tower soars above the campus as a testament to one man who dared to take a chance on a fledgling hospital in Memphis, Tennessee. More than 50 years ago, Pinkel was criticized by many in the medical community for pursuing a cure for acute lymphoblastic leukemia, which was assumed to be incurable.

"I was told I was throwing away my career," Pinkel recalls of his early days at St. Jude. "I said, 'Well, it's a good way to throw it away.'"

A place for hopeful causes

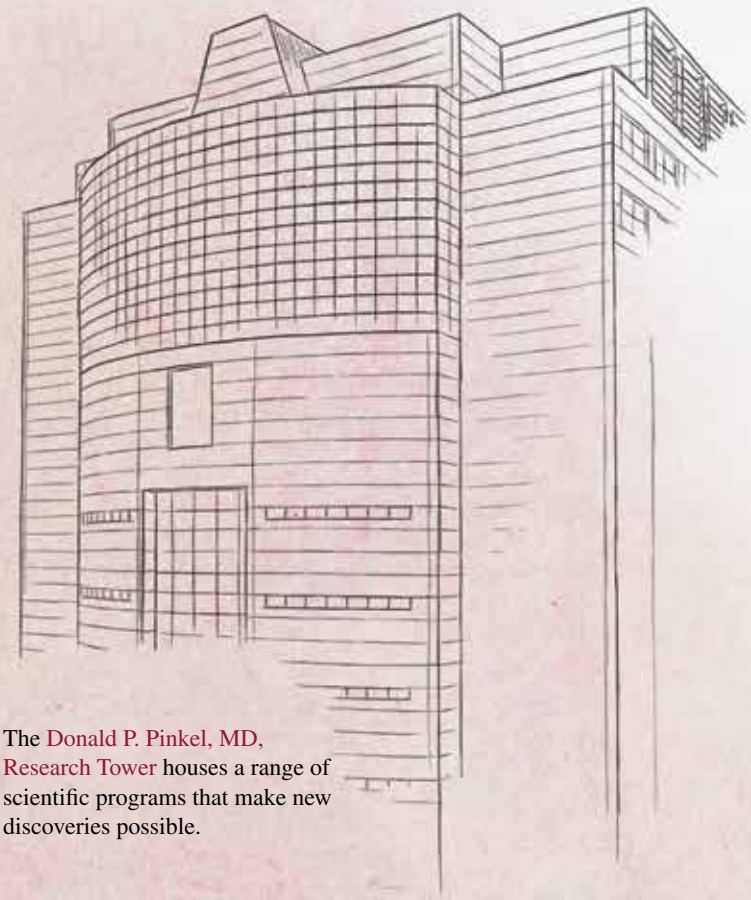
When Pinkel pulled his station wagon onto campus in November of 1961, he beheld an edifice of concrete, scaffolding and mud. The building's only completed room was his office—from which dangled a solitary phone line and an electrical cable.

As the hospital's first employee, Pinkel immediately set about recruiting researchers and clinicians to join him in a quixotic quest to find cures for children with pediatric cancer and other life-threatening diseases.

"We are here for a hopeful cause, not hopeless," Pinkel told the scientists he recruited. "We can do it."

"It's because of what Dr. Pinkel accomplished on this campus—because of his leadership, because of the people he recruited —that St. Jude exists today."

– James R. Downing, MD
St. Jude president and chief executive officer



The Donald P. Pinkel, MD, Research Tower houses a range of scientific programs that make new discoveries possible.

Science plus compassion

At St. Jude, Pinkel created a culture of great science, designing basic research programs and innovative clinical trials that systematically built upon incremental successes. Under his leadership, the survival rate for acute lymphoblastic leukemia rose from 4 percent to 50 percent within a decade. Today, that survival rate is nearly 95 percent, with quality-of-life measures rising in tandem with survival.

As a passionate advocate for children, Pinkel laid the groundwork for St. Jude to flourish. Always, he coupled science with compassion. Early in his tenure, Pinkel noticed that many of the patients from low-income areas were malnourished, which hindered their ability to survive treatment. As a result, Pinkel created a program that developed into the federally funded Special Supplemental Nutrition Program for Women, Infants and Children.

"Dr. Pinkel dared to dream big," says James R. Downing, MD, St. Jude president and chief executive officer. "He dreamed big in partnership with hospital founder Danny Thomas and with the early leaders of this organization.

"It's an honor to dedicate a building in his name and to never let that legacy disappear," Downing continued. "His legacy has to be what pushes us forward. We continue to be a place where great science is melded with great humanity. We care for patients and their families as they enter the most difficult journeys they could ever imagine, and we walk with them side by side throughout those journeys. We owe a real debt of gratitude to the work that Dr. Pinkel accomplished here." ■

Watch the video: **stjude.org/pinkel-legacy-video**

Pinkel's "Total Therapy" studies revolutionized the treatment of acute lymphoblastic leukemia. Each subsequent trial has built upon knowledge gleaned from preceding studies. *See page 20 to learn about the Total Therapy Study 17.*

THE TOTAL PACKAGE

A new precision medicine study aims to push leukemia and lymphoma survival rates ever higher while reducing side effects.

By Elizabeth Jane Walker

ILLUSTRATION BY DREAMSTIME

The word sliced through Wendi Brantner like a sharpened blade: *leukemia*. At that moment, the universe contracted, explanations muffled by the roar of a mother's frantic heartbeat.

"I didn't cry; I was just trying to breathe," Wendi recalls. "Your whole life changes in one second."

Looking back, there had been clues: worrisome bruises, a lackluster appetite, night sweats. But 12-year-old Brooke and her parents had discounted those minor ailments. Then a scooter mishap required X-rays to rule out a broken arm.

"Please check her blood while she's here," Wendi told the doctor.

The arm was not broken, but Brooke's blood sample teemed with immature white blood cells. Wendi and her husband, Mark, rushed their daughter to the St. Jude Children's Research Hospital affiliate in their hometown, where clinicians diagnosed acute lymphoblastic leukemia (ALL).

"We're sending you to the mother ship," the staff told the Brantners. "You're leaving for Memphis tomorrow."

Success builds on success

Brooke and her family learned she would be one of the first four patients to enter Total Therapy Study 17 for children with leukemia or lymphoma. This new clinical trial represents the culmination of a half-century of innovative research and clinical care.

Fifty-five years ago, most medical centers offered single-drug treatments that saved about four out of every 100 patients. Then St. Jude scientists announced a "total" strategy that involved a combination of anti-cancer drugs. The revolutionary protocol yielded cures, and the world took note.

During the ensuing years, each iteration in the Total Therapy series built upon knowledge gleaned from preceding studies. Today, St. Jude leads the world in the research and treatment of ALL. The 17th trial in the series is designed to save more children while improving their quality of life during treatment and beyond.

"At St. Jude, we have 94 percent survival, but we want to increase it to 100 percent," explains oncologist Hiroto Inaba, MD, PhD, who heads Total 17. "To reach 100 percent, we must take a new approach."

That tactic incorporates precision medicine—a discipline that uses genetic factors to tailor therapy. By harnessing technology and melding it with phenomenal research and clinical care, Inaba and his colleagues intend to further increase survival rates while reducing long-term side effects.

Practical genomics

Every child who enrolls in Total 17 will undergo genomic testing of both normal tissue and leukemia cells to guide therapy.

Genes in normal tissues determine our eye and hair color, as well as many other traits. But genes can also predispose children to cancer or regulate medication response.

Years ago, St. Jude researchers discovered that children with a certain variant genetic type could not clear a common chemotherapy drug from their bodies, so the medication could build to dangerously high levels. For those patients, a much smaller dose had the same effect that a larger dose would have in children with common genetic profiles. As a result, St. Jude developed a genetic test that is now used by hospitals worldwide to screen children before administering that drug.

Every child who enrolls in Total 17 will undergo genomic testing of both normal tissue and leukemia cells to guide therapy.

Total 17 will incorporate this kind of new testing for several medications, including a drug that can cause neurological problems such as foot-drop more frequently in children with a specific genetic type.

"Genomics will also change the chemotherapy," Inaba explains. "Leukemia cells carry abnormal genetic changes—so-called mutations—that produce cancerous cells and promote their growth. Using genomic data of leukemia cells, we can identify many abnormal mutations that may be targetable by new agents. If a patient has these lesions or is not responding well to treatment, we can add those agents to therapy to improve the responses."

Allergy avoidance

One important medication for ALL treatment is called asparaginase. But some children develop severe allergies to that drug. Those reactions can range from skin rashes to low blood pressure or respiratory problems. In such cases, the medication can stop working and response to chemotherapy may worsen. Alternative medicine is available and important for these patients, but it only works for a few days instead of for two or three weeks—meaning it must be given every few days to be effective.

SETH DIXON

By harnessing technology and melding it with phenomenal research and clinical care, Hiroto Inaba, MD, PhD, and his colleagues intend to increase survival rates while reducing long-term side effects for children such as 12-year-old Brooke Brantner.

"If you can prevent those allergies, the drug works better without severe side effects and it decreases hospital visits," Inaba explains.

Allergies are caused by antibody formation, so clinicians hope to avoid allergic reactions by dispensing a drug called rituximab to children like Brooke, who has a type of ALL that affects B cells. Rituximab prevents antibodies from forming.

"This method has not been used in other trials," Inaba says. "We hope that by giving rituximab early in therapy we can prevent antibody formation and the allergic reactions."

Early response

Success builds upon early vigilance. That's why evaluations occur early and often in Total 17. After the second and sixth weeks of therapy, clinicians conduct tests to find out whether cancer cells persist.

"With a microscope, we can detect maybe one out of 20 cells," Inaba explains. "But if even 1 percent is there, the cancer will come back. With our detection level, we can find one out of 10,000 to a million cells. This is a more sensitive way to identify who is a high-risk patient and who can be cured with standard agents."

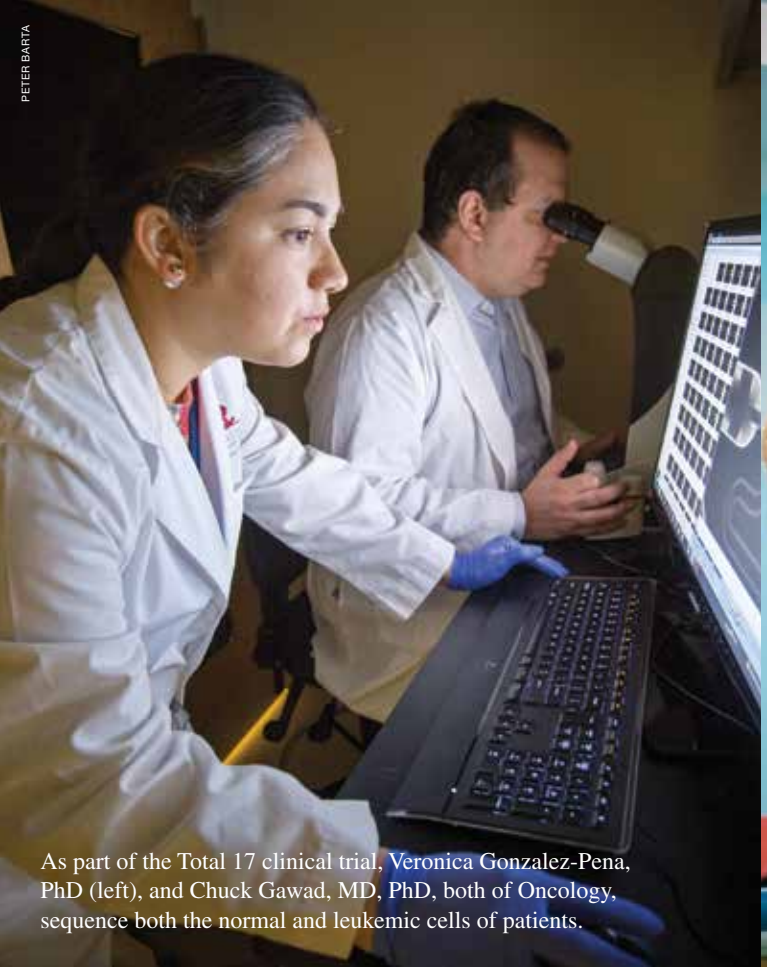
If leukemic cells remain, a patient with B-cell ALL receives immunotherapy, which is a treatment that marshals the patient's own immune system to eradicate cancer cells. If leukemic cells continue to persist after immunotherapy, then the child may require a bone marrow transplant.

Problem prevention

One crucial aspect of Total 17 is the emphasis on quality-of-life issues. St. Jude staff are determined to enable survivors to thrive into adulthood.

Several years ago, St. Jude completely stopped giving brain irradiation to children with ALL. Instead, all patients with that disease receive chemotherapy given through the spinal fluid. This has remarkably improved issues with IQ, memory, growth and the occurrence of second cancers. However, attention problems have persisted. To combat attention issues, St. Jude will test the use of computer software designed to increase attention and working memory.

In addition, through genomic testing, scientists are able



PETER BARTA

As part of the Total 17 clinical trial, Veronica Gonzalez-Pena, PhD (left), and Chuck Gawad, MD, PhD, both of Oncology, sequence both the normal and leukemic cells of patients.

SETH DIXON

Kiri Ness, PhD, of St. Jude Epidemiology and Cancer Control, helps Brooke Brantner understand how standing on a vibrating plate could help prevent bone density loss.

to determine which patients require more chemotherapy administered into the spinal fluid. If a child has lower-risk disease, that individual will receive lower frequencies of treatment, thus avoiding the potential for attention problems.

Because the steroids used in treatment may affect bone density, clinicians will use an intervention that requires the patient to stand on a vibrating plate—a therapy that may prevent bone density loss.

Finding cures more quickly

As the largest clinical trial ever run by St. Jude, Total 17 aims to treat 1,000 children—a massive undertaking that requires the collaboration of institutions throughout the U.S. By enrolling many children in the study, scientists can accrue data more quickly and share their findings worldwide.

"ALL is now divided into more than 20 subgroups," Inaba explains. "To study that, we need a large number of patients. I think such a high-quality, meticulous study can only be done by St. Jude. Our strength is the quality of our genomic testing and our dedicated patient care. But we also want to prove that the St. Jude way can be exportable to other institutions."

Attitude of gratitude

After completing the first month of therapy, Brooke remains upbeat and optimistic. Today, she colors an intricate picture during a seven-hour chemotherapy infusion. Although fighting fatigue, the sixth-grader is talkative.

"Mommy, the only thing that has energy is my mouth," says Brooke, who anticipates the day she can return to a normal life of riding bicycles and hanging out with friends; petting her dog, Snickers; and snuggling with her black cats, Perky, Ninja and Allison.

Although Wendi also anticipates that future homecoming, she says she appreciates the excellent medical care her daughter is receiving.

"This has been the most amazing experience," she says. "You don't feel sadness here; you feel hope and love and comfort. I'm so grateful to be here, and I couldn't imagine a better place for Brooke." ■

research highlights

Scientists learn to shutter flu 'factories'


PETER BARTA

Paul Thomas, PhD, and Heather Smallwood, PhD

The influenza virus is like an efficiency expert who arrives to launch production of a new product and to dramatically increase factory output. In this case, the "factories" are flu-infected lung cells whose output is more virus.

St. Jude scientists have a new strategy to shut down these flu factories. The method aims to dial back production of new flu virus to ease flu symptoms and speed recovery.

Researchers showed that the flu virus revs up the metabolism of flu-infected cells. They also found drugs, including the experimental cancer drug BEZ235, that can restore normal cell metabolism. As metabolism slowed so did flu virus production. Then flu symptoms eased, and survival rates in model systems increased.

In contrast, current anti-flu drugs work by directly targeting the flu virus.

"Targeting infected cells rather than the flu virus should help to avoid the problem of the virus mutating and becoming resistant to the drugs," said Paul Thomas, PhD, of St. Jude Immunology. "Some flu strains are already resistant to available anti-viral drugs. Flu-related complications remain a leading cause of hospitalization and death worldwide for the very young, the very old and those with chronic illnesses or compromised immune systems. This is another possible tool to combat the infection."

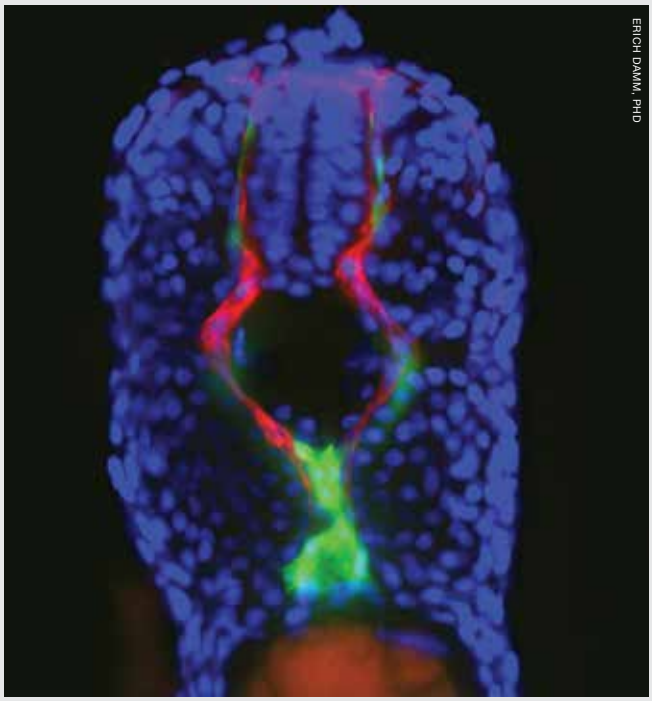
The research appeared in *Cell Reports*.

Finding offers clues for making 'donor blood' for therapeutic use

For patients with cancer and blood diseases, bone marrow transplantation can be life-saving. But a lack of donors remains a problem.

Like private investigators on a stakeout, St. Jude scientists used patience and video surveillance-like tools to identify cells that trigger blood cell development. The findings offer clues for making blood-forming cells in the laboratory that may ultimately help improve access to bone marrow transplantation.

Wilson Clements, PhD, of St. Jude Hematology, and his colleagues used strategies such as time-lapse video to identify cells that direct master cells to become blood cells. A report on this work appeared in *Nature Cell Biology.*


ERICH DAMM, PHD

A fluorescent image of blood-forming cells

Downing, Mullighan receive national awards

PETER BARTA

Charles Mullighan, MBBS, MD (left), and James R. Downing, MD

Two St. Jude scientists were recently recognized for their achievements in cancer research.

President and Chief Executive Officer James R. Downing, MD, received the 2017 Society of Memorial Sloan Kettering Prize, which recognizes an individual who has made exceptional and significant contributions to the field of pediatric oncology.

"Dr. Downing's leadership and vision in the field of pediatric oncology are truly monumental," said Andrew Kung, MD, PhD, chair of Pediatrics at Memorial Sloan Kettering. "Because of his discoveries, we have seen a true impact and major advances for pediatric patients globally. Furthermore, these advances are important as they make a difference to the littlest and most vulnerable patients."

Charles Mullighan, MBBS, MD, of St. Jude Pathology, received the National Cancer Institute Outstanding Investigator Award. He and his lab have used genomic profiling and experimental modeling to make significant advances in identifying and understanding high-risk and relapsed leukemia. Award recipients are cancer researchers who have served as principal investigators on recent NCI grants and who have demonstrated outstanding productivity.

Researchers unlock immunity 'black box'

A research team led by St. Jude immunologists has revealed a previously unknown immune machinery that goes awry to trigger an inflammatory skin disorder that may accompany cancer, infections or inflammatory bowel disease.

Mapping the biological machinery underlying the disease's inflammation is important because drugs targeting similar inflammatory disorders are not available. Currently, the only treatments for such disorders are strong immunosuppressive drugs that also render patients susceptible to infection.

The researchers discovered that a protein known as IL-1 alpha is a master immune switch that provokes an uncontrolled immune response. The scientists also found several key molecules that drive inflammation and tissue damage.

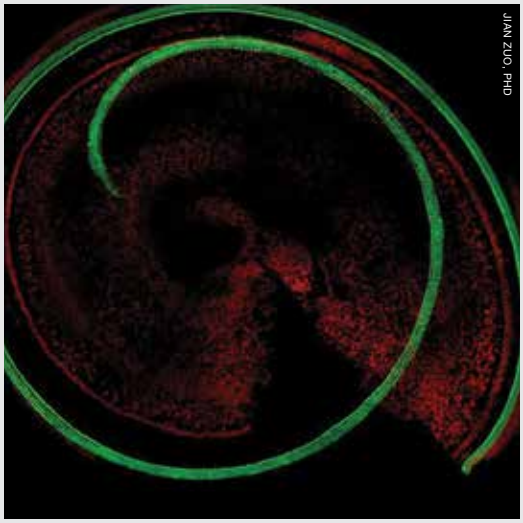
PETER BARTA

Thirumala-Devi Kanneganti, PhD

"This is quite an important finding," said Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology. "IL-1 alpha was discovered more than 45 years ago, but we have not known how it is regulated and how it functions. And our lab is one of the very few in the country studying IL-1 alpha."

A report on the study appeared in the journal *Immunity*.

Hearing what Mother Nature has to say



The cochlea in the inner ear

We are born with about 16,000 auditory hair cells. These cells are in the cochlea of the inner ear. They are needed to translate sound waves—from the softest rustling leaves to the loudest thunder clap—into nerve impulses that are interpreted in the brain.

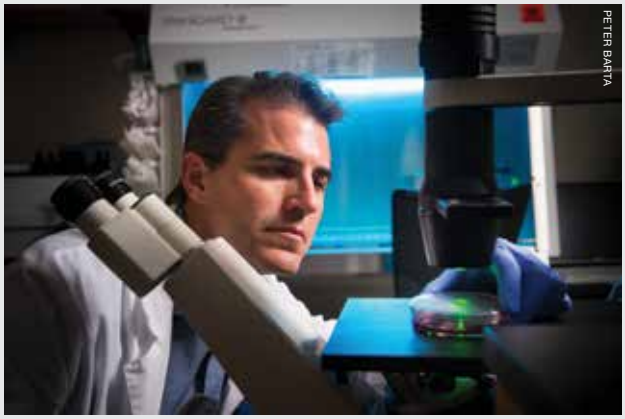
Hearing is lost for good if too many hair cells are damaged due to aging, loud noise or illness; or by certain drugs, including chemotherapy agents used to treat certain childhood cancers. That is because unlike fish or birds, humans cannot regrow these cells.

In the lab, St. Jude scientists used clues from nature to advance efforts to regrow hair cells in humans. By switching some genes on and off in specific inner-ear cells, scientists caused those cells to look and act like immature auditory hair cells.

"We looked to Mother Nature for answers, and we were rewarded," said Jian Zuo, PhD, of St. Jude Developmental Neurobiology. "The results suggest that regenerating auditory hair cells will likely require multiple factors to stimulate the process."

The research appeared in *Cell Reports*.

Discovery offers clues to cancer's origins



Michael Dyer, PhD

A team from the St. Jude – Washington University Pediatric Cancer Genome Project has mapped the intricate changes that cause immature cells to change into mature neurons in the retina. The retina is the thin membrane in the eye that is stimulated by light. Retinoblastoma is a rare cancer of the retina.

The researchers also mapped the epigenome of retinoblastoma cells as they turn cancerous. While the "genome" of thousands of individual genes is like data stored on a computer disk, the "epigenome" is like a computer program that controls how stored data are read. Malfunctions in the epigenome can drive cancers and degenerative diseases.

Scientists have been trying to crack the "epigenetic code"—the specific changes in the organization of the nucleus that cause a cell to transform from an immature cell to a specialized cell.

"This study narrowed down the developmental window when the normal cell becomes a tumor cell," said Michael Dyer, PhD, St. Jude Developmental Neurobiology chair. Instead of happening during cell division, the event occurred when cells transitioned from rapid growth to differentiation. "This insight will allow us to focus on that stage to better understand how retinoblastomas originate," Dyer said.

The work appeared in the journal *Neuron*.

The Power of Science

David Phillips, PhD, and Mary Phillips

Former St. Jude faculty member helps fund sickle cell disease research at the hospital.

By Kerry Healy

David Phillips, PhD, and his wife, Mary, are firm believers in the power of medical science to find better treatments and cures. Phillips, a distinguished scientist, professor and biotech entrepreneur, is a former researcher for St. Jude Children's Research Hospital.

The couple recently made a generous gift in support of the hospital's sickle cell disease research.

"The focus of my work at St. Jude was initially to study membranes of red cells, which subsequently led us to platelets and their role in thrombosis (the formation of blood clots)," Phillips says. "St. Jude has always had a sickle cell program, and I became interested in the disease early in my career."

Phillips served for 12 years in the hospital's Biochemistry department, first as a postdoctoral fellow in the laboratory of his mentor, Martin Morrison, PhD, and later as a faculty member. The couple and their two sons then returned to their native California, where he worked as a senior scientist at the Gladstone Foundation Laboratories for Cardiovascular Disease and as a professor at the University of California, San Francisco.

"Since leaving UCSF, I have had the opportunity to co-found three biotech companies," Phillips says. "Two of these, COR Therapeutics and Portola Pharmaceuticals, were involved in the discovery and development of novel antithrombotics." These drugs prevent the formation of blood clots.

This work rekindled the Phillips' interest in sickle cell disease. Understanding the recurring pain, organ damage and early death faced by many of these patients, Phillips and his wife resolved to financially participate in research at St. Jude.

Under the direction of Mitchell Weiss, MD, PhD, St. Jude Hematology chair, scientists are using a sophisticated gene editing technique to modify sickle cell patients' DNA to correct the disease in the lab.

"It's exciting to see the technology at St. Jude," Phillips says. "The work they are doing is just terrific and has potential to revolutionize the treatment of sickle cell disease.

"The hospital has made a great commitment in terms of sickle cell disease—to the patients and to the research," he says.

"St. Jude is a place of great integrity and innovation," Mary adds. ■

> "We want to help find a cure. We want to make the lives of these patients better."

A Calling to CARE

SETH DIXON

For one childhood cancer survivor, nursing is not a career, but a calling.

By Ashley McTyre, RN

When the idea of a medical career first crossed my mind, I was a 10-year-old patient at St. Jude Children's Research Hospital receiving treatment for the bone cancer osteosarcoma. During the most fearful time of my life, my St. Jude nurses cared for me and for my entire family. That experience inspired me to do the same for others.

"At St. Jude, I work beside amazing co-workers as part of an incredible team united in a mission to save lives."

JUSTIN VENEMAN

Ashley McTyre, RN, enjoys taking care of St. Jude patients Rylee Hale (top), and Elizabeth Wampler (bottom).

For the past three years, I've had the privilege of working among some of those same nurses and doctors.

At St. Jude, I've learned to cherish every moment. Life is precious, and each day is truly a gift. I've learned to celebrate the milestones throughout treatment, no matter how big or small. I've also learned that patient care is not just about the patient, but about the entire family.

I want our patients and families to know that this is not just a career for me, but a calling. When you care for these families, they become a piece of your heart. I want to bring them joy even in their darkest hours.

I'm just a small part of an amazing team that works together for every child and family who enters the doors of St. Jude. These precious kids have taught me how to persevere. It's wonderful to walk into their rooms and see their faces light up or to see a smile spread across a parent's face. I want them to feel the love and concern I have for them.

At St. Jude, I work beside amazing co-workers as part of an incredible team united in a mission to save lives. Our nurses and doctors are exceptional in their pursuit of excellence. We work extremely hard, but we laugh together, we cry together and we share life together.

I'm blessed and honored to be a part of this wonderful hospital—the one that saved my life and now is giving me the great privilege and great responsibility to care for others walking the same path. ■

Ashley McTyre, RN, is a pediatric oncology nurse in the Solid Tumor/Neuro-Oncology Inpatient Unit at St. Jude.

Their future starts with your legacy.

"I decided to leave St. Jude in my will because I want to continue helping the children just as my mother did."

—Carol Ayoub

St. Jude patients
Abigail (left), leukemia
and Gracie (right), leukemia

Establish a lifesaving legacy with St. Jude.

A gift to St. Jude in her will costs Carol nothing now, yet gives her the satisfaction of knowing her legacy will continue into the future, helping to save the lives of children, like Abigail and Gracie, battling cancer and other life-threatening illnesses.

Begin your legacy today.

1-800-910-3188 | stjude.org/legacy

St. Jude Children's Research® Hospital
ALSAC • Danny Thomas, Founder
Finding cures. Saving children.

St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
501 St. Jude Place
Memphis, TN 38105

Non-Profit Org.
U.S. POSTAGE PAID
St. Jude Children's Research Hospital

Top billing

U.S. News & World Report recently ranked St. Jude as the nation's No. 1 pediatric cancer hospital in its "Best Children's Hospitals" list. St. Jude President and Chief Executive Officer James R. Downing, MD, joined patients Sophia Kaplanis (center) and Tashayla Clayton in celebrating the ranking.

St. Jude is the only National Cancer Institute–designated Comprehensive Cancer Center devoted solely to children, having received the NCI's highest ranking of "exceptional. The hospital has top survival rates for some of the most aggressive childhood cancers, including acute lymphoblastic leukemia and medulloblastoma. St. Jude creates more cancer clinical trials than any other children's hospital in the U.S., and unlike most hospitals, no family receives a bill from St. Jude for anything, including treatment, travel, housing or food.

SETH DIXON

Finding cures. Saving children.