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

LINDSEY GRUWELL **HEADRICK**

PETER BARTA

Super-conducting magnet

Charalampos Babis Kalodimos, PhD, Structural Biology chair (left) and Youlin Xia, director of the Center for Biomolecular NMR Spectroscopy, supervise delivery of the world's largest superconducting magnet. The 1.1 GHz nuclear magnetic resonance (NMR) spectrometer will enable scientists to look deeper into a cell than ever before. A million times stronger than the earth's magnetic field, the 10-ton, $10 million magnet will help scientists understand health and disease at the molecular and atomic level.

Cover Story

Features

News and Highlights

Life after St. Jude

SETH DIXON

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ON THE COVER: Photo of Lindsey Gruwell Headrick by Seth Dixon

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.

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Research Highlights

Childhood cancer affects 11.5 million years of life

A NEW STUDY shows there is a much greater burden of childhood cancer in low- and middle-income countries than previously thought.

A St. Jude – Institute for Health Metrics and Evaluation study is changing how pediatric cancer is viewed worldwide. Researchers looked at the number of years of life affected by cancer. It is the first time this metric has been used to analyze the childhood cancer burden globally.

Evaluating impact by years of life affected may provide a more complete view of global cancer burden. In childhood cancer, early deaths mean many years of life lost. Survivors can also live for many years with chronic disability.

"Previous estimates put the childhood cancer burden in the hundreds of thousands globally," said Nickhill Bhakta, MD, of St. Jude Global Pediatric Medicine. "By looking at a different metric, disability-adjusted life years, we can now show for the first time that this burden is significant and underappreciated in both the cancer and child health communities."

The study shows that globally in 2017 about 11.5 million years of life were affected due to childhood cancer. Of these, 97.3% were due to years of life lost.

Most of this burden occurs in low- and middle-income countries in Asia, Africa, and Central and South America. This metric is comparable across diseases. The study's results may help experts set public health priorities.

This work was published in *Lancet Oncology*.

Lisa Force, MD, and Nickhill Bhakta, MD

Research Highlights

SETH DIXON

Diantha van de Vlekkert and Alessandra d'Azzo, PhD

We can learn from rare disorders

RARE DISEASES CAN help answer questions about cell biology and common health problems.

Take sialidosis. It's caused by mutations in the gene encoding the lysosomal enzyme NEU1. Deficiency of this enzyme disrupts the normal function of muscles and many other organs. As many as 1 to 4 people per 200,000 inherit this life-threatening childhood disease.

Alessandra d'Azzo, PhD, of St. Jude Genetics studies sialidosis and NEU1. Her research into sialidosis has also provided clues about cancer, Alzheimer's disease and aging.

Her team recently linked another health problem with NEU1 deficiency: Fibrosis.

Fibrosis is the build-up of connective tissue in the heart, lungs and other organs. This disorder interferes with organ function. The cause is often unknown.

The scientists found how NEU1 deficiency fuels the expansion of connective tissue into muscle and other organs.

"The results suggest that NEU1 may be helpful for identifying those at risk for developing fibrosis or monitoring its progression," d'Azzo said.

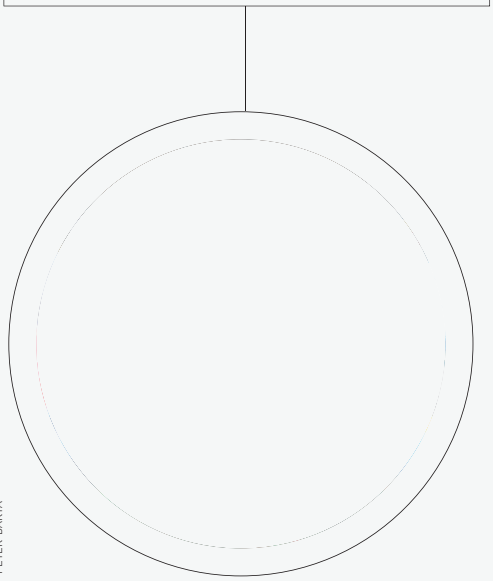
A report on this work appeared in the journal *Science Advances*.

Researchers find genetic trigger that compromises immunotherapy

AN INTERNATIONAL research team has discovered a gene that triggers a process called "exhaustion" in the T cells used to battle cancer in immunotherapy.

The gene, called *Tox*, launches a process that remodels the cells' machinery to weaken their ability to attack cancer cells, as well as infections. Such immunotherapy – in which a cancer patient's own immune cells are activated to detect tell-tale proteins called antigens on cancer cells – is highly promising. However, T cell exhaustion has proven a daunting barrier to the therapy.

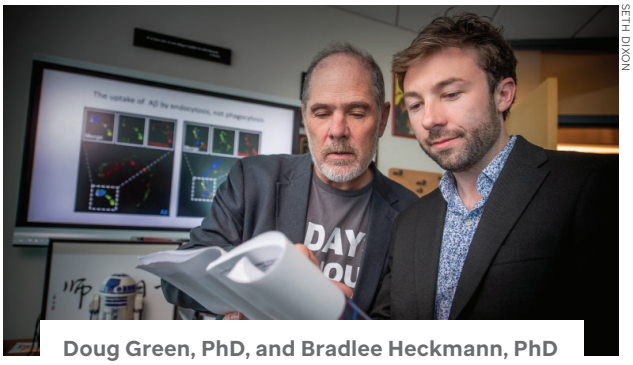
The discovery, published in the journal *Nature*, could lead to diagnostic tests to detect T cell exhaustion. The researchers hope their basic findings will also result in techniques to prevent this process.



PETER BARTA

Yiping Fan, PhD, and Ben Youngblood, PhD

Pathway discovered: prevents buildup of Alzheimer's protein



SETH DIXON

Doug Green, PhD, and Bradlee Heckmann, PhD

RESEARCHERS studying the immune response to cancer have discovered a pathway that clears a toxic protein that is a hallmark of Alzheimer's disease.

The pathway works by preventing the buildup of a protein called beta-amyloid. The protein accumulates in the brains of Alzheimer's patients and disrupts brain function.

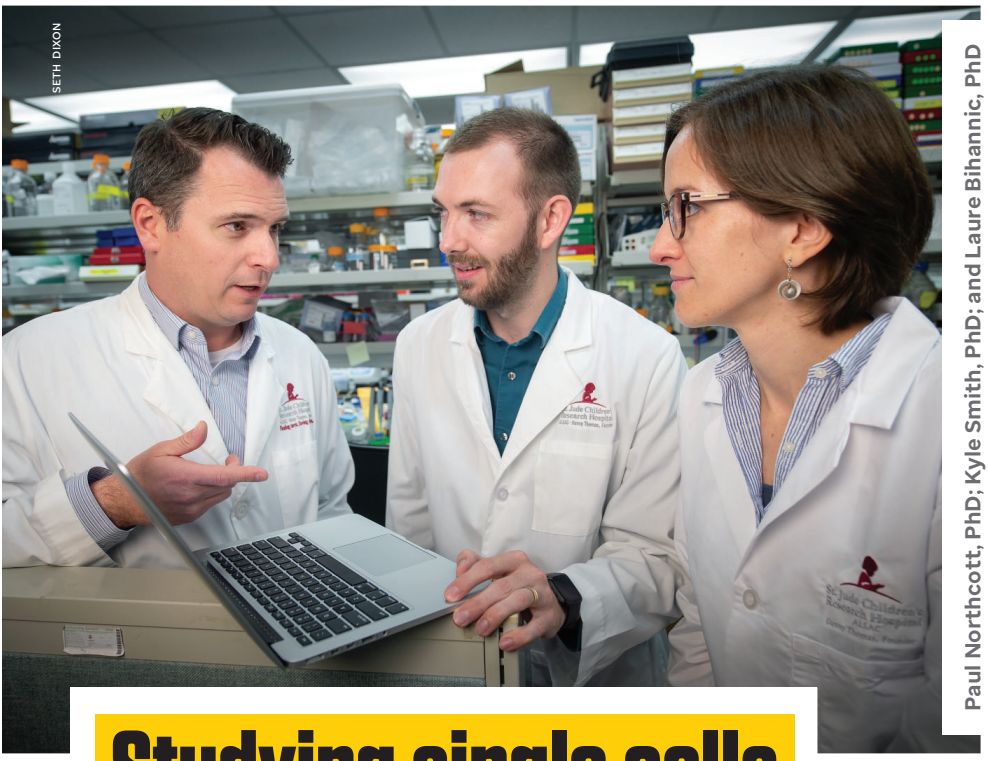
The shorthand name for the pathway is LANDO. This pathway also regulates inflammation, which can help rally the immune system against cancer. Chronic inflammation contributes to diseases like Alzheimer's.

Without LANDO, beta-amyloid accumulated rapidly in mouse brains. The mice showed signs of memory loss and other problems that mimic Alzheimer's disease. Researchers are exploring ways to regulate the pathway.

"That's how science works," said Douglas Green, PhD, St. Jude Immunology chair. "When you follow the data you never know where it will lead."

Cell published a report on this work.

Research Highlights



SETH DIXON

Paul Northcott, PhD; Kyle Smith, PhD; and Laure Bihannic, PhD

Studying single cells to understand a type of pediatric brain tumor

MEDULLOBLASTOMA is the most common malignant childhood brain tumor. It has four subtypes. Two of them, Groups 3 and 4, account for 60% of cases. They are the least understood.

Scientists completed the most in-depth study to date of medulloblastoma subtypes. To do that, they studied single cells. This helped shed light on how the cells become cancerous.

"The ability to look at these single cells propelled us 10 steps forward in understanding how the types of medulloblastoma arise, what drives them and how we can make treatments more effective," said Paul Northcott, PhD, of St. Jude Developmental Neurobiology.

The scientists found the first cell of origin for Group 4. They also learned more about the relationship between Groups 3 and 4.

The findings may help scientists create lab models of the disease and design future clinical trials.

St. Jude worked on the project with Massachusetts General Hospital, the Broad Institute of MIT and Harvard, Dana-Farber Cancer Institute and others.

Nature published a report on this work.

BRCA2 gene linked to non-Hodgkin lymphoma risk

A ST. JUDE STUDY linked inherited mutations in the *BRCA2* gene with a higher risk of non-Hodgkin lymphoma.

The work focused on childhood cancer survivors. The team looked at 1,380 survivors of pediatric lymphoma.

"*BRCA* genes have been linked to adult cancer for many years," said Zhaoming Wang, PhD, of the Epidemiology and Cancer Control and Computational Biology departments. "Our study shows a relationship between *BRCA2* and non-Hodgkin lymphoma in childhood cancer survivors."

Genetic counseling and *BRCA2* testing could be useful for survivors of childhood non-Hodgkin lymphoma. Survivors with a family history of *BRCA2*-associated cancers may also be tested.

A report on this work appeared in *JAMA Oncology*.

By Elizabeth Jane Walker

A blue-sky process yields new projects designed to accelerate the mission of St. Jude.

The Sky's the Limit

SOME EXCITING NEW PROJECTS ARE POPPING UP at St. Jude Children's Research Hospital. They're audacious in scope. Optimistic. Filled with wonder and hope, creativity and grit.

Since its founding in 1962, St. Jude clinicians and researchers have asked and answered "what-if" questions that have changed the landscape of childhood catastrophic diseases. Today, the hospital is guided by a strategic plan that outlines a bold strategy for the future. But other opportunities arise constantly. Technologies evolve. Priorities expand.

What if there were a way to identify and pursue bold new projects that could further transform science and medicine?

Now there is. It's called the blue-sky process.

"We want to challenge people to come up with new ideas that have a game-changing impact," explains James R. Downing, MD, St. Jude president and chief executive officer. "We want to look beyond the priorities of our strategic plan to identify unique opportunities that will accelerate our mission-critical objectives and test novel scientific and clinical approaches."

All faculty and staff members can submit blue-sky ideas. Proposals that are deemed innovative and impactful receive funding, and the work begins. On the following pages, you'll get a glimpse of seven questions we're working to answer.

PETER BARTA

What if ... we could prevent adult cancers by vaccinating children?

DID YOU KNOW 1 out of every 4 people in America is infected with a virus that causes cancer? Each year, more than 31,000 individuals are diagnosed with cancer caused by the human papillomavirus (HPV).

But wait — There's good news. A vaccine is available. When given to boys and girls in their early teens, the two-part vaccine helps them avoid infection and subsequent cancer development.

Despite that simple fix, HPV vaccination remains low. In fact, the nation's lowest immunization rates and highest number of HPV-related cancers occur in the region where St. Jude is located.

"Pediatric cancers can't be prevented, but we can reduce the risk of preventable cancers later in life," says Charles Roberts, MD, PhD, director of the St. Jude Comprehensive Cancer Center. "Our goal is to reduce cancer deaths by establishing a premier HPV prevention initiative."

This blue-sky project features collaborations with local, regional and national partners, as well as state and federal policy changes. Through the HPV cancer prevention blue-sky initiative, St. Jude will help lead the way in increasing vaccination rates.

"Together, we can help children eliminate their risk of HPV-associated cancers," Roberts says.

What if ... we could ease the transition to survivorship?

NO MORE CHEMO parties at St. Jude are joyful celebrations for patients completing treatment. But what happens after the confetti falls? For many families, the time of transition away from daily hospital visits is stressful, even scary.

"How will my child re-adjust to school?"

"Does a bruise or sniffle mean the cancer has returned?"

"What happens if I have a question in the months before our follow-up visit?"

The Transition Oncology Program (TOP) provides a safety net for patients who have finished treatment but are not yet eligible to enroll in the After Completion of Therapy (ACT) clinic, which generally occurs five years after diagnosis. Thanks to TOP, patients receive an extra layer of support from a multidisciplinary team.

"If you think of the primary oncology teams as the active cancer specialists, and the ACT team as the long-term survivor specialists, then you can think about the TOP team as being specialists for that in-between time of transition and uncertainty," explains the program's director, Emily Browne, DNP. "We have social workers, psychologists, nurse practitioners, school liaisons, and rehabilitation specialists ready to assess and address patients' physical, cognitive and psychosocial concerns."

PETER BARTA

What if ... we could give children worldwide a fighting chance for survival?

ONE CHILD LIVES in the U.S., while another hails from a developing nation. Which of those children would be more likely to survive a bout with cancer? Too often, the answer depends on where the child lives. Worldwide, more than 80% of children with cancer live in low- and middle-income countries. Most of those children will die from their diseases.

A program called St. Jude Global has already been making strides to improve survival rates. But what if St. Jude teamed up with World Health Organization (WHO) to turbo-charge that effort?

Thanks to a blue-sky initiative, that's what has happened. The result is the WHO Global Initiative for Childhood Cancer. As St. Jude works bottom-up with childhood cancer providers globally, WHO works top-down with governments, civil society and health-system leaders. St. Jude and WHO staff will analyze policies, medical workforce capacity and infrastructure. Together with other global stakeholders, they will develop and implement plans to improve the care for children with cancer around the world.

"This initiative unites health care providers, advocates and researchers from around the globe," says Carlos Rodriguez-Galindo, MD, Global Pediatric Medicine chair. "It marks the start of a new era in the worldwide fight for the lives of children with cancer."

What if ... we freely share discoveries with even more scientists?

PHOTOS BY SETH DIXON

WHEN ST. JUDE and Washington University launched the Pediatric Cancer Genome Project in 2010, the goal was to share data from that project with researchers worldwide.

In 2018, St. Jude launched an online data-sharing and collaboration platform called St. Jude Cloud. Suddenly, researchers had access to the world's largest public collection of childhood cancer genomics data. Researchers across the globe accessed the information and tools and performed computational analyses. But for many scientists, the process was cumbersome and time consuming — requiring significant computing resources and expertise to seamlessly download the data.

Thanks to the blue-sky process, St. Jude is enhancing the cloud infrastructure, tools and datasets. With more than 10,000 genomes, St. Jude Cloud holds more childhood cancer data than any other repository. The cloud is now user friendly for members of the scientific community.

"The design of St. Jude Cloud from its inception was to create a site that was not only useful for individuals with advanced computing skills, but that could be effectively used by clinicians and other researchers who might have limited computer skills," says Jinghui Zhang, PhD, St. Jude Computational Biology chair. "We think we've been successful in developing such a site."

SETH DIXON

What if … we find a new way to model pediatric diseases?

SCIENTISTS NOW HAVE a new way to model pediatric diseases — to study aspects of normal human biology and better determine how childhood diseases develop.

It starts when a patient or family member donates blood or skin cells. In the lab, scientists convert those cells into an immature state called induced pluripotent stem cells, or iPSCs. Researchers then guide the cells to differentiate into cell and organ-like structures that resemble various body tissues.

A blue-sky project will create a St. Jude core facility that uses samples donated by St. Jude patients to develop models for studying childhood cancers and neurological disorders. The models can also be used to assess how tumor-specific genetic mutations respond to new therapies. Scientists will use these models to assess the impact of gene-editing technologies on diseases caused by single gene defects, such as sickle cell disease.

"The generated iPSC cells and resulting models will be a shared resource for St. Jude investigators, but it's really for researchers around the globe," explains Michael Dyer, PhD, St. Jude Developmental Neurobiology chair and Howard Hughes Medical Institute investigator. "By freely sharing these models, we aim to accelerate research worldwide."

PETER BARTA

What if ... we could save the lives of kids with hemophilia worldwide?

CHILDREN WITH hemophilia B can have life-threatening bleeds because they lack a protein that causes the blood to clot normally. In the U.S., children with the severe form of the disease take protein-replacement therapy, which can cost about $1 million over their lifetimes.

In resource-challenged countries, most patients cannot afford this therapy, suffering severe bleeds that cause deformities and death.

How can we help those children?

At St. Jude, researchers have developed a gene therapy that can significantly decrease or eliminate patients' need for replacement therapy.

What if we could use this single-injection therapy for children around the world? St. Jude researchers have a blue-sky plan. It involves a feasibility study in low- and middle-income countries. A positive outcome could lead to a public-private partnership that might save the lives of children around the globe.

"We need to develop the protocol and get it approved, make sure the countries chosen have the right regulatory infrastructures and that the institutions have adequate support to monitor the patients," says Ulrike Reiss, MD, of St. Jude Hematology. "It's an exciting project with far-reaching possibilities."

What if ... we could understand the biology of neurologic disorders?

FOR DECADES, St. Jude clinicians and researchers have sought cures for catastrophic diseases such as cancer, sickle cell and HIV. But what about children with neurologic disorders? About 1 in 6 children has some form of neurologic disability — ranging from neurodevelopmental or movement disorders to neuromuscular diseases. Early intervention can prevent or slow the progression of these diseases.

The Center for Translational Neuroscience will build on a strong foundation of discovery science in cell biology and neuroscience and add additional faculty, projects and research capabilities to push the frontier in neurological diseases. As scientists work with clinicians to move these discoveries into the clinic, they will accelerate the pace of clinical trials and implement new cutting-edge therapies.

"We are expanding the scope of catastrophic pediatric diseases to be addressed by St. Jude," says J. Paul Taylor, MD, PhD, St. Jude Cell and Molecular Biology chair and Howard Hughes Medical Institute investigator. "Neurological diseases are among the greatest burden of catastrophic illness in children, and we are addressing this head on."

PETER BARTA

Where Leukemia Hides, the Immune System Seeks

Research challenges the notion that cancer cells must contain multiple mutations to prompt an immune response.

By Erin Podolak

MANY OF US HAVE PLAYED HIDE-AND-SEEK either as children or with our own kids. The basic principles of this backyard classic capture one of the central aspects of the human immune system: Our bodies are locked in a constant game of hide-and-seek. Things that might hurt us (such as viruses or cancer cells) try to hide, and the immune system seeks to find them before they cause problems.

Harnessing the power of the immune system to treat cancer has revitalized the field of immunotherapy in the last decade. However, this revolution in care has been slower to arrive in pediatrics. Drugs called checkpoint inhibitors modify the communication between cancer cells and immune cells. These drugs have helped achieve long-term success against some forms of cancer in adults but have been largely unsuccessful in children.

A mutation on a cancer cell is like posting a billboard that says, "Here I am; come get me." Without this signal, the immune system may not as easily identify cancer cells. Like other pediatric cancers, acute lymphoblastic leukemia (ALL) does not typically harbor many mutations. Some researchers have suggested that immunotherapies may not work as well for young patients because childhood cancers have fewer genetic mutations than adult cancers.

Research by Paul Thomas, PhD, of St. Jude Immunology challenges this notion, overturning researchers' assumptions about how ALL and the immune system communicate.

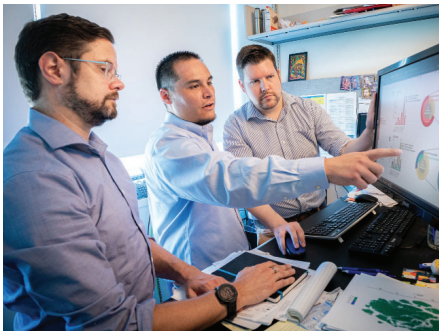
SPYING ON THE IMMUNE SYSTEM

To better understand how the immune system responds to ALL, Thomas and his team looked at specialized immune cells called CD8+ T cells. These immune cells attack cancer cells by recognizing patient-specific mutations.

Surprisingly, the researchers found that CD8+ T cells recognize 68%–86% of mutations found in pediatric ALL.

"In the game of hide-and-seek, leukemia is losing. It can't stay hidden from the immune system; quite the opposite, in fact," Thomas explains. "The immune system finds the leukemia, which shows us that the number of mutations present in a specific type of cancer does not necessarily dictate the ability of the immune system to recognize those cells as cancerous."

PETER BARTA



From lab to clinic

"We've shown that it is possible for the immune system to effectively target ALL. Now, it is a matter of finding the right therapy," says Anthony Zamora, PhD (center), who collaborated with (from left) Paul Thomas, PhD, and Jeremy Crawford, PhD, on the discovery.

Recently, the researchers published an article in *Science Translational Medicine* explaining why the immune system can recognize ALL in such high numbers. The scientists drew a comparison between the way the immune system responds to viruses and cancer.

Large viruses — like tumors that contain many mutations — have more potential targets for the immune system to detect. This leads to a process called immunodominance, where the immune system response focuses on a limited number of the most important viral targets. This process may be at work in childhood ALL, where the immune system is still focusing on the most important cancerous targets but may be relying on a greater percentage of those mutations to figure out what to attack.

"In the game of hide-and-seek, leukemia is losing. It can't stay hidden from the immune system; quite the opposite, in fact."
– Paul Thomas, PhD

HINTING AT A DIFFERENT TREATMENT

Immunotherapy for pediatric cancers is just starting to take root. These types of strategies may play an important role in the future of pediatric ALL treatment, particularly for patients whose disease has relapsed, and for whom conventional therapies are ineffective. Although some investigators may have written off immunotherapies such as checkpoint inhibitors for pediatrics, Thomas and his team have now shown that these strategies could be viable.

Additional research on immunotherapy for ALL will look to identify different ways of revving up T cells to attack leukemic cells. One potential path forward for immunotherapy for ALL is through cellular therapy approaches where T cells are modified to increase the specificity and magnitude of their response.

"We've shown that it is possible for the immune system to effectively target ALL," said Anthony Zamora, PhD, a postdoctoral fellow in Thomas' laboratory. "Now, it is a matter of finding the right therapy."

BRAVE New World

A new mobility program seeks to help critically ill patients return to normal activities as soon as possible.

By Mike O'Kelly

PAULA ELSENER REMEMBERS sitting by her son's side in the St. Jude Pediatric Intensive Care Unit (PICU) for 25 long days. Time seemed to bend. The calendar flipped from December 2018 to January 2019. The days dragged and seemed to blur together. Her 17-year-old son, Tristan, had beaten cancer a year earlier and now faced a new foe — acute myeloid leukemia — as a result of his treatment.

A few days into Tristan's PICU stay, he was placed on a ventilator because he was too weak to breathe on his own. Paula's days consisted of three segments: "before rounds," "rounds" and "after rounds." During rounds, she discussed Tristan's condition with his clinical team. She was hopeful, anxiously awaiting the moment he would open his blue eyes again.

While Tristan was sedated, Physical Therapist Amanda Curry and Occupational Therapist Sarah Schwartzberg of St. Jude Rehabilitation Services visited him to introduce mobility techniques and to teach Paula how she could help.

"They taught me exercises and worked on passive stretches for Tristan, knowing that if he didn't keep moving he would lose mobility," Paula says. "I would pick up Tristan's leg and move it in certain directions and massage his arms."

STEP BY STEP

When Tristan awoke, he was weak and unable to move his arms and legs. His first goal was to hold his phone and turn on the power button. He slowly gained the strength for hand movements while the rehab team worked to sit him up in bed and, later, helped him rest in a wheelchair. After moving to an inpatient room, Tristan stood. Then he walked with a walker. Then he walked with a therapist. After 38 days, he was discharged to outpatient visits.

These guidelines for critical care patients are part of a new initiative at St. Jude called BRAVE (Beginning Restorative Activities Very Early). They are designed to help mobilize patients as soon as possible to decrease their time in the PICU, delirium and ventilation time.

WHAT'S EARLY MOBILITY?

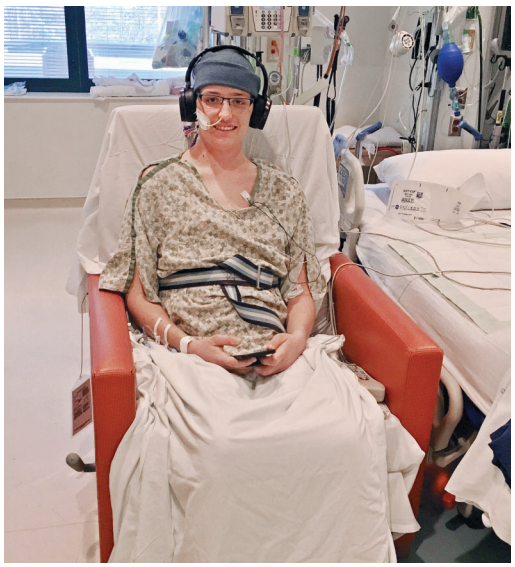
St. Jude patients range in age from newborns to older teens with varying degrees of illness. So, the definition of mobility is different for each patient.

"Early mobility is much more than just walking," Curry says. "It could be passive range of motion, or something as simple as turning a patient in bed or moving an infant into their parents' arms. The overall goal is to help our patients return to their regular activities as soon as possible."

Children begin to lose muscle mass after only two or three days of immobility in the PICU. That can lead to additional concerns once they awaken from sedation. The BRAVE program will help establish a baseline of mobility for each child upon admission to the PICU. Clinicians will assess patients daily and carefully document and study the progress.

Gaining momentum

Seven months after leaving the St. Jude Pediatric Intensive Care Unit, Tristan joins Physical Therapist Amanda Curry in an activity to evaluate how far he can walk in six minutes.



ANN-MARGARET HEDGES

"By focusing on early mobility, we have a concentrated approach to not only focus on short-term outcomes but also to help our patients improve long-term functioning after they are taken off sedation and leave the PICU," says Saad Ghafoor, MD, of St. Jude Critical Care.

MAKING STRIDES

These early techniques were invaluable for Tristan, who is now making strides toward increasing his activity level at his family's North Carolina home between monthly check-ups at St. Jude. He gets winded during half-mile walks, but he tracks his progress with a step counter.

"We're still working on his strength and endurance, but he has certainly come a long way," says Paula, who pauses for a moment as Tristan walks up and down the stairs of their home as part of his therapy.

"Developing that bond with our therapists early in the PICU was beneficial for Tristan and me, and it continues throughout our St. Jude experience," she says. "That consistency of care is crucial."

"By focusing on early mobility, we have a concentrated approach to not only focus on short-term outcomes but also to help our patients improve long-term functioning after they are taken off sedation and leave the PICU."
– Saad Ghafoor, MD

Together: Powered by St. Jude

By Keith Crabtree, PhD

A new online resource brings families and St. Jude experts together to face pediatric cancer.

LOOKING BACK, Jillian Bolding says tending to her son's gastrostomy tube (G-tube) was difficult. In 2017, her 7-year-old son, Alexander, was diagnosed with medulloblastoma, a brain tumor. She and her husband, David, turned to St. Jude Children's Research Hospital for help.

"It's not just about the cancer," Jillian says, recalling her G-tube struggles. "It's about the other things that go along with it. I wish there had been somewhere for us to find information in one place."

The tube, needed to deliver drugs and food, was inserted through Alexander's abdomen and into his stomach. When asked, Jillian didn't hesitate to share photos of its use and care with other families via a new online resource for pediatric cancer called Together.

GERM OF AN IDEA

In 2014, James Downing, MD, St. Jude president and chief executive officer, asked a simple question: "Can St. Jude develop a website that has everything families need to know?"

When faced with questions after a cancer diagnosis, many parents turn to the Internet for answers. Which sites are trustworthy? It's hard for parents to know what to click and what to ignore.

Downing wanted St. Jude to build an authoritative resource where families all over the world — not just those at St. Jude — could learn about pediatric cancer, its diagnosis and treatment, care and support, and life after cancer.

BUILT FOR FAMILIES

Diane Roberts, director of medical content and patient outreach, says the Together name reflects a key St. Jude ethos: "We're in this together with patients and families."

Patients and families have been involved every step of the way, offering input about their information needs and preferences as well as sharing their experiences in support of other families facing similar journeys.

The launch of Together in September 2018 was a first step. The site now contains more than 450 pages, including 118 medication summaries, 67 videos and 20 medical illustrations. Earlier this year, the Together team won the Center for Plain Language's ClearMark award for best website, topping the Centers for Disease Control and Prevention.

"Every single page was developed from the ground up," Roberts says, noting that more than 200 St. Jude subject-matter experts made Together possible. St. Jude pediatric oncologist Jamie Flerlage, MD, understands the significance of this effort.

"One thing that is very important to me is having an up-to-date and trustworthy site for patients and families to go to," Flerlage says. "There is a need for something reliable, and it brought all of these experts together."

FILLING A GLOBAL NEED

In the last year, people from countries large and small — China and Croatia, India and Iceland — have accessed Together. Last count: 151 countries, all 50 states and all 10 Canadian provinces.

The need for this resource is clear. Earlier this year, Roberts attended a pediatric oncology meeting in Europe.

"It was remarkable," she says. "We had people from over 35 countries approach us."

This highlighted the next step — translating the site into multiple languages.

The Spanish Together site is up, and Together will be available in five additional languages before 2020 with more planned.

PAY IT FORWARD

Roberts talks about a "pay-it-forward" attitude. She sees it again and again: patients, families and health care professionals coming together to provide a resource so that no family has to face pediatric cancer alone.

"It's not just about helping my patients, it's about helping all children with cancer," Flerlage says. "This website is another example of sharing this wealth of knowledge and resources we have at St. Jude with as many people as possible."

Alexander, who turned 9 on his first day of school, loves fishing, bugs and playing Minecraft. If someone asks a question, he says, "I don't have a second belly button. This is actually from my G-tube."

"I knew the photos of his G-tube would benefit other moms," Jillian says. "I did it in the hope of helping other mamas."

VISIT TOGETHER:
https://together.stjude.org
SUGGESTIONS WELCOMED AT
together@stjude.org.

Together users hail from countries that include:

Albania
Algeria
American Samoa
Antigua & Barbuda
Argentina
Armenia
Australia
Austria
Azerbaijan
Bahamas
Bahrain
Bangladesh
Barbados
Belarus
Belgium
Benin
Bhutan
Bolivia
Bosnia & Herzegovina
Botswana
Brazil
British Virgin Islands
Brunei
Bulgaria
Burkina Faso
Cambodia
Cameroon
Canada
Chile
China
Colombia
Costa Rica
Croatia
Cyprus
Czechia
Democratic Republic of the Congo
Denmark
Dominican Republic
Ecuador
Egypt
Estonia
Ethiopia
Fiji
Finland
France
Georgia
Germany
Ghana
Greece
Grenada
Guadeloupe
Guam
Guatemala
Guyana
Haiti
Honduras
Hong Kong
Hungary
Iceland
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Jordan
Kenya
Kosovo
Kuwait
Kyrgyzstan
Laos
Latvia
Lebanon
Liberia
Libya
Lithuania
Luxembourg
Macao
Malawi
Malaysia
Maldives
Malta
Mauritius
Mexico
Moldova
Mongolia
Montenegro
Morocco
Myanmar (Burma)
Namibia
Nepal
Netherlands
New Zealand
Nicaragua
Nigeria
North Macedonia
Northern Mariana Islands
Norway
Oman
Pakistan
Palestine
Panama
Papua New Guinea
Peru
Philippines
Poland
Portugal
Puerto Rico
Qatar
Romania
Rwanda
Russia
Saudi Arabia
Serbia
Sierra Leone
Singapore
Slovakia
Slovenia
Somalia
South Africa
South Korea
South Sudan
Spain
Sri Lanka
St. Kitts & Nevis
St. Lucia
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Sweden
Switzerland
Syria
Taiwan
Tanzania
Thailand
Trinidad & Tobago
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Uganda
Ukraine
United Arab Emirates
United Kingdom
United States
Uruguay
Venezuela
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Zambia
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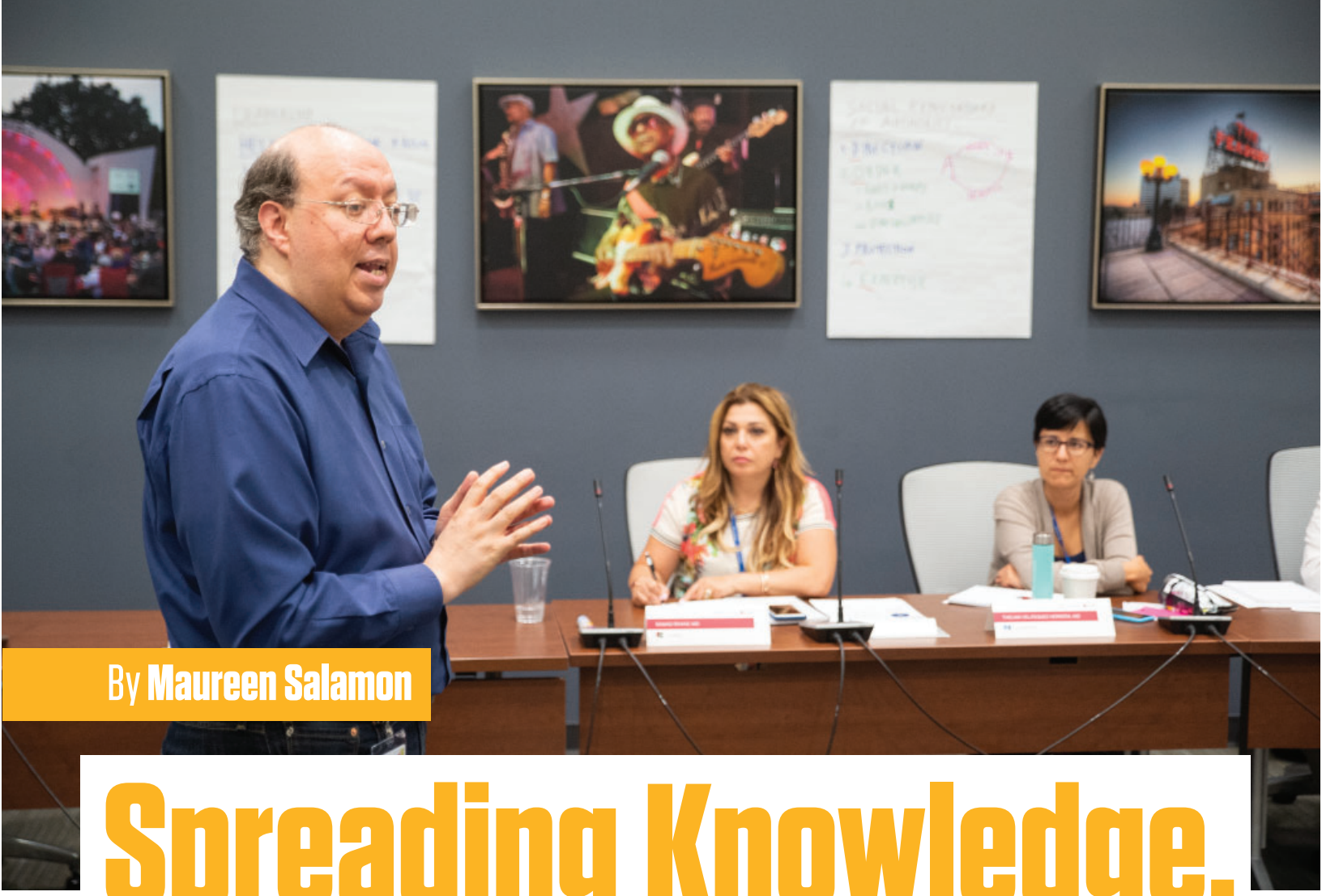


By Maureen Salamon

Spreading Knowledge, Saving Children

Unique master's program in Global Child Health trains health care professionals around the world.

AS A GIRL GROWING UP IN INDIA, Shaloo Puri, MD, had few career choices. After choosing medicine – and a career in global health at institutions such as Harvard and World Health Organization – she yearned to inspire others as an educator.

In 2018, she arrived in Memphis to develop and direct a unique master's program in the St. Jude Children's Research Hospital Graduate School of Biomedical Sciences. As Puri and her colleagues train health care professionals from around the world in global child health, they'll spread the impact of St. Jude far beyond its Tennessee roots.

FIRST-CLASS PROGRAM

The Master of Science program in Global Child Health incorporates the world-renowned faculty of the Graduate School with the expertise of the St. Jude Global Pediatric Medicine department.

The program's online courses in research methods, population sciences, global health and health systems are tailored to child health. Students also gain management, leadership and communication skills. The inaugural class of 10 students from 10 countries consists of seasoned clinicians and health administrators.

JUSTIN VENEMAN

Inspiring impact

"There are lots of master's programs out there and some similar ones in prominent places, but we have a niche because ours is focused in pediatrics," says Stephen White, DPhil, president and dean of the St. Jude Children's Research Hospital Graduate School of Biomedical Sciences.

SETH DIXON

Stephen White, DPhil

PETER BARTA

Shaloo Puri, MD

JUSTIN VENEMAN

Students in the program travel periodically to St. Jude for on-campus workshops while remaining in their professional roles. As they return home and complete online coursework, they can immediately apply what they've learned to reach the most vulnerable in their countries.

"We all have the same goal, which is to improve the care of children with cancer in our countries," says student Liliana Vasquez, MD, who hails from the Ministry of Health in Peru. "This program is going to change the future of many children with cancer in developing countries, by training leaders who will make changes in the system."

A SINGULAR FOCUS

The new master's program comes several years after the launch of the St. Jude Children's Research Hospital Graduate School of Biomedical Sciences, where three cohorts of students are currently pursuing doctorates. The program aligns with the goals of St. Jude Global, which brings the hospital's clinical practices and treatments to the world.

"One of the big ways of doing that is to teach the teachers," explains Stephen White, DPhil, the school's president and dean. "There are lots of master's programs out there and some similar ones in prominent places, but we have a niche because ours is focused in pediatrics."

The students will learn to assimilate scientific evidence and apply analytical tools and integrative thinking to develop and implement evidence-based programs and policies. Those skills, complemented by leadership and management training, will help them address needs in their own clinics and hospitals. As they educate their colleagues and implement new processes, the students can help improve children's care.

The students will also write master's theses that propose projects to solve important child health issues. Select projects will be considered for funding by St. Jude .

"We're creating agents of change by providing health care professionals around the world with skills and knowledge to improve treatment, care and survival rates of children with cancer and other illnesses," Puri says. "That perfectly aligns with the values and mission of St. Jude ."

MAKING AN IMPACT

Adriana Porras, MD, works in the only children's hospital in Costa Rica. She often treats immigrant children with cancer and other dire illnesses who live in an overflowing hospital shelter.

When Porras attended student orientation, she quickly became inspired.

"Much of the money at St. Jude comes from donations, and that made me think it's something that could be done in my country," she says. "We're 5 million people, and if each of us gave something it would add up to a lot of money to buy equipment, hire more people and increase the capacity of our shelter."

Transformational training

"We're creating agents of change by providing health care professionals around the world with skills and knowledge to improve treatment, care and survival rates of children with cancer and other illnesses," says Shaloo Puri, MD. "That perfectly aligns with the values and mission of St. Jude ."

The students' fire-in-the-belly quality resonated with White and Puri, who interviewed all candidates and selected those representing a diverse set of cultures and viewpoints.

"We're going to help them develop a systems approach to child health and determine how they can impact the health system that serves an individual child," Puri says. "In a few years, we'll be able to see how this will impact the status of childhood cancers around the world."

By **Jane Langille**

SETH DIXON

Seventy percent of patients lack perfectly matched family members. It can be difficult to find a matched donor in bone marrow registries. In those cases, a haploidentical, or half-matched, transplant may be an option.

Half Match, Whole Hope

A new study for half-matched transplants aims to cure high-risk blood cancers.

EVER SINCE 7-year-old Clayton Pinner was diagnosed with a rare form of B-cell acute lymphoblastic leukemia (ALL) in November 2018, he has wanted to know everything about his cancer and his treatments. At St. Jude, Clayton's nickname is "BossMan" — a moniker that's even emblazoned on his T-shirts and shoes.

Clayton's treatment began when he enrolled in a St. Jude clinical trial that used targeted therapy to attack his leukemia.

"The best available chemotherapy decreased his level of disease, but some cancer remained," recalls Aimee Talleur, MD, of St. Jude Bone Marrow Transplantation and Cellular Therapy. "Clayton's B-cell ALL has a genetic factor called hypodiploid, which only affects about 2% of patients, making it harder to treat."

Clayton received CAR T-cell therapy, an approach that engineers a patient's own disease-fighting T cells to target and destroy cancer cells. That treatment successfully eliminated his cancer cells, but his normal B cells started to return — a warning sign of potential relapse.

Clayton's best option for a permanent cure was a blood stem cell transplant. But no family member was a perfect match, and none was found in bone marrow registries.

Fortunately, there was another option. Clayton enrolled in a new trial for patients who lack matched donors. The study, called HAP2HCT, aims to kill any remaining cancer cells, reduce the risk of graft-versus-host disease, and help patients recover a strong immune system as quickly as possible.

The ultimate gift

Clayton's mom, Natalie, donated blood stem cells through a process that collects and separates stem cells from blood taken from a vein in the arm. "Clayton received my cells just 21 days from when they saw warning signs that his leukemia might come back," she says. "I don't think things happen that fast anywhere else."

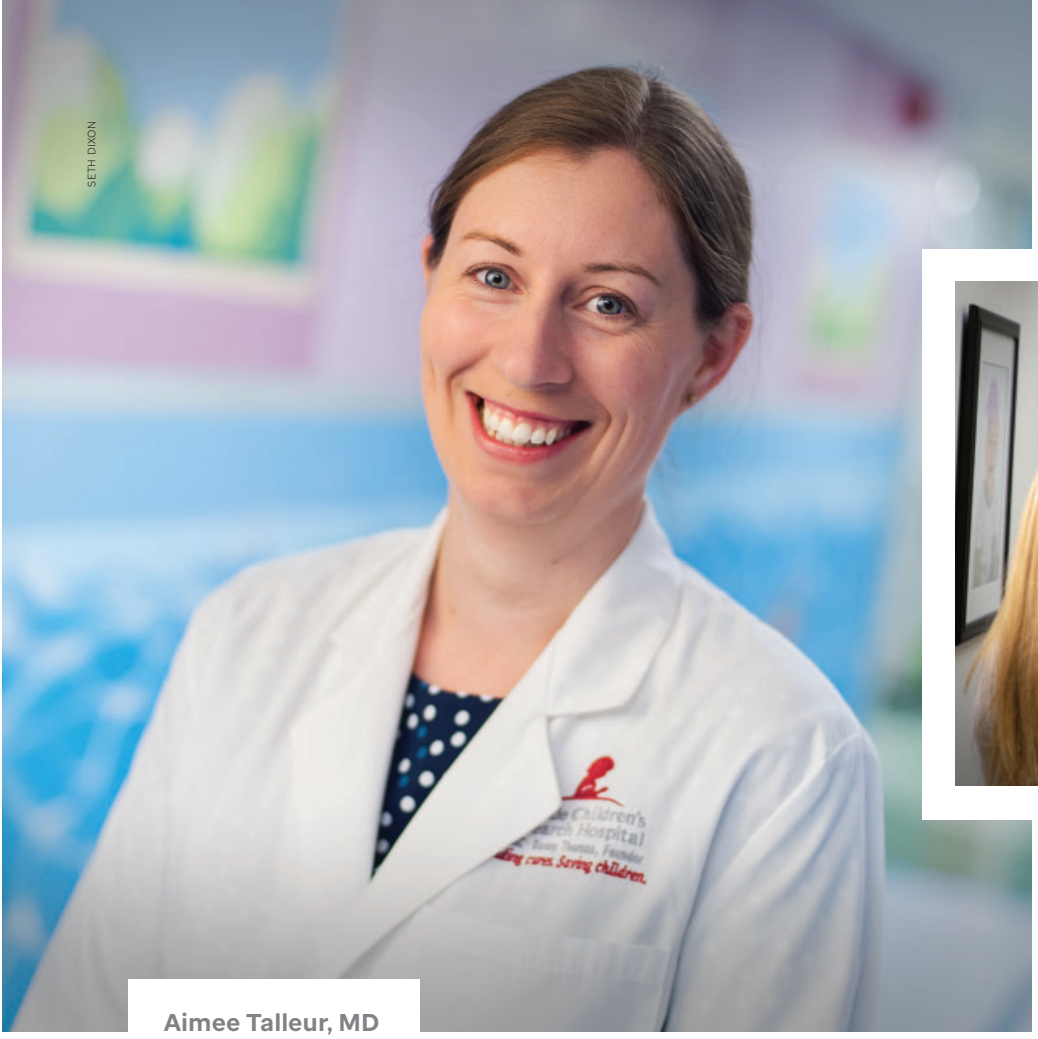
THE BEST CHOICE

A transplant can be an option for children who have blood cancers that have not responded to other treatments.

Immature blood stem cells found in bone marrow develop into all types of blood cells. An allogeneic transplant replaces damaged stem cells with healthy ones from another person. Proteins called human leukocyte antigen (HLA) markers must match on the donor and recipient cells. If the match is not perfect, the donor's cells may attack the patient's cells, a condition called graft-versus-host disease.

Seventy percent of patients lack perfectly matched family members. It can be difficult to find a matched donor in bone marrow registries. In those cases, a haploidentical, or half-matched, transplant may be an option. Biological parents are always half-matches for their children, and biological siblings have a 50% chance of being a half-match for one another.

With one of the largest pediatric bone marrow transplant programs in the world, St. Jude has performed thousands of transplants since 1982. For nearly two decades, St. Jude researchers have been



SETH DIXON

Aimee Talleur, MD

ANN-MARGARET HEDGES

Brandon Triplett, MD

pioneering and refining haploidentical transplants to push survival rates higher.

MOM AS DONOR

First, Clayton received chemotherapy to destroy his bone marrow. Natalie Pinner, Clayton's mom, donated blood stem cells through a process that collects and separates stem cells from blood taken from a vein in the arm.

"Clayton received my cells just 21 days from when they saw warning signs that his leukemia might come back," Natalie says. "I don't think things happen that fast anywhere else."

About two weeks after the infusion, Natalie's stem cells were creating new blood cells in Clayton's bone marrow. At that point, he received a second infusion from Natalie of her donor memory cells — mature white blood cells that remember how to prevent people from becoming sick from common infections.

Before the infusions, Natalie's donor cells were engineered in the lab to remove certain types of T cells: those with cell surface receptors made up of an alpha protein linked to a beta protein, and those that express a molecule called CD45RA.

"We take out the T cells that can make patients sick and leave those that can fight infection and any remaining leukemia cells," explains Brandon Triplett, MD, chief of the hospital's Bone Marrow Transplant Clinical Service. "If we remove all of the T cells, recipients experience less graft-versus-host disease, but there are more infections and relapses."

An earlier trial called HAPNK1 used CD45RA-depleted donor memory cells in haploidentical transplants. Scientists noted promising results among the 70 patients.

"We saw some of the best outcomes ever," says Triplett, who led the trial. "The relapse rate and the risk of dying from complications were very low, and life-threatening viral infections were well-controlled."

Patients in HAPNK1 received donor memory cells in one dose. In HAP2HCT, doctors are monitoring patients weekly for 15 weeks and treating them with smaller doses of donor memory cells as required. Clayton also received a drug that attaches to T cells at one end and to leukemia cells at the other. This drug activates the T cells to destroy leukemia cells while stimulating the growth of more T cells.

FULL CIRCLE

Clayton has faced cancer with a maturity far beyond his years. After understanding the rationale for each treatment, he said, "You've gotta do what you've gotta do."

The boy painted the motto on his hospital room's window to encourage other children undergoing treatments.

Natalie says it's interesting how things come full circle.

"I volunteered at St. Jude on Saturdays when I was in high school," she says. "I ran the Happy Cart for the Child Life program, taking toys to children. Now it's my son who is enjoying toys from the cart."

When he grows up, "Boss Man" wants to be a cancer researcher and find more ways to fight cancer.

"St. Jude has been a blessing to us," Natalie says. "Everyone is on the same team. We are where we are because other children signed up for clinical trials. It's rewarding to think that down the road, Clayton's experience is going to help other children."

SETH DIXON

How do cells organize proteins without membranes? St. Jude scientists unlock the mysteries of liquid-liquid phase separation.

Organizing Organelles

By **Erin Podolak**

The first step of organization involves sorting — picture shirts on one side of your closet, pants on the other. This process also applies to cells. They need to stay organized to efficiently accomplish various tasks.

Cells find ways to sort and separate proteins and other cell components. They do that through liquid-liquid phase separation (LLPS). It's the same process that governs the way oil forms droplets in water.

Organelles are bodies within a cell that are surrounded by membranes and serve specific functions. Cell biologists have long known that alongside traditional organelles there were cellular bodies without membranes. No one had an explanation for these membraneless organelles. Then, a decade ago, things changed. Membraneless organelles were found to behave like liquid droplets. LLPS was proposed to explain how a cell organizes certain proteins without enclosing them in a membrane.

"This field went unappreciated for years," says J. Paul Taylor, PhD, St. Jude Cell and Molecular Biology chair. "But once we started to look at liquid-liquid phase separation, just about every scientist studying any biological process realized this is relevant to their work."

Now, researchers are studying LLPS to better understand membraneless organelles, the functions they serve and how errors in this process play a role in disease.

BIG IDEAS SHAPE NEW FIELD

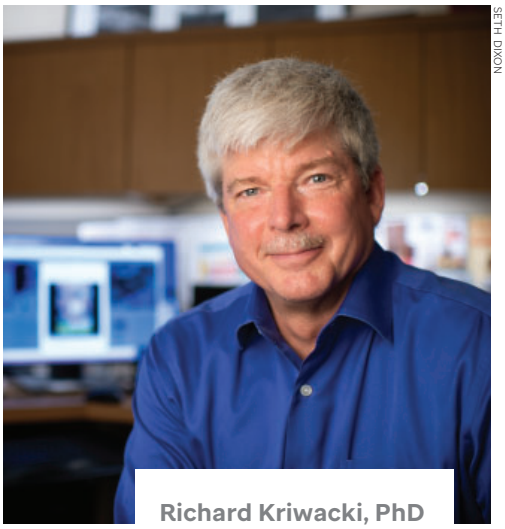
Richard Kriwacki, PhD, of St. Jude Structural Biology studies a membraneless organelle called the nucleolus. He discovered how the nucleolus produces molecular machines called ribosomes using LLPS.

The protein and RNA building blocks of the ribosomes are held in a liquid phase by a protein called nucleophosmin through phase separation. This enables the ribosomes' component proteins and RNA to bind each other properly, allowing ribosome subunits to assemble.

"We revealed the mechanism for how phase separation contributes to a critical biological process," Kriwacki explains.

SETH DIXON

Tanja Mittag, PhD



SETH DIXON

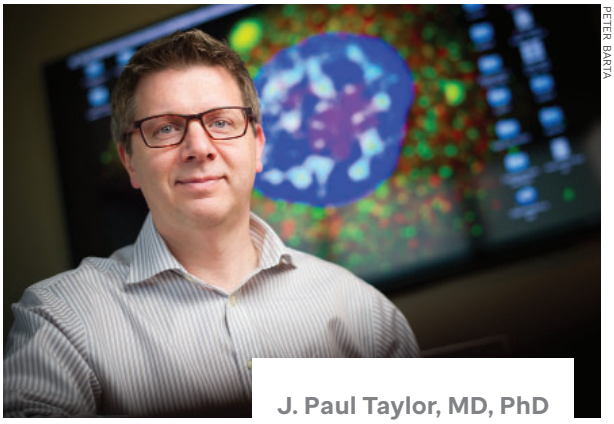
Richard Kriwacki, PhD

We're only scratching the surface of understanding the driving forces for phase separation and what can happen when these processes go awry."
– Tanja Mittag, PhD

ORDER IN DISORDER

Tanja Mittag, PhD, of St. Jude Structural Biology seeks to understand how interactions between intrinsically disordered proteins, notable for their lack of structure, can drive LLPS. Mittag and Taylor were among the first to show that an intrinsically disordered region in a protein is enough for it to phase separate. One-third of all proteins are intrinsically disordered. While not all of these easily phase separate, this suggests LLPS may guide the interactions of many more proteins than initially thought.

"This highlights the scale at which liquid-liquid phase separation underlies the inner working of a cell, as well as the importance of intrinsically disordered proteins," Mittag says. "But we're only scratching the surface of understanding the driving forces for phase separation and what can happen when these processes go awry."



PETER BARTA

J. Paul Taylor, MD, PhD

REVELATIONS

Taylor studies neurodegenerative disorders, which have only recently been linked to abnormal phase separation. Mittag and Taylor found that some mutations that underlie neurodegenerative diseases can also drive LLPS. Taylor then showed that some of these mutations can also drive pediatric cancers.

"Mutations can modify the concentration threshold at which phase separations occur," Taylor says. "Lowering the threshold can make phase separation more likely to happen, disturbing biological processes and at times leading to disease."

Kriwacki is also studying LLPS in neurodegenerative disorders, providing insight into how the process can contribute to amyotrophic lateral sclerosis (ALS). He is studying abnormal proteins found in abundance in ALS and how undergoing LLPS disturbs the nucleolus and contributes to cell death.

Genes that control cell growth can be hijacked by cancer to allow for uncontrolled development. Mittag recently showed that mutations in the tumor suppressor gene *SPOP* contribute to cancer by disrupting LLPS.

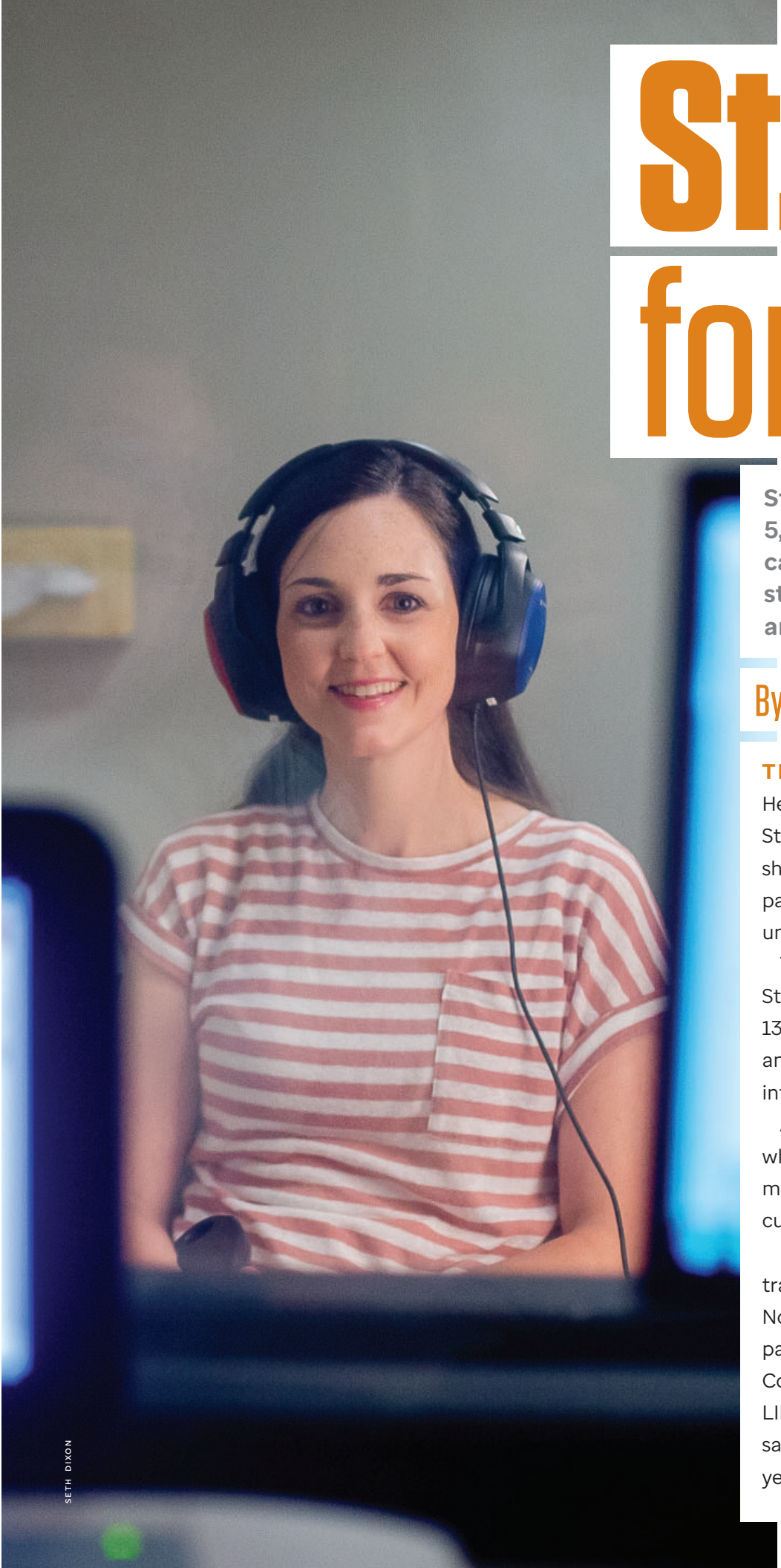
A NEW FRAMEWORK

This research provides a framework for scientists to explore how drugs could modify LLPS to achieve therapeutic results.

"It would be like targeting the cell's abnormal equilibrium to prod it back into balance," Taylor says.

There is great potential for treatments to target LLPS to modify protein interactions in a cell. But there are also challenges to surmount — like the fleeting nature of phase separation. Still, researchers say they relish the opportunity to work in an up-and-coming field.

"The phase separation work at St. Jude and elsewhere is rewriting how we understand cell biology," Kriwacki says. "We're going to need to revise the textbooks."



SETH DIXON

St. Jude for LIFE

St. Jude welcomes its 5,000th patient back to campus in an extraordinary study for today's survivors and tomorrow's patients.

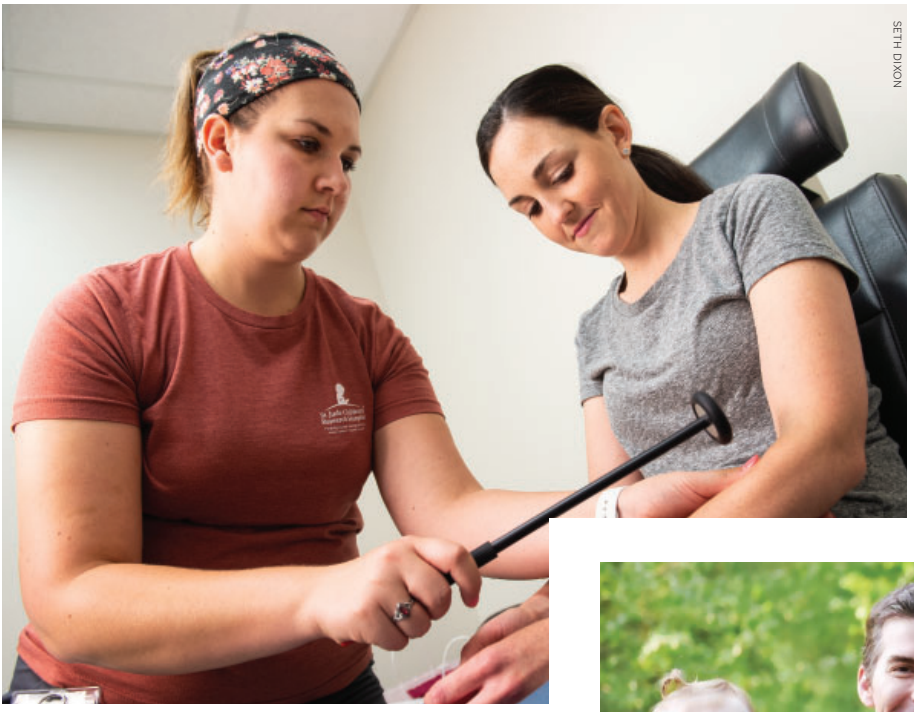
By **Elizabeth Jane Walker**

THE FIRST TIME Lindsey Gruwell Headrick passed through the doors of St. Jude Children's Research Hospital, she was a 9-year-old leukemia patient, paralyzed from a stroke and unable to speak.

The second time she turned to St. Jude for help, Lindsey was a 13-year-old swimmer, facing a relapse and another two-and-a-half years of intensive treatment.

A third bout with cancer occurred when she was 19. After a bone marrow transplant, she left St. Jude cured.

In the summer of 2019, Lindsey traveled to Memphis yet again. Now 30 years old, she arrived as a participant in the St. Jude Lifetime Cohort study, also known as St. Jude LIFE. It's a research project that may save the lives of other children in years to come.



SETH DIXON

ANN-MARGARET HEDGES

Les Robison, PhD, and Melissa Hudson, MD

Today's research for tomorrow

Lindsey Gruwell Headrick and her husband, David, have three daughters (from left), Josie, Jane and Annie. Lindsey is the 5,000th survivor to complete medical evaluations through the St. Jude LIFE long-term follow-up study.

GIVING BACK

More than 5,825 survivors have enrolled in St. Jude LIFE. This study focuses on cancer patients who were treated between 1962 and July of 2012. The hospital brings them back to the hospital for health screenings for the rest of their lives. Lindsey is the 5,000th person to take part in the study's medical evaluations.

It's a win-win for Lindsey and other participants. Not only do they learn about their own health status, but they also provide researchers with insights that help current and future survivors worldwide.

Most survivors experience some side effects of cancer and its treatment. Some children received chemotherapy that affects hearing or fertility. Others required radiation therapy that puts them at risk for secondary cancers or heart issues. Certain diseases carry their own long-term side effects such as memory loss or learning problems. The possibilities are endless, based on the individuals and the therapies they received.

INTENSIVE VISIT

As part of her initial St. Jude LIFE visit, Lindsey spent three exhausting but exhilarating days on campus. She spent nearly two hours doing mental calisthenics, in the form of brain-teasers and memory tests. Then she laced up her sneakers to run on a treadmill and stand on a shifting platform to evaluate her balance. There were blood tests and bone density studies. Hearing and eye exams. Genetic counseling sessions and skin biopsies. She filled out food questionnaires, took part in a psychological exam and described her health habits.

As she moved from place to place, Lindsey also met old caregivers and new patients just starting their journeys. She roamed familiar halls and explored the new facilities that have been constructed since her last visit. She celebrated the changes and contemplated the impact the hospital had on her life.

"By being in the LIFE study, I'm giving back a little to St. Jude research and I'm staying connected to the hospital," Lindsey explains. "The data collection is essential to progression and growth for the future. What they gather from me might help improve treatment regimens or decrease lasting side effects of those who face this cancer journey.

"It is beyond my pleasure to participate in a study that will help future patients, their treatments and quality of life."

SYSTEMATIC TESTING

The beauty of St. Jude LIFE is that every survivor receives the same comprehensive evaluations. Similar programs at other institutions screen survivors based on specific risk factors known to be associated with that patient's treatment. But St. Jude LIFE performs a much more thorough evaluation.

"The systematic assessment of St. Jude LIFE is unique," says Melissa Hudson, MD, who serves as the study's co-principal investigator along with Les Robison, PhD, St. Jude Epidemiology and Cancer Control chair.

"No other center is doing this in a population that has such a wide age diversity," adds Hudson, who is the hospital's Cancer Survivorship Division director. "We have very, very long-term survivors, some of whom are approaching 70 years old. Other centers typically get much of their data from health registries. They don't have access to the level of detail that we do — information about behavioral issues and detailed clinical assessments."

WHAT WE'VE LEARNED

St. Jude LIFE is now the largest cohort of clinically assessed childhood cancer survivors in the world.

Researchers have published more than 120 papers in medical and scientific journals, sharing insights they've gleaned from the massive amounts of data collected. The discoveries include findings in a broad range of areas — from memory issues and fertility to secondary cancer risks and quality of life.

The St. Jude LIFE study found that adult survivors of childhood cancer have a nearly two-fold greater cumulative burden of chronic health problems than the general public. A large percentage of these survivors have undiagnosed conditions that could benefit from early interventions to preserve their health. For instance, scientists learned that survivors in their mid-30s are apt to display frailty typically seen in elderly individuals. As a result, researchers are developing ways to reverse these issues in survivors and prevent them in current patients.

Whole-genome sequencing of St. Jude LIFE participants also revealed that almost 6% had inherited mutations in one of 60 genes that can lead to cancer. That number was about 10-fold greater than among people with no childhood cancer history. This finding helps clinicians pinpoint which survivors should be given priority for genetic testing.

"We've learned that we should counsel all of our survivors about the genetic risk underpinning their type of cancer and the potential for subsequent cancers," Hudson says.

Discoveries emerging from the study are having a dramatic impact on the lives of childhood cancer survivors.

"The results are already informing the guidelines we're giving survivors," Hudson says. "And the findings are helping us develop interventions to preserve survivors' health as they age."

A PRESENT AND A FUTURE

As part of the St. Jude LIFE evaluation, Lindsey learned about her specific health risks as a childhood cancer survivor. The experience reminded her of a pivotal discussion she had with her physician after her bone marrow transplant.

"At St. Jude, I felt like I'd been in a bubble, protected," she says, "and now I was going out into the world where even the trees around me would have fungal spores. But my doctor told me, 'When we're driving to work, we have a risk that we're going to get into an accident and die, but we take that risk. Go back to college and do what you want to do. Whatever comes, we'll deal with it.'"

Lindsey took his advice and finished her nursing degree.

"Since age 9, I had been in the oncology environment," she explains. "That's where my heart was."

So, it makes sense that Lindsey, the mother of three beautiful daughters, now works in a hospital caring for children with cancer.

"St. Jude has literally given me everything I have now," she says, "the present and a future."

ANN-MARGARET HEDGES

Beyond Benefit: Healthy Volunteers

AS ST. JUDE LIFE researchers pore over data generated by thousands of survivors, they need to know how the results compare with those of people who have never had childhood cancer or its therapy. That's where healthy volunteers come in: people like Kirk Johnston.

Johnston volunteered to undergo testing so that scientists would have a yardstick by which to gauge the health of former patients.

"I thought it would be a great way to help St. Jude," says Johnston. "I don't know of any other place where you could get such a comprehensive view of your current health," he says.

The control subjects' contributions are crucial, according to Melissa Hudson, MD, Cancer Survivorship Division director.

"As scientists, we need to know whether our findings with survivors are different than what we'd expect to see in people who have not been exposed to cancer therapies," she says. "For example, we might observe that our survivors have premature menopause or high blood pressure, diabetes, obesity or high cholesterol. Are their rates different from other people who live in this region? The control group can help us know the answer to those questions."

Johnston says the volunteer experience was a fulfilling way to give back.

"St. Jude is a special place," he says. "It was an honor to be able to help with the research and to be checked out by such an amazing team."

By Elizabeth Jane Walker

APRIL BROWN / ABC PHOTOGRAPHY

Life after Treatment

Hoop Dreams

One retinoblastoma survivor celebrates a dramatic comeback.

THE HIGH SCHOOL GYM reverberates with cheers as point guard Simon Stacy dribbles, pivots and shoots — electrifying the crowd with his speed and coordination.

What makes Simon different than any other basketball standout is his back story. It's one of courage, determination and possibilities.

When Simon was 5 years old, his mom, Sharon Chancellor, noticed a white spot in his eye. At their local hospital, a physician ordered an MRI.

"A little while later, the doctor burst through the door," Sharon recalls. "He and his nurse were crying."

Retinoblastoma, a malignant eye cancer, had already caused blindness in Simon's right eye. Soon, he and his mom were racing toward St. Jude Children's Research Hospital.

To prevent the disease from spreading, St. Jude surgeon Matthew Wilson, MD, removed the affected eye. Aggressive chemotherapy and 35 intensive radiation treatments followed.

Sharon, a single mom, had four other children at home. Simon's grandparents, church groups, schools and neighbors rallied to help, providing resources and caregivers. When Simon missed his kindergarten graduation, teachers placed a single rose in his chair, a poignant symbol of support.

"His grandparents and the people in our town completely took care of my kids," Sharon says.

Meanwhile, St. Jude oncologist Ibrahim Qaddoumi, MD, and his colleagues showed care and concern for both Simon and his mom.

"They helped me as much as they helped my son," Sharon admits.

Simon eventually returned home, where he demonstrated prowess on the gridiron, baseball diamond and basketball court. Recently, his high school basketball coach began to discuss the possibility of Simon playing college ball. Today, the high school senior spends up to four hours a day running and weightlifting before hitting the court.

When Simon returns for appointments in the St. Jude After Completion of Therapy Clinic, he leans down to hug clinicians who used to tower over him.

"Basketball is really fun," Simon tells them. "There's the joy of playing it and how it makes me feel. There's the friendship that I have with my teammates.

"And then there's the surprise on the faces of people who find out I've only got one eye and yet I'm playing as well as I am," he says with a chuckle. "I like that."

PETER BARTA

Creative approach to discovery

ST. JUDE structural biologist Eric Enemark, PhD, and others recently captured an atomic-scale image of the structure of DNA replication machinery. Enemark began to ponder that structure. He thought it might help solve a mystery at the heart of cell division. Using scrap lumber, he built a simple model. This low-tech machine shows how double-stranded DNA could begin separating to single-stranded DNA, which can be copied in advance of cell division. *Nature Communications* published a report on his research.

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PETER BARTA

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Advancing research

Now under construction, the Advanced Research Center will serve as a hub of interaction and discovery. The 625,000-square-foot center is one of the largest active research construction projects in the U.S. Opening in 2021, the eight-story facility will have the capacity to serve more than 1,000 scientists.