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## Promise

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# Promise

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**On the cover:**  
*Lukas Etchison*  
*Photo by Peter Barta*

# Meanwhile, in Memphis

By Elizabeth Jane Walker

Long before a little boy in Puerto Rico received news that his leukemia had returned, a St. Jude team of scientists and physicians had already been collaborating to create a therapy that might someday save his life.

**“Y**our child has...” In the millisecond before the word is spoken, life hangs in the balance. An inhalation of outrageous hope; an exhalation of gut-wrenching fear.

Then the word *relapsed* drops like a boulder onto a mother’s heart.

When doctors at a Puerto Rican hospital uttered that word to Jessica Lopez-Montanez, her son was just completing two-and-a-half years of treatment for acute lymphoblastic leukemia (ALL). Although ALL is the most common form of childhood cancer, Christopher’s battle had suddenly become decidedly uncommon, the family’s end-of-therapy celebration short-lived.

## Curing the toughest cases

For children with newly diagnosed ALL, the survival rate is about 94 percent. But when the disease returns during or soon after the end of therapy, the outlook is not as rosy. Christopher’s local hospital offered few options for a

child with a high-risk relapse. Fortunately, Christopher’s hometown medical team learned about a new clinical trial that had recently opened thousands of miles away in Memphis, Tennessee. This regimen combined chemotherapy with immunotherapy, a treatment that uses the immune system to help fight cancer.

The entire time that Christopher had been undergoing initial therapy in Puerto Rico, scientists at St. Jude Children’s Research Hospital had been preparing for this clinical trial—conducting research that might someday save his life.

## A global resource

Jessica had heard of St. Jude long before her son ever relapsed. During his treatment, she had read books and combed the Internet for details about his disease.

“The thing is, when a mother has a son who is sick, she is always trying to search and find out what’s the best thing for him,” she says. “So I always had hope.”

When she and her family arrived in Memphis, Jessica was confident that they had found the right place.

“I had seen St. Jude on TV, but it was more than I had expected. I thought, ‘He is going to live. He is going to receive good treatment here, and he is going to be well,’” she recalls.

At St. Jude, the 10-year-old enrolled in a clinical trial created especially for children with relapsed leukemia. For years, researchers worldwide had been trying to find a way to raise survival rates for children like Christopher. But survival rates had plateaued.

“For the last 20 years, leukemia study groups around the world had tried different things,” explains Deepa Bhojwani, MD, of St. Jude Oncology. “They tried



giving more intense chemotherapy; giving it in different combinations; giving chemo that hadn't been given during front-line treatment. Everybody's results were exactly the same: no improvement."

Children with high-risk disease—like Christopher, whose disease relapsed during or soon after the end of treatment—had about a 30 percent survival rate. For children with standard-risk relapsed disease, the survival rate was 50 percent.

"A team of people from different areas at St. Jude came together to find an answer," Bhojwani continues. "We knew that intensifying the chemotherapy was not the answer. We needed to add something novel to the treatment.

"That's when we thought about combining chemotherapy and immunotherapy in one block to attack the disease from different angles."

### Meeting the challenge

Children in the St. Jude clinical trial have either B-cell ALL (a cancer that affects white blood cells called B lymphocytes) or B-cell lymphoblastic lymphoma (a type of non-Hodgkin lymphoma). Like Christopher, participants have either relapsed or their disease has not responded to initial therapy.

A test developed at St. Jude allows clinicians to closely monitor each child's response to treatment. That test can detect even one leukemic cell among 10,000 normal cells, called minimal residual disease, or MRD. In the St. Jude clinical trial, if MRD is discovered after any block of chemotherapy, that child receives more intensive therapy.

Children in the clinical trial receive chemotherapy as well as a monoclonal antibody that has been used mostly with lymphoma treatments in the past.

The antibody kills the leukemia cells more effectively when natural killer (NK) cells are added. The NK cells are

harvested from the parent and infused into the patient. NK cells can also directly kill leukemia cells.

After that, children with standard-risk disease receive another two years of chemotherapy. Patients with high-risk disease—such as Christopher—undergo bone marrow transplants as soon as they have no evidence of MRD.

Christopher's mom served as his NK cell donor, as well as his bone marrow donor.

"This clinical trial is a good option to get the leukemia very well controlled and, if they are high-risk, to get the children to transplant," Bhojwani explains. "Our hope is that the kids will not relapse again."

Throughout the process, Christopher asked questions. He read about his condition and his medications. Then he quizzed his clinical team so that he would understand each step of the process.



PETER BARTIA

*Now 12 years old, Christopher continues to visit St. Jude regularly for follow-up appointments. When he returns home, the straight-A student plays basketball and participates in track and field. He plans on pursuing a career as a chef.*

“I used to draw leukemia cells and explain to him about leukemia and its treatment,” Bhojwani recalls. “Because I couldn’t speak Spanish well, our interpreter would explain to him what I was saying as I drew the cells and described the mechanisms. I was impressed with how inquisitive Christopher was and how much he understood about the mechanisms involved in leukemia treatment.”

## One-two punch

The St. Jude clinical trial takes a unique approach to treating children who have relapsed ALL and lymphoma.

“This therapy is novel, and it has the potential to really improve outcomes,” Bhojwani says. “This combo regimen has not been done anywhere else.”

The exceptional supportive care at St. Jude enables children undergoing treatment to receive preventive antibiotics and meticulous follow-up care to help them avoid infections. The transplant team consists of individuals who have years of experience in performing high-risk transplants, especially haploidentical, or half-matched, transplants that use parents as donors.

The clinical trial is also providing scientists with a way to better understand why some children have disease that is more resistant to treatment than other children and why relapsed disease is more difficult to treat.

## A place of rebirth

Throughout his treatment, Christopher provided support to other children at St. Jude. “Christopher had a sense of peace and tranquility,” Jessica says. “He would share his insights with other kids that were sick. He would reassure them and encourage them to let the doctors know if they had any problems.”

After Christopher completed his transplant, he attended a special celebration.

His mom and stepdad had put their wedding plans on hold for the years that Christopher was undergoing treatment. Once the crisis was over, the couple knew the perfect time and place to say their vows: St. Jude.

“My child comes first,” Jessica explains, “so he was our sole focus for a long time. But once we found out that he was going to be okay, we wanted to be united in the place where he had been reborn—the place where he got cured from cancer.” ■



PETER BARTA

*During an inpatient stay, Christopher enjoyed playing games with Mari Dallas, MD, of St. Jude Bone Marrow Transplantation and Cellular Therapy.*



JUSTIN VENEMAN

*After Christopher’s transplant, his mom and stepdad married at St. Jude. The couple had put their wedding plans on hold during Christopher’s treatment. “We wanted to be united in the place where he had been reborn—the place where he got cured from cancer,” Jessica explains.*

## Relapsed acute lymphoblastic leukemia

- Relapsed acute lymphoblastic leukemia (ALL) is the fifth most common childhood malignancy.
- Approximately 15%–20% of U.S. children with ALL will relapse.
- Treating relapsed ALL has become increasingly challenging, largely due to resistance to therapy.
- New targets for the treatment and prevention of relapsed ALL and lymphoma are needed, which is why St. Jude has opened a clinical trial for children with these diseases.



# Look

## A Deeper



How do children with the eye cancer retinoblastoma fare as they grow into adulthood? St. Jude researchers uncover answers.

By Anita Houk

**T**erry Aldridge was 8 months old in 1964, when his mom's sister noticed a problem with his eye. "My aunt was visiting and holding me," Aldridge says. "She told my mother, 'Ruth, there's something wrong... There's a white dot in the brown of his eye.' "So they rushed me to the doctor. He looked at me and

talked to another doctor. That doctor told my mother, 'That eye is going to have to come out today, or he might lose his other eye.'"

Aldridge had retinoblastoma, a cancer of the retina, the part of the eye that senses light and sends images through the optic nerve to the brain. Fifty years ago, when Aldridge



*Terry Aldridge, who lost an eye to cancer in 1964, took part in a study of long-term retinoblastoma survivors from St. Jude. Like Aldridge, most of the participants work full time, live independently and have achieved other important milestones.*

arrived at St. Jude Children’s Research Hospital, treatment consisted of eye removal, chemotherapy and external beam radiation.

“They removed my left eye,” Aldridge explains. “I got my first prosthesis when I was 8 months old.

“I don’t feel I have any limitations,” Aldridge continues. “I’m not going to lie: I wish it hadn’t happened. But this is what happened, and I’ve had to live with it. I know I’ve been turned down from jobs on account of it—but I also know that I’ve been blessed.”

### Good news for survivors

As one of the hospital’s early patients, Aldridge is among the older members in the St. Jude Lifetime Cohort Study (also called St. Jude LIFE), which follows St. Jude cancer survivors through adulthood. Aldridge’s experience is typical of most of the 69 adult retinoblastoma survivors who were evaluated in a recent study. Results of that study, which appeared in the journal *Cancer*, showed that most of those survivors have

normal cognitive function, with the vast majority working full time, living independently and achieving other important milestones.

Earlier studies compared patients who had cancer in one eye to those with cancer in both eyes. But the St. Jude study looked deeper, says clinical psychologist Tara Brinkman, PhD, of St. Jude Epidemiology and Cancer Control. The child’s age at diagnosis—rather than the extent of disease—emerged as a crucial factor.

“Survivors diagnosed before 1 year of age performed better on measures of verbal intelligence, verbal learning, and short- and long-term memory,” Brinkman explains. “Verbal processing seems to be enhanced in survivors who were diagnosed younger than that age.

“We know the visual system develops rapidly,” she continues. “The earlier the disease appears, the greater the opportunity for the brain to adapt and compensate for disruption to the system. This highlights the importance of early intervention and rehabilitation for these children.”



## Welcome surprises

Brinkman and her colleagues discovered that most of the long-term survivors in the study were doing well. Seventy percent of study participants were living independently, 62 percent were married or living with a partner, 58 percent had completed college or postgraduate education and 75 percent were employed full time.

In the areas of verbal intelligence, attention and memory, retinoblastoma survivors performed within normal ranges. Fine motor skills showed a dip, but in nonverbal reasoning and the ability to learn new information over a series of trials, the survivors were above the norm.

“It was a little bit surprising, given the very young age at which they’re treated and the fact that they receive intensive therapies, including surgery, chemotherapy and, historically, radiation

therapy,” Brinkman says. “We expected that they might be at risk for some cognitive deficits. Generally, cancer survivors treated at a young age are at risk for cognitive or social difficulties later on, whereas this retinoblastoma group seems to be doing particularly well.”

## A disease of the very young

Retinoblastoma is a cancer of early childhood. The eye tumor can even affect developing fetuses. The disease usually is diagnosed when a child is 1 to 2 years old, with the first noticeable sign often being a cloudy white pupil—a white-eye in a photo, rather than the normal red-eye effect. Today, as compared to when Aldridge was treated as a baby, retinoblastoma treatment can be finely focused, including chemotherapy injections and novel therapies.

Rachel Brennan, MD, of St. Jude Oncology, has a particular interest in retinoblastoma, its therapy and late

effects. She has treated children as young as 3 weeks old and as old as 10 years.

“With better than 95 percent survival rate when retinoblastoma is confined to the eye, you have to be extremely careful with the therapy,” Brennan says.

“You’re curing 2-year-olds who have decades of

life ahead of them. With high survival rates, you want to make sure therapies can be tailored to the patient—to provide enough therapy but not over-treat. It’s a very fine line. Long-term, retinoblastoma survivors do very well. But the question is: For those who do not do as well, where are the deficits?”

**“A cancer survivor is a survivor for life. We want those survivors to live the fullest lives they can. So the treatment team is looking long-term, at the very edge of the horizon.”**



*Tara Brinkman, PhD, of St. Jude Epidemiology and Cancer Control, talks with a St. Jude survivor. “We know the visual system develops rapidly,” Brinkman says. Her recent study highlights the importance of early intervention and rehabilitation for children with retinoblastoma.*

## The horizon's edge

Brennan recently worked with St. Jude Psychology chair Sean Phipps, PhD, and others on the first-known study to follow developmental function of extremely young retinoblastoma patients. The results, published in the *Journal of Clinical Oncology*, were unexpected. Developmental functioning among the children, tested at 6 months and 1, 2, 3 and 5 years, slowly declined until age 5. Many of the 5-year-olds scored significantly below average. The decline was most pronounced in children whose treatment consisted solely of surgical removal of the eye, with no additional therapy. The researchers suspect that children who did not receive additional treatments may have had a reduced exposure to rehabilitative services.

Phipps and his team will conduct further studies to examine whether the declines continue over time, level off or lead to subsequent recovery.

"We are going to bring these kids back when they hit age 10 and assess them again," Phipps says. "At that age, we can assess them in a much more finely grained way and look at issues such as attention and working memory, processing speed and other neuropsychological factors."

Why is it important to study these patients on a long-term basis?

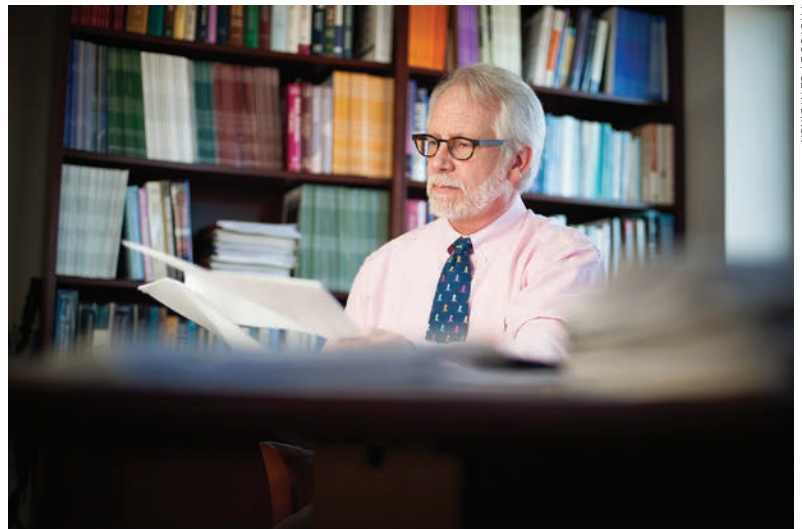
"A cancer survivor is a survivor for life," Brennan says. "We want those survivors to live the fullest lives they can. So the treatment team is looking long-term, at the very edge of the horizon."

St. Jude is using functional imaging to examine brain development and to evaluate how the brain compensates in the wake of retinoblastoma.

"We're really trying to move our survivor projects forward," Brennan says. "The psychology team is bringing the survivors back five years out. It's no small task, so we want to be asking the right questions. I love this group of patients; I love the cooperation at St. Jude."

## Encouraging other survivors

The phenomenal thing, Brennan adds, is that the children compensate well. "They're incredible," she says.



PHOTOS BY SETH DIXON

*Psychology chair Sean Phipps, PhD, and his colleagues are examining the developmental function of extremely young retinoblastoma patients.*



*"We want those survivors to live the fullest lives they can. So the treatment team is looking long-term, at the very edge of the horizon," says Rachel Brennan, MD.*

And their parents?

"I trust these parents," Brennan says. "A parent's job is to know when something is wrong with their children and to advocate."

Terry Aldridge couldn't agree more about the importance of parents. "I was blessed to have a mother like mine, a great mother," says Aldridge, who is now a father and grandfather himself. "She sacrificed for me.

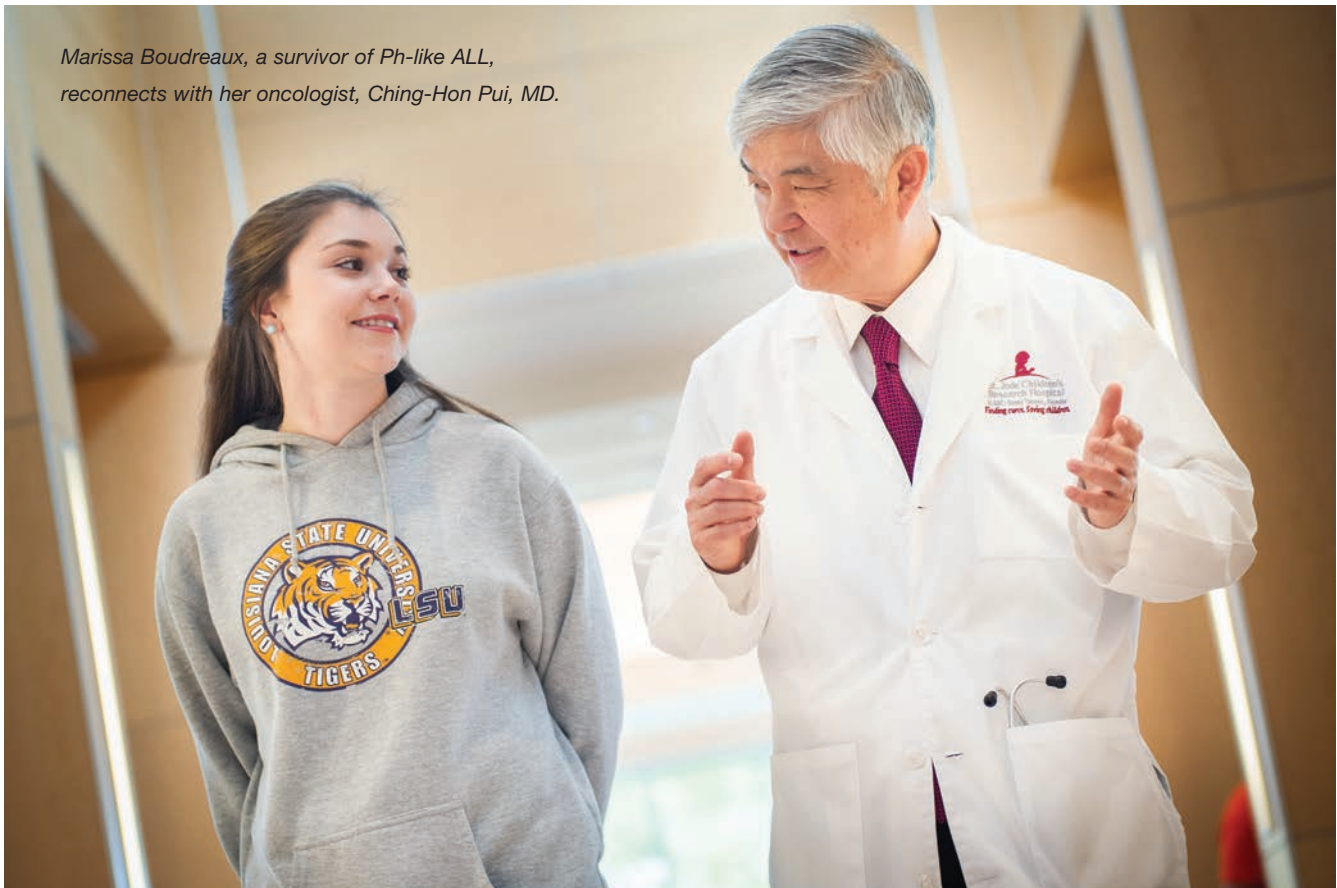
"So, now, if there's anything I possibly can do to help a mother and her child, I want to do it. I want to help. I tell them: 'Be encouraged. Don't give up. Have hope.'" ■



# Making Progress with Ph-like ALL

By Ginger Porter

*Marissa Boudreaux, a survivor of Ph-like ALL, reconnects with her oncologist, Ching-Hon Pui, MD.*



SETH DIXON

A few short years ago, St. Jude helped identify a novel leukemia subtype called Ph-like ALL. Since that time, the hospital has taken dramatic steps toward identifying and treating patients with this disease.

**M**arissa Boudreaux was almost 8 years old when her battle with acute lymphoblastic leukemia (ALL) began. In 2005, the little girl enrolled in a St. Jude Children's Research Hospital clinical trial that adjusted her treatment based on early responses to chemotherapy. Because of careful monitoring and treatment, Marissa was cured. Physicians now know that she had a yet-undiscovered genetic

subtype of ALL called Philadelphia chromosome-like ALL (Ph-like ALL). Clues gleaned from her case and those of other children have helped scientists identify the Ph-like ALL subtype, as well as improve treatments for future patients.

“I would go through it again tenfold if it would help someone else,” the now 17-year-old Louisiana native says.

## New directions

Under the care of Ching-Hon Pui, MD, St. Jude Oncology chair, Marissa enrolled in a clinical trial that used risk-directed chemotherapy to treat B-ALL, a cancer that affects white blood cells called B lymphocytes. Treatment intensity was monitored and adjusted based on minimal residual disease (MRD), or the percentage of leukemic cells remaining in the bone marrow after treatment. This method of evaluating treatment response was pioneered at St. Jude.

Pui and his colleagues recently published a *Journal of Clinical Oncology* paper showing how children with Ph-like ALL fared in that study. The researchers showed that modifying treatment based on early responses to chemotherapy made life-saving differences to many children and adolescents with the subtype.

Throughout the world, five-year survival rates for Ph-like ALL have hovered at 62 percent. But in the St. Jude clinical trial, Pui and his colleagues reported that 92.5 percent of patients with Ph-like ALL were alive five years after their cancer was discovered.

“This study shows that by measuring minimal residual disease and using the results to guide treatment intensity, patients with Ph-like ALL who have a poor initial response to chemotherapy can, with more intensive treatment, often be rescued and enjoy the same high rates of survival as other patients,” Pui explains.

## Assigning risk

Scientists once classified all children with Ph-like ALL as high-risk. By taking into account such factors as patient age and white blood cell count at diagnosis, and adjusting therapy based on MRD levels, St. Jude researchers demonstrated that Ph-like ALL is not uniformly high-risk. As a result of that study, St. Jude now classifies Ph-like ALL risk groups as low, standard or high, in part depending on the number of cancer cells found in the bone marrow by pathologists. Low-risk patients have less than one cancer cell in 10,000 in the bone marrow after remission induction

chemotherapy. High-risk patients have one cancer cell in 100. Standard patients fall in the middle.

In the St. Jude clinical trial, 40 percent of Ph-like ALL patients were classified as having low-risk disease, making them candidates for less-intensive treatment.

“You don’t want to treat everyone intensively, since a substantial proportion of patients would be over-treated,” Pui explains. “Children with Ph-like ALL who achieve a negative MRD status after remission induction should do just fine with low-risk therapy.”

Pui says children with high MRD levels should not only receive intensive chemotherapy but also further testing. Patients with genetic lesions responsive to specific groups of drugs can then be identified to spare them from bone marrow transplantation.

## From lab to clinic

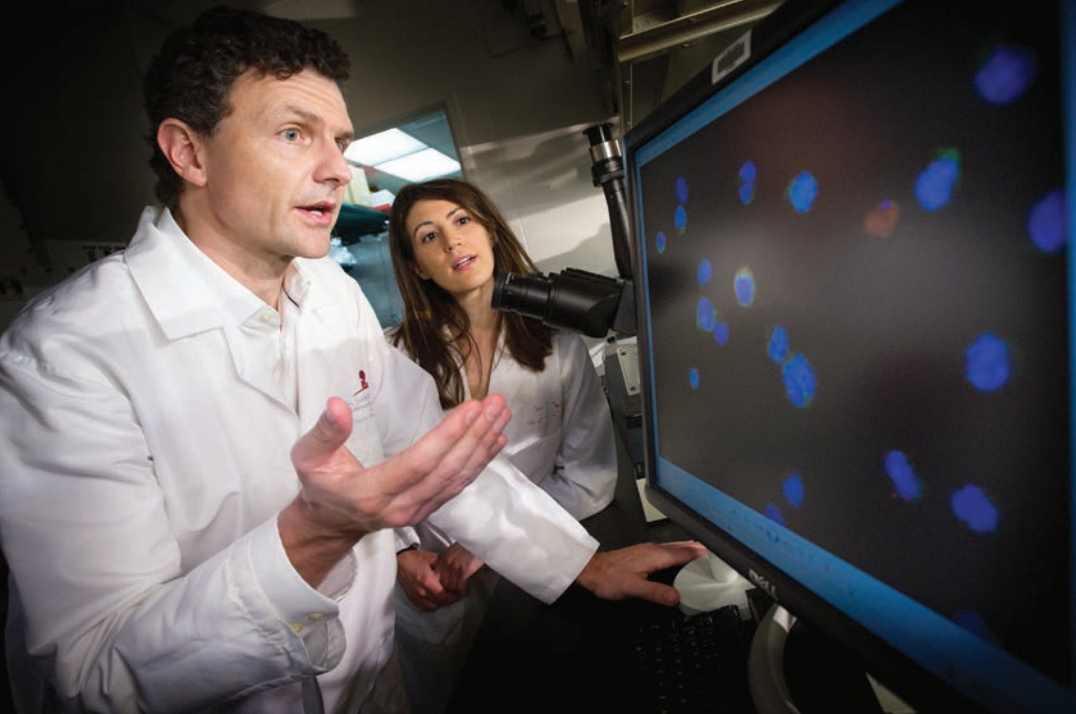
In 2009, St. Jude pathologist Charles Mullighan, MD, MBBS(Hons), helped discover and describe Ph-like



ANN MARGARET HEDGES

Today, physicians understand that Marissa Boudreaux (pictured with Pui in 2005) had a leukemia subtype known as Ph-like ALL.





St. Jude pathologist Charles Mullighan, MD, MBBS(Hons), helped discover and describe Ph-like ALL.

ALL. Recently, he led a study that details how often the subtype occurs and pinpoints which genetic changes drive development of the disease.

That study, published in the *New England Journal of Medicine*, involved 1,725 B-ALL patients between ages 1 and 39. Scientists used next-generation sequencing to identify the genetic missteps that lead to Ph-like ALL. The research was part of the Pediatric Cancer Genome Project, a collaboration between St. Jude and Washington University School of Medicine in St. Louis. The complete normal and tumor genomes of 700 young cancer patients have been sequenced as a result of the project.

“In this study, we were able to identify the full range of genetic changes, the driving force of leukemia in cases of Ph-like ALL,” Mullighan says. “We identified multiple new genetic changes, but at the end of the day, they activate only a limited number of cell growth pathways. And those pathways can be inhibited with drugs which are already available.”

The results pave the way for clinical trials to see if drugs called tyrosine kinase inhibitors (TKIs) can improve outcomes.

Two drugs called dasatinib and imatinib are examples of TKIs that have been used to treat Ph-positive leukemia in children and adults. Researchers recently used these drugs to treat a small group of patients whose Ph-like ALL had not responded to chemotherapy. Five of those eight patients

remain in remission with no detectable cancer. A national clinical trial is being planned, using existing TKIs to treat children with Ph-like ALL.

“There are children and adults alive today as a result of this research,” Mullighan says. “It has truly made a difference for at least a handful of people, and that number is likely to grow.

“At St. Jude, we will soon be sequencing every child with cancer, and we will be able to rapidly identify those with Ph-like ALL,”

Mullighan continues. “We’re

proud that we’ve been able to identify this subtype and move toward an effective treatment in such a short period of time. It’s the most exciting and satisfying project I’ve been involved with.”

## More than magic

Marissa’s experience at St. Jude not only saved her life but also directed it. The college sophomore is now preparing for a career as a labor and delivery nurse. “I want to witness life not only as a survivor, but also as one who will help to bring it into the world,” she says.

Ten years ago, Marissa could never have dreamed that her treatment would one day affect the lives of other children. She remembers 2005 as the year her brother and father had surgery, Hurricane Katrina hit her hometown and she received a cancer diagnosis. She remembers Pui, not as a celebrated researcher, but as a doctor who entertained her with magic tricks.

“He had a magic set kit with little foam balls under plastic cups. He would do a trick and frustrate me,” she says. “Then he would stick a pen through a dollar bill, and there would be no hole in it. Being 9, I was like, ‘Oh my gosh.’”

Marissa’s mom, Tanya, recalls Pui’s swift attention when Marissa had complications or when she had questions.

“He was always there, always reachable,” she says. “We love Dr. Pui. We love St. Jude.”■



# Sneezing Seals, Virulent Virus

**St. Jude scientists discover that a flu virus deadly to some harbor seals also poses a threat to humans.**

By Anita Houk

**L**ook at those soft, brown eyes, that adorable nose, the movement-sensitive whiskers and winsome smile.

Meet the Atlantic harbor seal. This mostly marine neighbor raises its young on beaches, pleasing human onlookers with its barks and yawns and tricks.

Who would think that an illness in this population would rock New Englanders and spark scientific studies?

In the autumn of 2011, more than 160 seal pups, sleek and furry and dying, washed ashore and sounded an influenza alarm.

A mutated form of the avian virus H3N8 influenza A was the culprit. It had jumped from birds (likely waterfowl) to harbor seals.

## **Could it threaten us?**

“The big concern was obviously whether it would infect humans,” says Infectious Diseases researcher Stacey Schultz-Cherry, PhD, a lead investigator in a St. Jude Children’s





Research Hospital study that appeared in the journal *Nature Communications*.

Although no human illness was linked to that harbor seal virus, scientists noted that strains of H3N8 have also been detected in horses, dogs, donkeys and pigs. The virus is believed to have triggered a human flu pandemic in the 1880s.

## A red flag

St. Jude scientists discovered that two mutations in the hemagglutinin protein and a change in the *PB2* gene were the culprits in the recent harbor seal event.

Schultz-Cherry explains, “At St. Jude, we didn’t do anything with the seals themselves; all of our work was in the lab. When we saw that H3N8 could grow well in mammalian cells and could transmit disease, we wanted to know: If this virus came in contact with humans, would we have any protection against it?”

In short: No.

Investigators found no evidence of human immunity to this H3N8 strain and no evidence that seasonal flu vaccines would thwart it.

“Our study raises a red flag about the threat this strain poses to humans who are exposed to animals infected with the virus,” Schultz-Cherry says. “We need to do a human risk assessment study.”

## Worldwide resource

Risk of infection is a major concern at St. Jude, where insight into contagious diseases is critical to treating immune-compromised cancer patients.

“Doing these studies is so important at St. Jude, because we have a susceptible population,” Schultz-Cherry explains.

St. Jude influenza research began in the 1970s with work spearheaded by internationally renowned scientist Robert Webster, PhD, who now holds the Rose Marie Thomas Chair in Infectious Diseases. As a result of Webster’s work, the scientific community learned that aquatic birds are the reservoir for influenza A viruses.

Since 1975, St. Jude has been a World Health Organization (WHO) Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds. Today, St. Jude remains on the forefront of flu research.

“We help decide which influenza strains are going to be in the vaccines,” says Schultz-Cherry, deputy director of the St. Jude WHO center, “and St. Jude helps make vaccine seed stock for the pandemic viruses.”

St. Jude is also one of five U.S. research institutions designated as a Center of Excellence for Influenza Research and Surveillance by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health.

So, when the complexity of the New England harbor seal deaths emerged, St. Jude was asked to assist.

“The virus is really sloppy. When it grows, it can’t fix any mistakes—kind of like turning off spell-check. It just types away, makes mistakes and has no way to backspace and delete.”

## Calculating risks

Originally, the event involved investigation of five harbor seals, mostly pups that were in generally good physical condition, not malnourished. After avian H3N8 influenza A was confirmed, state and federal officials collected more samples from harbor seals stranded in

Maine, New Hampshire and Massachusetts.

In the St. Jude study, scientists found that H3N8 naturally acquired genetic changes.

“Either by going into the seals or by going seal to seal, that virus mutated,” Schultz-Cherry explains. “And the virus is really sloppy. When it grows, it can’t fix any mistakes—kind of like turning off spell-check. It just types away, makes mistakes and has no way to backspace and delete. Sometimes you see changes that make a virus better suited for a new mammal, or that make it grow more effectively to be able to transmit.”

At St. Jude, Schultz-Cherry and her colleagues look at those genetic changes and spot concerns that might indicate a need to produce new antivirals or vaccines.

“We want to know if these new influenza strains come from animals or birds, if they are going to create a public health problem and if so, how serious would that problem be? Would it affect everybody, or just pose a risk to people who have compromised immune systems, such as our



St. Jude patients? We do risk assessment studies: What is the risk to the public? Do we have therapies or vaccines or antivirals that are going to work against these infections?

“You couldn’t do work like this any place else. That’s why I came here—to move this work forward from the laboratory to the bigger area of public health for children.”

### Sealed with a kiss

So how does this unique H3N8 move from harbor

seals to other mammals?

Scientists learned that the virus is transmitted through respiratory droplets.

Would that imply sneezing seals?

“Absolutely right!” Schultz-Cherry says. “How do you get influenza but through aerosols—coughing, sneezing?”

“People shouldn’t be afraid of seals,” Schultz-Cherry continues, with a laugh. “Still, I wouldn’t run up and kiss one.” ■

## Why conduct flu research at St. Jude?

- Flu infections remain a **leading cause of illness and death** worldwide.
- The study of influenza is critical to cancer patients because their diseases or treatments may weaken their immune systems, putting them at **increased risk for infections** such as the flu.
- During an average U.S. flu season, the virus is linked to about **36,000 deaths** and **114,000 hospitalizations**.
- St. Jude is **home to the only World Health Organization Collaborating Center** for Studies on the Ecology of Influenza in Animals and Birds.
- St. Jude is designated as a **Center of Excellence for Influenza Research and Surveillance** by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH).

PHOTOS BY SETH DIXON



*“Our study raises a red flag about the threat this strain poses to humans who are exposed to animals infected with the virus,” explains Infectious Diseases researcher Stacey Schultz-Cherry, PhD. The next step, she says, is to conduct a human risk assessment study.*



# A Fertile Future

*The new St. Jude Fertility Clinic offers options to some current patients, as well as to long-term survivors.*

**By Elizabeth Jane Walker**

**F**ifteen-year-old Alexis Gilmore has a message for the children she may have years from now: “I loved you long before I ever knew you.”

Cancer ravaged Alexis’ reproductive organs when she was a toddler. After puberty, she was haunted by the possibility that she might never have children of her own.

“It really bothered me,” Alexis says.

When St. Jude Children’s Research Hospital opened a fertility clinic for its patients in June of 2014, Alexis’ heart leapt. She knew that she was at high risk of early menopause; her uterus had been removed during cancer treatment, and one of her ovaries had already ceased to function. Could doctors possibly harvest the eggs in her remaining ovary for future use? She was determined to find out.



PHOTOS BY PETER BARTA

*While undergoing fertility preservation procedures at St. Jude, Alexis Gilmore created a baby book that she can show to her children someday.*

## High expectations

Soon after the clinic's opening, Alexis met with its staff and began making plans to harvest her eggs, which would then be frozen and stored. While her peers lounged by the pool or hung out at the mall, Alexis injected hormones. Underwent frequent ultrasounds. Prepared for an egg-harvesting procedure. Created a baby book.

A baby book?

"I'm a teenager, so of course I always take selfies," she explains. "I thought I'd use those pictures to make a book so my kids would know what I went through for them. I've got pictures of the pregnancy test, of me before my first ultrasound, and then a photo of my mom and me. They're really fun pictures, because I was so excited."

From Alexis' right ovary, doctors obtained more than two dozen mature eggs.

"St. Jude isn't a hospital that forgets you once you're done with your cancer treatment," Alexis says. "The hospital offers things like this because they really care."

James Klosky, PhD, of St. Jude Psychology, agrees.

"At St. Jude, we're committed to providing options to survivors," he says. "In many cases, survivorship comes at a cost. We want to offer interventions to relieve some of those difficulties."

Located on the St. Jude campus, the Fertility Clinic is available to both current patients and long-term survivors

like Alexis. The service offers hope to interested patients whose age, treatment stage and disease status make them eligible to participate. Not only does St. Jude cover the cost of harvesting eggs or sperm, but the hospital also covers the cost of storing those samples until patients reach age 35.

"I don't know of any other institution in the United States that offers such a service," says William Kutteh, MD, PhD, medical director of the clinic.

Alexis' mom says she's thankful that St. Jude takes steps to ensure the quality of life of survivors.

"I just wanted her to live," Tamatha Gilmore says, "but St. Jude thinks of everything."

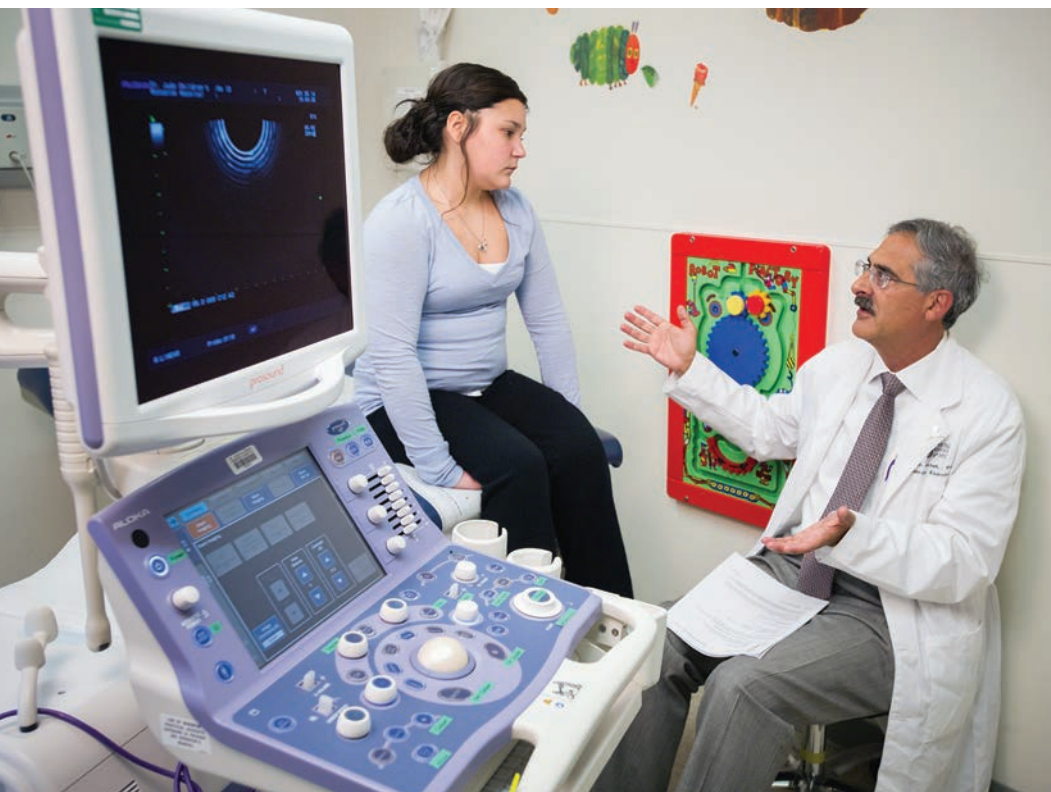
## The possible dream

Like Alexis, many cancer patients have a high risk of infertility as a side effect of surgery, radiation therapy, chemotherapy or the disease itself. As survival rates have improved, fertility preservation has become increasingly important to patients and families. Klosky estimates that half of adolescent and young adult male cancer patients are at increased risk for infertility, with about 10 percent of female childhood cancer survivors having acute ovarian failure and an additional 15 percent entering menopause prematurely.

"In my long experience, the issue of fertility is second only to death as a concern of parents of newly diagnosed

children," says St. Jude Clinical Director Larry Kun, MD, who has treated children at St. Jude for three decades. Patients also perceive the issue as significant, says Klosky, who recently published a study in which adolescent males ranked having children among their top three life goals.

Lukas Etchison has a firsthand



*In the St. Jude Fertility Clinic, 19-year-old Bailie Reed and William Kutteh, MD, PhD, discuss reproductive concerns. Located on the St. Jude campus, the clinic is available to both current patients and long-term survivors, such as Bailie.*





*Lukas Etchison arrived at St. Jude last fall to begin treatment for the brain tumor medulloblastoma. One of his chief concerns was fertility preservation. “Because of this service, cancer survivors can go on to live normal lives, doing all the things that they dream of doing and that they think about as they’re growing up,” says his mom, Denise.*

understanding of that sentiment. In September 2014, the Oklahoma native was diagnosed with a brain tumor called medulloblastoma. The cancer’s tentacles had spread into his spine. Therapy consists of 30 radiation treatments and four months of chemotherapy. One of Lukas’ first questions was whether the regimen might affect his ability to father children. The answer was yes.

“I definitely want to have a family someday,” Lukas says. “I’ve watched my parents, who’ve seemed happy raising my sister and me. I’d like to do the same thing, down the road.”

Soon after his arrival at St. Jude, Lukas met with Klosky to discuss fertility issues; as a result, the young man decided to bank his sperm. As Lukas faces the next few months of grueling treatments, he and his parents say they have one less complication to worry about.

“Because of this clinic, cancer survivors can go on to live normal lives, doing all the things that they dream of doing and that they think about as they’re growing up,” says Lukas’ mom, Denise.

## Beyond the birds and bees

In the Fertility Clinic, Kutteh and Klosky meet with patients and their families—listening to concerns, discussing options. Patients visiting the clinic may be new to St. Jude, like Lukas, or long-term survivors, such as Alexis.

“Not only do we see newly diagnosed patients, but we also see young adult patients who were treated here as children and who now want to get a better understanding of their fertility status,” Klosky explains.

He is quick to point out that the service is not appropriate for everyone.

“There are many, many features—whether cultural, religious, developmental or psychological—that can affect a family’s interest or perspective in terms of fertility preservation,” he says.

Some medical considerations may also prevent banking of sperm or eggs. Some children have not yet entered puberty, which medically precludes them from donating eggs or sperm. Other patients must begin treatment immediately in order to save their lives—and that treatment may also affect

their fertility. Females may be particularly affected in such a situation, since harvesting eggs requires several weeks of hormone therapy followed by a surgical procedure.

Kutteh and Klosky work in tandem to address these and other issues.

“Dr. Kutteh focuses more on fertility preservation interventions, whereas I focus more on decision-making, psychological adjustment to fertility differences, and maintaining a sense of peace regardless of what preservation decision is made,” Klosky explains. “We want our patients to be aware of and engaged in discussions related to fertility risk, and to be satisfied with their decisions, whatever those may be.”

### Beating the clock

Many times, Klosky and Kutteh feel like they are playing a “beat-the-clock” game—rushing to preserve fertility before cancer treatment begins.

One teenager recently arrived at St. Jude with a brain tumor. The head and spinal radiation necessary to save her life would also decimate her potential to have children. She and her parents wanted to bank and freeze her eggs, but the hormone treatments required to stimulate the ovaries would take 10 to 14 days. Because the girl’s tumor was aggressive, radiation therapy had to begin right away. With each radiation treatment, her fertility level diminished.

“There was a battle of who was going to win before her ovaries got wiped out,” Kutteh recalls. “I tracked her

egg quality hormones. By the time we harvested the eggs, she had the egg quality of a 42-year-old woman. We just barely made it. We got 25 eggs, 23 of which were mature and are now in the freezer. The pregnancy rate in the future is predicted based on the number of mature eggs you get. With 23, she is in good shape.”

### Parenthood possibilities

St. Jude is currently the only hospital in the U.S. to cover the expenses associated with harvesting and storing sperm and eggs until patients reach age 35. That policy eliminates one of the greatest barriers to fertility preservation for many childhood cancer patients: cost.

The knowledge that they have samples “in the bank” gives many patients a sense of assurance, according to Klosky.

“Research has shown that even if their materials are never used, just knowing that they’re available promotes significant reductions in fertility-related distress,” he says.

When patients reach the point at which they want to use those stored materials, they will be responsible for the cost of any necessary assistive reproductive technologies.

The St. Jude Fertility Clinic has given Alexis a sense of assurance—a glimpse of a future that may include motherhood. Perhaps, years from now, an infant with blonde hair and sparkling eyes will wrap a tiny, starfish hand around one of its mommy’s fingers.

And Alexis will smile. ■



*Alexis Gilmore meets with James Klosky, PhD, of St. Jude Psychology. “Here at St. Jude, we’re committed to providing options to survivors,” he says. “In many cases, survivorship comes at a cost. We want to offer interventions to relieve some of those difficulties.”*





# The Power of ST. JUDE

*"When you start giving to St. Jude, it is amazing what follows. You reap joy by helping these children," says J. Howard Johnson, pictured with his wife, Brenda.*

Faith binds donor to Danny Thomas and to the hospital he founded.

By Kerry Healy

**S**t. Jude Children's Research Hospital is named for a man who lived nearly 2,000 years ago. Yet St. Jude Thaddeus still has the power to inspire the lives of men like hospital supporter J. Howard Johnson.

Howard grew up in a Catholic household of modest means in Southern California. His family instilled in him the importance of giving, and his mother prayed often to St. Jude Thaddeus—a devotion she passed on to Howard. "It's part of my DNA," he says.

A 1961 alumnus of the University of Southern California School of Law, Howard married Brenda LaGrange in 1968. His career path changed course several times before he reached the pinnacle of his professional life, founding Targus Group International, a leading maker of computer carrying cases and other computer accessories.

While building this highly successful business, Howard weathered periods of struggle and uncertainty. In those times he turned to St. Jude, the patron saint of hopeless causes, just as the hospital's founder, Danny Thomas, had done. Through their shared faith, Howard feels a kinship to Thomas and the hospital he built.

"There is a premise that underlies the foundations of this hospital that stems from Danny Thomas' faith and convictions," Howard says. "I don't think this incredible place would exist without the support of the patron saint."

As Howard's business thrived, he remembered the values he had learned as a child. Howard leads by example, and he is guided

by and believes in the power of faith. Howard and Brenda say they feel blessed in many ways, including their four healthy children and nine grandchildren. Supporting St. Jude is one of the couple's ways of giving back.

The couple generously supports St. Jude through the J. Howard & Brenda LaGrange Johnson Family Foundation. In addition, they hosted a dinner in their hometown of New York to give other St. Jude donors in the area an opportunity to learn about the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project. In 2014, Howard received The Cardinal Stritch Donor of the Year Award, which is named in honor of Danny Thomas' spiritual mentor. The award recognizes donors who have made a significant financial commitment to St. Jude.

On a recent visit to St. Jude, Howard and Brenda were impressed by the hospital's research and care.

"St. Jude exemplifies what a child-friendly environment should be," Brenda says. Howard adds, "Their achievements at all levels are astounding, and I do not question that St. Jude is going to continue to excel in all their fields of interest."

In spite of all they have done for the hospital, Howard says the rewards he and his family have received in return are much greater.

"When you start giving to St. Jude, it is amazing what follows," he says. "You reap joy by helping these children. I am 100 percent convinced of that." ■

# Research Highlights

## Gene therapy provides life-changing relief from hemophilia

People with severe hemophilia B, a bleeding disorder, are at risk of serious health problems and early death. To manage their disease, they endure lifelong injections of a blood clotting protein.

Now, gene therapy developed at St. Jude, University College London (UCL) and the Royal Free Hospital has transformed life for 10 men with severe hemophilia B.

Years after receiving a single DNA treatment, the men continue to produce their own clotting factor with minimal side effects. This treatment has significantly decreased their reliance on injections. Some now participate in sports like soccer without worrying about bleeding.

“The results so far have made a profound difference in the lives of study participants by dramatically reducing their risk of bleeding,” said Andrew Davidoff, MD, St. Jude Surgery chair. “This study provides the first clear demonstration of the long-term safety and efficacy of gene therapy.”

Injections of blood clotting protein can cost \$250,000 a year. The researchers estimate that overall spending on injections of the missing protein has declined more than \$2.5 million for study participants. The findings were published in the *New England Journal of Medicine*.

## The power of phone calls for protecting the heart

Certain treatments for childhood cancer, while effective, can lead to serious heart problems later in life. For childhood cancer survivors, regular heart checkups can save lives. Yet despite the potential benefits, many survivors fail to get recommended checkups on schedule.

St. Jude researchers and their colleagues worked with 472 at-risk survivors to try a new approach. Results from the study showed that two brief phone counseling sessions from a nurse

practitioner, added to a written care plan, doubled the chances of survivors getting recommended heart screenings.

“This intervention offers a model for how to motivate other cancer survivors to be more proactive about their health,” said Melissa Hudson, MD, of St. Jude Oncology. Researchers are now working on ways to implement the approach more widely.

The findings were published in the *Journal of Clinical Oncology*.



## Science meets art

Trey Oguin of St. Jude Immunology discusses one of the images on display at the fourth annual Art of Science reception in Memphis. This collaborative project pairs St. Jude scientists with local artists. Researchers meet with their artist partners to share and discuss biomedical images from their research, which the artists use as inspiration for their works of art.





## First Lady visits St. Jude

During a visit to St. Jude, First Lady Michelle Obama poses for a selfie with patient Courtney Davis. As part of her historic visit, Mrs. Obama toured the hospital; spoke with patients, families and staff members; and answered a variety of lighthearted and thoughtful questions from patients during a question-and-answer session. Mrs. Obama joins Nancy Reagan, Barbara Bush and Hillary Rodham Clinton as First Ladies who have visited St. Jude.

## Two genes are double trouble in Ewing sarcoma

New secrets have been revealed by a detailed study of Ewing sarcoma, a cancer of the bone and soft tissue. Mutations in two genes appear to work together to drive cancer growth and reduce the chances a patient will survive. Mutations in the genes, *STAG2* and *TP53*, were previously linked to Ewing, but their

combined impact on survival was unknown.

“This is an important step in developing more effective diagnosis and treatment,” said Jinghui Zhang, PhD, of St. Jude Computational Biology. New clinical trials are being planned at St. Jude to test therapies that may be effective for Ewing

patients with these mutations.

The work, published in the journal *Cancer Discovery*, was a collaboration between the St. Jude – Washington University Pediatric Cancer Genome Project and the Institut Curie-Inserm through the International Cancer Genome Consortium.

## Launching a three-pronged attack against Ewing

St. Jude scientists have discovered a promising new triple-drug therapy for Ewing sarcoma. This is good news, as survival rates have been stalled for nearly two decades, and remain dismal for patients whose disease has spread or reappeared after treatment.

In laboratory studies, many tumors treated with the triple-

drug therapy disappeared and did not return. The therapy consisted of two drugs currently used to treat Ewing sarcoma, plus experimental drugs called PARP inhibitors that interfere with a cellular process called DNA repair. Clinical trials are now being planned to evaluate the therapy in patients.

The findings were published in the journal *Cell Reports*.

# Highlights

## A new connection between diet and disease

The human gut is home to trillions of bacteria and other microbes, known collectively as the intestinal microbiome. Changes in its makeup have been linked to diseases ranging from cancer to inflammatory disorders, though how has been poorly understood.

Intriguing results from St. Jude scientists now shed light on this connection. They found that diet-induced changes in the gut microbiome can alter susceptibility to an autoinflammatory bone disease. The key connection appears to be an immune molecule

called IL-1beta, which promotes inflammation and is influenced by the dietary changes.

“These results are exciting because they help to explain how environmental factors like diet can influence susceptibility to autoinflammatory diseases,” said Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology. “While multiple lines of evidence have suggested that diet can impact human disease, the scientific mechanism involved was a mystery.”

The findings were published in the journal *Nature*.

## Protecting fertility in boys with cancer

Chemotherapy saves lives, but often at a price. For men who were treated during childhood with drugs called alkylating agents, that price can be fertility (*see related article, page 15*).

A St. Jude study of 214 such men revealed that over half of them had abnormal sperm levels years after their cancer treatment, with a quarter producing no sperm at all. The researchers used the data to determine the cumulative chemotherapy dose that poses a strong risk to male fertility. The information should help guide decisions for young patients who may want to have biological

children of their own someday.

“Fertility preservation is important to patients and families, which is why at St. Jude we provide fertility counseling and preservation for active patients,” said Daniel Green, MD, of St. Jude Epidemiology and Cancer Control. “Until now, however, there was little information to guide clinicians, families and patients trying to assess the risk alkylating agents will pose to sperm production years in the future.”

The study appeared in the journal *Lancet Oncology*.

## Survivors' Day reunites St. Jude patients, caregivers

More than 350 individuals returned to the hospital for Survivors' Day 2014. Survivors and their families received updates and information about survivorship during a series of workshops. Participants also attended a panel discussion in which survivors shared their stories and received answers to questions about battling childhood cancer. Melissa Hudson, MD, Cancer Survivorship Division director (second from right), visits with survivors who now work on the hospital's campus: (from left) Gabby Salinas of Chemical Biology and Therapeutics, Shane Glover of Biomedical Engineering, and Miguel Betances of ALSAC.





By Leigh Ann Roman

*Thirty-four years ago, Diane Lavallee began her relationship with St. Jude. Last summer, she and her husband, Victor, visited the hospital for the second time, finding the St. Jude Pathway of Hope brick they had purchased.*

donation is about \$24 a month. The St. Jude Partners In Hope program includes 750,000 people who donated more than \$134 million in the last fiscal year—an amount that could cover the operating cost of St. Jude for 67 days.

St. Jude Partners In Hope like Lavallee are vital to the hospital's mission, says ALSAC President and CEO Richard Shadyac Jr.

"Every day, families come to the hospital desperate for lifesaving care because they've been told that St. Jude provides their best hope for survival," he says. "Supporters in the monthly giving program ensure that we have the steady flow of funds needed to help our doctors and scientists treat critically ill children in need of cures."

Lavallee's connection to the St. Jude mission is rooted in her deep love for children. Once a stay-at-home mom who ran an in-home daycare, she is now office manager of a local furniture store, where she keeps a St. Jude "cuss cup."

"During the holidays, anybody who swears at work has to pay the cuss cup," Lavallee says of the good-natured collection she started 10 years ago. Contributions have allowed her to send an additional \$75 to \$175 to St. Jude annually.

Lavallee and her husband, Victor, have visited the hospital twice—once 10 years ago, and again this past summer.

After the first visit, Lavallee upped her monthly contribution. "It was a very moving and humbling experience. We didn't see any sadness. All the children seemed to be happy," she says.

When they returned this year, the couple found the brick they had purchased on the Pathway of Hope, another way of supporting the hospital.

Lavallee keeps St. Jude in mind when good fortune comes her way, giving 10 percent of any pay raise or tax refund to St. Jude. Victor supports her commitment to the hospital, as well.

"He says there is nothing we can't do for kids," she says. "Not just for our kids, but for any kids." ■

**Learn more about St. Jude Partners In Hope**

**1-800-822-6344**

[partnersinhope.org](http://partnersinhope.org)



## A Partner for Life

Meet one of the more  
than **750,000** dedicated  
**Partners In Hope.**

**T**hirty-four years ago, Diane Lavallee was on bed rest during her second pregnancy when she saw an infomercial about St. Jude Children's Research Hospital. She immediately joined the monthly giving program and has been a loyal supporter ever since.

"Seeing all those faces of innocent children and what was happening to them made me cry. I started thinking about the baby I was carrying and what I would do if that were me," says Lavallee, a Massachusetts resident. "I felt that I needed to help in some little way—that God had blessed me with one healthy child and another on the way."

When Lavallee joined the program, the monthly donation request was just \$7. Today, the average St. Jude Partner In Hope

By Jack Nicklaus

## Fore **THE KIDS**

Golf history's greatest icon explains his support of St. Jude and children's health care.



Visiting with St. Jude patients are (from left) Howard Milstein, Jack Nicklaus and Barbara Nicklaus.

**I**t is said there is no exercise better for the heart than reaching down and lifting people up. Early in our lives, my wife, Barbara, and I pledged that if we were ever in a position to help others, we would—and that extended hand would most often go to children.

Our path to philanthropy can be traced back to an alarming moment for us in 1966. Our daughter Nan was just 11 months old, and she was struggling to breathe. In fact, she was basically choking. At the hospital, they discovered she had inhaled a piece of crayon. She battled pneumonia and other complications while there, but the doctors and staff essentially

saved her life. It was at that time we began to make a strong commitment to children's health care.

Fast-forward to 2004, when we created the Nicklaus Children's Health Care Foundation to provide access to world-class health care for children, and to support cutting-edge programs focused on the diagnosis, prevention and treatment of childhood diseases and disorders. Part of that mission hinges on forming strategic partnerships with like-minded organizations, such as

St. Jude Children's Research Hospital.

I visited St. Jude with Barbara and my business partner, Howard Milstein, last spring, when we announced that the charitable program tied into the sales of our Nicklaus Golf Ball line was expanding to benefit St. Jude. We have always loved and supported St. Jude, and our visit allowed us to observe firsthand the extraordinary work being done. We met wonderfully inspiring children and incredibly dedicated and passionate hospital staff. It was an emotional few hours, but we left motivated and even more driven about our mission.

When we launched the Nicklaus Golf

Ball line last fall, we wanted to determine a way these balls could help save young lives as much as save golfers strokes. We decided that for each dozen golf balls sold through *nicklaus.com*, the Nicklaus Companies would make a donation to St. Jude and the Nicklaus Children's Health Care Foundation. Because of support from our friends at FedEx, online customers also receive free domestic shipping, and if FedEx delivery services are used, more money is donated to St. Jude. Customers can also make voluntary contributions at checkout, and to date, nearly 80 percent have chosen this option. That says so much about the game of golf and the people who play it.

Supporting organizations that impact young lives means the world to Barbara and me. My career in golf has blessed our family of five kids and 22 grandkids, and the philanthropic model of our Nicklaus Golf Balls allows golfers of all ages and abilities to spread that blessing to those who need it most—such as the children and families impacted each and every day by St. Jude. ■

*Golf legend Jack Nicklaus, nicknamed the "Golden Bear," is widely recognized as the greatest champion in the history of golf. He and his wife, Barbara, have a long history of philanthropy. To purchase Nicklaus Golf Balls and help support St. Jude, visit [www.nicklaus.com](http://www.nicklaus.com).*



“I knew that I  
wanted to help  
St. Jude continue  
its lifesaving mission,  
so that the children  
and their parents  
could realize their  
dreams.”

—Nora Martinez



## Your gift gives back.

*St. Jude patient Charlee  
at age 3  
myelodysplastic syndrome*



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By including St. Jude in her estate plans, Nora Martinez is providing for her loved ones and helping to ensure that the lifesaving work of St. Jude doesn't stop until no child dies from cancer. Her legacy of compassion will continue to carry her values forward for future generations.

**Begin your legacy today. Call 1-800-910-3188 or visit [stjude.org/legacy](http://stjude.org/legacy).**

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## Champion for St. Jude

*St. Jude National Outreach Director Marlo Thomas reacts to thunderous applause during dedication ceremonies for the Marlo Thomas Center for Global Education and Collaboration in November. Thomas was honored for her tireless efforts to raise awareness and funds for the research and treatment of childhood cancer.*

*Celebrating her achievements were family, friends and dignitaries, including (at right) former U.S. Secretary of State Hillary Rodham Clinton. The 38,000-square-foot center will be the epicenter of a campus facility designed to usher in a new era of research, education, collaboration, care and treatment of childhood cancer.*



*Finding cures. Saving children.*