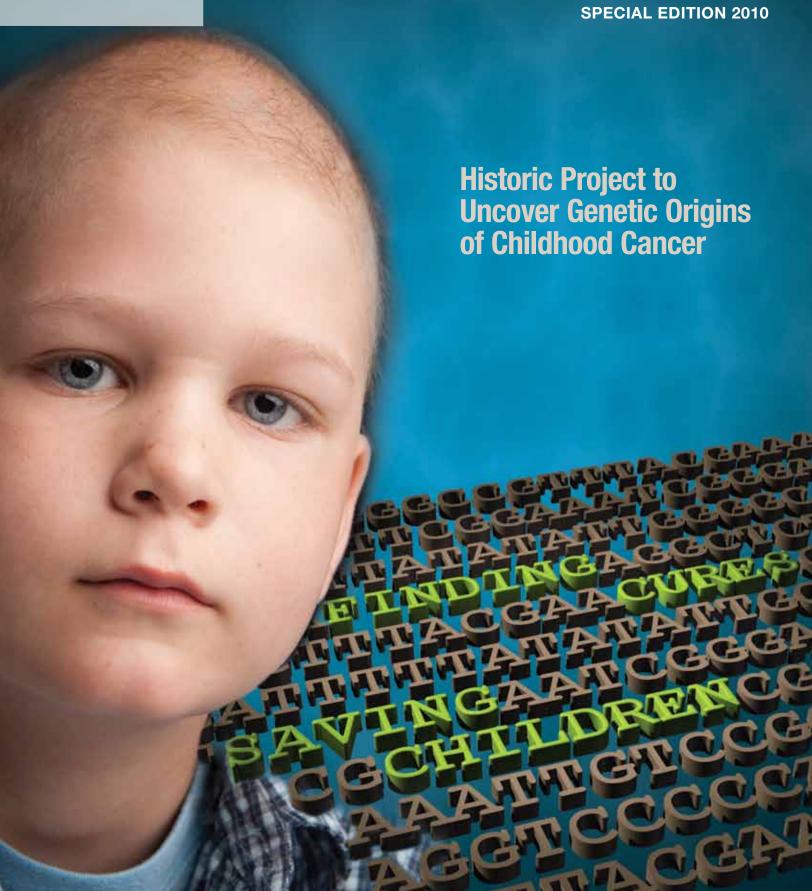
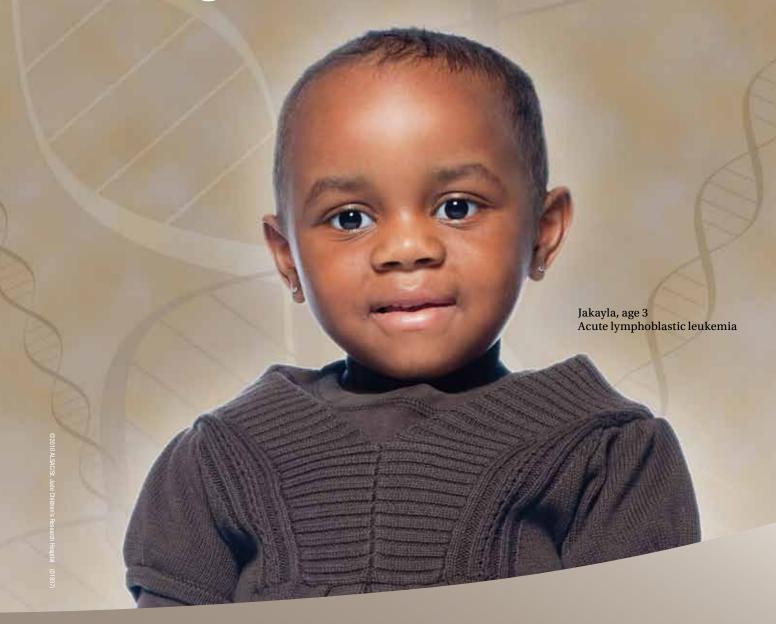


Promise



Join our most ambitious effort to fight childhood cancer.



St. Jude Children's Research Hospital transformed the way the world treats childhood cancer, leading to better care and increased survival. And now St. Jude scientists are poised to make extraordinary breakthroughs in our understanding of the underlying causes of this still deadly disease. St. Jude is embarking on a multi-million dollar project to sequence pediatric cancer genomes. The **St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project** offers the highest promise yet for lifesaving improvements in the diagnosis and treatment of the deadliest childhood cancers. Together with the support of our loyal donors, we are closer than ever to realizing Danny Thomas' dream of a day when no child will die in the dawn of life.

Find out more at www.stjude.org



Promise

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Promise

Special Edition, 2010

Cover story

2 History in the Making

Massive project aims at understanding the genetic origins of pediatric cancers.

Features

7 A Sparkling Alliance

Kay Jewelers shows its support of a historic project.

8 A Legacy of Life

The mother of one valiant child glimpses hope on the horizon.

10 Realizing the Dream

How you can support St. Jude and the new research project.

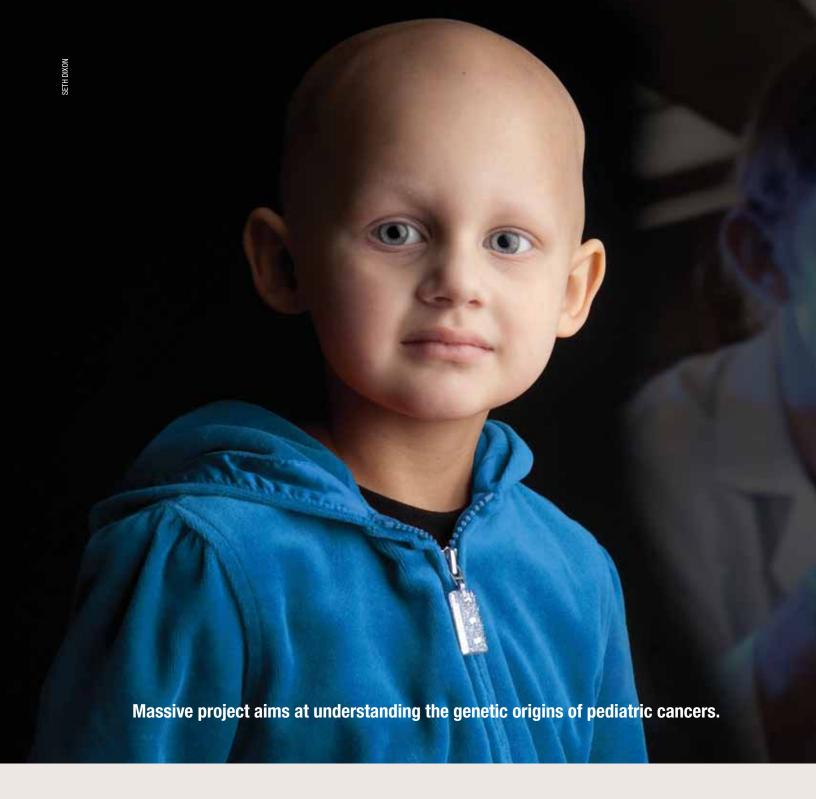
Perspective

12 Creating a Better Tomorrow

Dr. William E. Evans reflects on the significance and the promise of the Pediatric Cancer Genome Project.

St. Jude Children's Research Hospital's mission is to advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment. Consistent with the vision of our founder, Danny Thomas, no child is denied treatment based on race, religion or a family's ability to pay.

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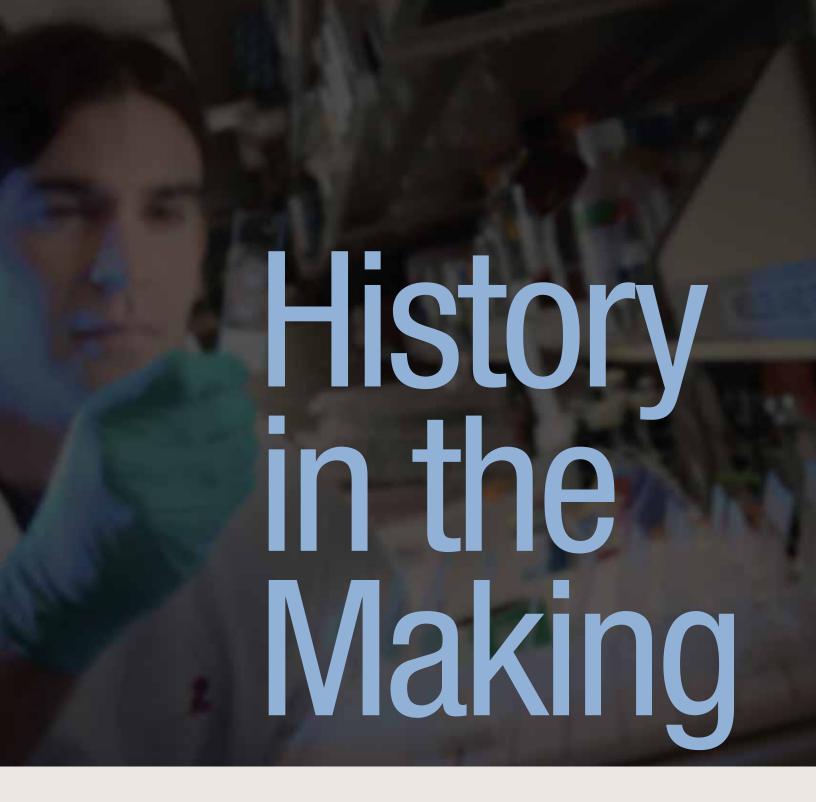


pproximately 106,800.
That's how many four-drawer filing cabinets would be necessary to store the raw data scientists expect to generate from an epic project to decode childhood cancer genomes.

St. Jude Children's Research Hospital and Washington University School of Medicine in St. Louis recently embarked on the largest initiative to date aimed at understanding the genetic origins of child-hood cancer. The team is joining forces to decode the genomes of more than 600 childhood cancer patients who have contributed tumor samples throughout the years.

Scientists in the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project will sequence the entire genomes of both normal and cancer cells from each patient, comparing differences in the DNA to identify genetic mistakes that lead to cancer.

"We are on the threshold of a revolution in our understanding of the origins of cancer. For the first time in history, we have the tools to identify all of the genetic abnormalities that turn a white blood cell into a leukemia cell or a brain cell into a brain tumor," says Dr. William E. Evans, St. Jude director and CEO.



"We believe it is from this foundation that advances for 21st century cancer diagnosis and treatment will come."

Today is the day

As a research institute since its inception, St. Jude has compiled one of the world's largest and most complete repositories of pediatric tumor tissues and normal DNA from the same patients, as well as all of the associated clinical and

biological annotations needed to fully understand these tumors.

"This tissue bank has been generated through St. Jude protocols and the acquisition of material from patients who were treated on those protocols," explains James Downing, MD, St. Jude scientific director.

The collection dates back to the 1970s and includes more than 50,000 tumor, bone marrow, blood and other biological samples. "This is virtually a treasure chest containing the answers we seek, but it has been awaiting the day when science and technology would allow us to analyze the tissues and reveal the answers. In many ways, today is that day," Evans says.

The samples donated by children undergoing treatment are essential to efforts to understand the origins of cancer. The tissue bank has also helped St. Jude scientists develop



"I think this will really be a wonderful opportunity for us to develop more optimal treatment and perhaps to develop measures to prevent the development of cancer in the first place," says Ching-Hon Pui, MD, Oncology chair (pictured with St. Jude patient Ishmael Wilson).



Approximately 200 brain tumors will be chosen for sequencing under the leadership of Brain Tumor Program co-leaders Amar Gajjar, MD, and Richard Gilbertson, MD, PhD. "Our current research has been based on a long-standing understanding of the anatomy of the brain, as well as an understanding of various genes involved in the diseases," says Gilbertson (shown working with colleague Jennifer Atkinson, PhD). "The Pediatric Cancer Genome Project will take our work to a higher level and enable us to make even more progress."

the experimental models crucial to determining which mutations drive cancer's development and spread.

"One of Danny Thomas' favorite sayings was, 'One child cured in Memphis is 1,000 children cured worldwide.' That is an eloquent way to express the importance of participation in clinical research," says Michael Kastan, MD, PhD, St. Jude Comprehensive Cancer Center director. "Every child who walks through the doors of St. Jude contributes to our education—to our ability to understand pediatric cancer. Our goal is to understand all of these tumors at the most basic level so we can develop new therapies. Clinical research allows us to do this.

"We are the only Comprehensive Cancer Center designated by the National Cancer Institute that is dedicated solely to the care of children," Kastan continues. "This makes us uniquely suited to conduct this research."

An outgrowth of the mission

The Pediatric Cancer Genome
Project focuses on childhood
leukemias, brain tumors and tumors
of bone, muscle and other connective
tissues called sarcomas. St. Jude
is providing DNA from tumor
and normal tissues of patients,
Washington University's Genome
Center is performing the wholegenome sequencing, and both are
participating in validation sequencing.
Researchers at both institutions
will collaborate to analyze the data
and make the information publicly
available once validated.

Earlier research by this group and others indicates that the many genetic abnormalities in childhood cancers will differ from those found in adult cancers.

"Pharmaceutical industries are not going to focus on pediatric

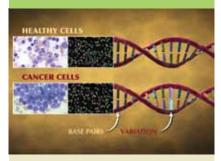
cancer because there is little financial motive for them to do that," Downing explains. Our mission is to advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment. That is why we need to tackle a problem that others will not tackle. It is our mission, our responsibility as a national resource."

Searching for variations

With 3 billion base pairs, the size of the human genome is staggering. As part of the project, scientists will sequence both the normal cells and cancer cells from more than 600 patients. Clayton Naeve, PhD, St. Jude chief information officer, has done the math.

"If you were to type up the 3 billion base pair human genome on standard typing paper, it would fill 89 four-drawer file cabinets," Naeve says. "We are proposing to do 1,200 of those, and that's just raw data. Overall, we anticipate this project producing about 2 petabytes, or 2 million gigabytes, of data during

Identifying Cancer Mutations



As part of the Pediatric Cancer Genome Project, scientists will isolate DNA from both the cancer cells and and a normal, healthy tissue sample from the same patient. The healthy cells give the scientists a reference DNA sequence to which they can compare genetic alterations in the patient's tumor cells.



"Pharmaceutical industries are not going to focus on pediatric cancer because there is little financial motive for them to do that," says St. Jude Scientific Director James Downing, MD (at left; pictured in his lab with colleague Charles Mullighan, MD, PhD). "And yet cancer is still the leading cause of death from disease among U.S. children over 1 year of age. So who will focus on pediatric cancers? That's why we're here."

the next three years. That is about five or six times more data than St. Jude has collected in its nearly 50-year history."

Earlier research to identify cancer mutations has typically focused only on the few hundred genes already suspected of being involved in the disease. While some recent studies have involved sequencing the 20,000 or so proteincoding genes in the genome, the whole-genome approach involved in the Pediatric Cancer Genome Project provides a more detailed and complete picture of all the mutations involved in a patient's cancer by examining both the protein-coding genes and the long stretches of DNA between genes, which may influence the ways the genes work. Such complete genomic sequencing is now possible because of recent advances that have made the technology faster and far less expensive.

Researchers involved in the project also will investigate how pediatric cancer is influenced by

other variations in the genome, including epigenetic changes, which are changes that alter the expression of genes but not the genes themselves. Researchers also will use DNA sequencing data to identify genetic markers that can help physicians decide the best treatment options for cancer patients, based on the genetic profile of their tumors.

"The tools we are using have evolved to the point where they are faster, more accurate and less expensive than they were just a year ago," Evans says. "But DNA sequence data alone does not equal new knowledge. It requires meticulous analyses and insightful interpretation to translate these sequence data into new knowledge that can lead to better treatments for childhood cancer."

Sharing results with the world

Details of the Pediatric Cancer Genome Project were announced in January 2010 at the National

The Role of Genes in Pediatric Cancer

Cancers are genetic diseases that are triggered by harmful changes in the DNA of normal cells.

The human genetic code is written in the four-letter alphabet of the DNA molecule—A, T, C and G. Cells can accumulate misspellings, or mutations, within the 3 billion DNA base pairs of the human genome.

Mutations remove regulatory controls, allowing cells to multiply and spread unchecked. Every cancer arises from a series of mutations, each of which alters a normal biological process in the cell and leads to the transformation of a normal cell to a malignant cell.

Until now, technology has limited scientists' ability to quickly assess the entire genome and identify most mutations. Only 350 of an estimated 2,000 cancer genes have been found; as a result, the genetic causes of most cancers remain elusive.

If scientists can pinpoint the critical mutations that drive these tumors, they can develop diagnostic and prognostic tests and identify targets for new, more effective treatments.

Investigators at St. Jude and Washington University will search the vast landscape of the human genome for the mutations that lead to childhood cancers.

Press Club in Washington, D.C. Among the presenters was Francis Collins, MD, PhD, director of the National Institutes of Health, who led the Human Genome Project, an international feat that paved the way for the Pediatric Cancer Genome Project. Collins praised St. Jude and



"It's an exciting time to be a cancer researcher," says Michael Dyer, PhD, who leads the Solid Malignancies Program, along with Alberto Pappo, MD. "This project will give us an unprecedented opportunity to integrate cancer genetics with developmental therapeutics in order to explore new treatments for pediatric solid tumors."

Washington University as leaders in pediatric cancer and cancer genomics.

"I am delighted to be here to cheer for and celebrate this wonderful partnership that's being announced to forever change the landscape of our understanding of pediatric cancers," he said. "What is done in this partnership between St. Jude and Washington University will provide the foundation upon which pediatric cancer diagnostics and therapeutics will be built in the future."

By combining St. Jude and Washington University talent, resources and experience, this initiative raises hopes of saving the lives of countless children worldwide by generating new knowledge about the biology of the disease and translating that into diagnostic tests and a new generation of more effective drugs.

The Pediatric Cancer Genome Project will include a public database where information, once validated, will be shared with the international scientific community, with the goal of accelerating progress in battling childhood cancer.

"Scientists will want to see the data as a foundation or a platform for discovery of what causes childhood cancers and how better to treat them," Evans says. "This is the hospital's next big contribution on behalf of all children with cancer. It allows us to fulfill the national and international leadership role that St. Jude has had for many years." ■



Leaders of the Pediatric Cancer Genome Project are (from left) Michael Kastan, MD, PhD, St. Jude Comprehensive Cancer Center director; Elaine Mardis, PhD, Washington University Genome Center co-director; James Downing, MD, St. Jude scientific director; Richard Wilson, PhD, Washington University Genome Center director; Larry Shapiro, MD, executive vice chancellor for Medical Affairs and dean of Washington University School of Medicine; and Dr. William E. Evans, St. Jude director and CEO.

A Sparkling **Alliance**

By Janice Hill

Kay Jewelers shows its support of the Pediatric Cancer Genome Project.

or more than a decade, Kay Jewelers has been a major partner in helping St. Jude Children's Research Hospital find cures and save children.

Now the company's dedication to the St. Jude mission is taking on a new dimension with its commitment to provide \$20 million as the lead sponsor of the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project.

"We are proud to be the lead sponsor for this historic research effort that holds such promise for saving children from cancer," says Mark Light, CEO of Kay Jewelers. "Year after year our employees have seen the remarkable progress being made at St. Jude, and we welcome the opportunity to be a part of this historic initiative that will transform the understanding and treatment of childhood cancer in the future."

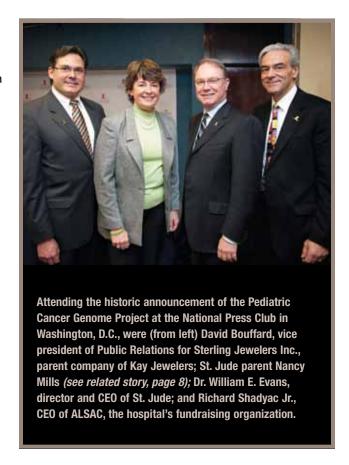
Rick Shadyac Jr., CEO of ALSAC, the hospital's fundraising organization, says Kay Jewelers' decision to support the genome project reflects the company's deep dedication to children.

"Kay Jewelers' leadership in supporting this groundbreaking project speaks volumes about the company's strong values, dedication to excellence and

"With this latest and largest commitment, Kay Jewelers will have a lasting impact on research that will lay the foundation for better ways to diagnose and treat cancer."

commitment to charitable giving that is children focused and research based," Shadyac says.

Kay Jewelers selected St. Jude as its national charity of choice in 1999 and has wholeheartedly stood behind the hospital's mission ever since. Each year, Kay Jewelers' parent company, Sterling Jewelers Inc., kicks off its support of St. Jude with an employee-giving campaign and the sale of holiday plush items, which this year included a



cuddly brown puppy wearing a winter hat and scarf named "Colby." The plush promotion continues to be a national success story and is augmented by employee giving, a Mother's Day promotion and a corporate donation.

Most recently, the company showed its dedication to St. Jude with a \$16 million multi-year commitment to remodel and significantly expand the St. Jude cafeteria, which is now named the Kay Kafe.

In addition, Kay Jewelers has provided valuable support to renovate the Solid Tumor Clinic, the patient registration area and the second-floor lobby in the hospital's Patient Care Center.

"Our partnership with Kay Jewelers has been invaluable in helping us provide the best in family-centered patient care over the last decade," Shadyac says. "Now, with this latest and largest commitment, Kay Jewelers will have a lasting impact on research that will lay the foundation for better ways to diagnose and treat cancer in the 21st century."



A Legacy of Life

The mother of a valiant St. Jude patient glimpses hope on the horizon for thousands of other children and their parents.

By Nancy Hula Mills

n July 2, 1997, I walked through the doors of St. Jude Children's Research Hospital with my 5-year-old daughter, Ali. That day, she looked just like any other 5-year-old. But within four hours we learned that Ali had cancer. The next day she returned for tests to determine exactly what type of cancer she had. After a bone marrow biopsy, CT scan, bone scan and MRI, my husband and I were told that Ali had stage IV neuroblastoma, a cancer that originates in the nerve tissues. She had a tumor from her abdomen to her neck, and the cancer was in her bone and her bone marrow.

Within 24 hours of walking through the door of St. Jude, we learned that our precious Ali had a very grim prognosis—she would probably only live for six months. She was admitted to the hospital that evening, and I stayed up all night and tried to figure out how in the world I was going to tell my 5-year-old that she had cancer.

During the following 18 months, she had surgery, round after round of chemotherapy and a bone marrow transplant. In August of 2001—four years after she had begun—Ali's treatment was complete. During those years, she had met and befriended many children at St. Jude, many of whom had not survived. Ali attended more "celebrations of life" by the age of 9 than I had attended in my entire life. She would say things like, "Mommy, when I die and I have a celebration of life, I want you to speak," or "I want this hymn played." That's abnormal talk for a typical 9-year-old, but a very typical comment from a child with cancer.

Ali was no longer the shy and naïve 5-year-old I had taken to St. Jude four years earlier. She began to flourish. She went to school; enjoyed being with her friends; hated French class; was a super ambassador for St. Jude; and she loved, loved, loved being a cheerleader.

I would like to say that was the end of our cancer story. I would like to tell you that Ali is enjoying her senior year in high school with her best friend, Elizabeth, and talking with her brother, Bobby, as he navigates through his freshman year in college. Unfortunately, there is a second chapter to Ali's cancer story. In January of 2004 her cancer came back—after six years of being cancer free and three years after she had completed treatment. Ali died April 12, 2005, at St. Jude—the place she'd grown up, the place she loved, the only place she wanted to be when she felt bad or was scared.

I remember that was the first time I ever walked out of St. Jude without her. That night, I looked up at the hospital's research tower and prayed that somehow through the research very few other parents would have to live out that nightmare.

Ali is only one child, and we are only one family who has been affected by cancer. There are thousands of others—with their own individual stories, with their special friends and family, and with the hope that there will be a cure for them.

In 1962 when St. Jude opened its doors, the survival rate for neuroblastoma was 10 percent. Ali would not have had any chance of survival at that point. Fortunately, due to the progress made from the beginning to the time of her diagnosis, Ali surpassed those six months. She lived eight fun-filled years because of the research prior to her diagnosis. However, that is not enough. The cure

rate for some childhood cancers is still below 50 percent.

Without research specific to childhood cancer, we will not move the needle fast enough toward a cure. Cancer is the No. 1 cause of death by disease in children over the age of 1. Without significant leaps in childhood cancer research, we will only make small advances. Simply stated, it means that if the research is done faster, a child dying with cancer today might be saved, and the parents might not have to watch their child die.

As a parent who has had to live through that nightmare, I am pleased and hopeful about the new Pediatric Cancer Genome Project. The information and data learned from Ali's case and many others just like her are now going to be used by doctors and researchers to help future children. Danny Thomas, the founder of St. Jude, once said, "No child should die in the dawn of life." Hopefully, with this project we will make that a reality for children with cancer.

Ali succumbed to cancer in 2005, when she was 13 years old. "The information and data learned from Ali's case and many others just like her are now going to be used by doctors and



Realizing the Dream

St. Jude needs your help to take a major step forward in curing childhood cancers. Here are a few ways to support St. Jude and the Pediatric Cancer Genome Project.

The St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project is the most ambitious research endeavor in the hospital's history, costing \$65 million over three years, with \$55 million coming from St. Jude. An investment now could yield enormous benefits for children with cancer. Your support can make it possible.

Here are just a few examples of how your gift can help contribute to the project.

Tools for Discovery

\$1 million Cost to develop and maintain a public database, which will allow our scientists to share

their findings with the global medical community.

\$670,000 Cost of one genome sequencing instrument.

Each machine will allow scientists to sequence one complete genome within days, when previous equipment required months to complete the task. A total of 20 instruments are needed for the project.

samples used in the project.

Steps to Discovery

\$83,000

\$25,000

\$70,000 The total costs to obtain and analyze the complete DNA sequence of one sample pair

(one normal genome and one tumor genome).

Cost to keep a single DNA sequencer

running for one month (including staff,

Liquid nitrogen freezers to maintain tissue

reagents and supplies).

\$15,000 The cost of computational analyses required

to determine the relative frequency of specific mutations within a given tumor type (leukemia, brain or solid tumor) and determining whether they provide clinically

useful information.

Numerous other funding and naming opportunities are available as you join with the hospital in this pioneering exploration into the origins of childhood cancer. The items listed are representative of the needs of this research project. Costs are approximate and will vary based upon actual costs incurred.

To learn more about ways you can make a meaningful gift in support of St. Jude and the Pediatric Cancer Genome Project, please call 1-800-395-1087 or e-mail giftplanning@stjude.org.





It was 41 years ago when my wife and I walked through the doors of St. Jude Children's Research Hospital with our baby boy, but it seems like it was yesterday. We had just learned that Jeffie, always so happy and healthy, had cancer in both of his eyes—double retinoblastoma. Our doctors at Shands Hospital at the University of Florida had sent us to this new hospital in Memphis called St. Jude because that was our greatest hope.

Full of fear, we didn't know what to expect.

What we found was a place of peace and tranquility and great compassion for Jeffie and our family. I will always know that everything that could have been done for Jeffie was done. He was treated by everyone as if he were their own child! The doctors used the most advanced treatment and all the knowledge available to try to save him. But it was not enough. They made it possible for us to have two more years with Jeffie, but we lost him on July 5, 1971, just short of his third birthday.

I'm very thankful there has been so much progress since I first heard those horrible words "Your child has cancer." But too many children continue to suffer and die; even though we have come so far, there is much that even the brightest and hardest working minds don't understand about this horrible disease.

That is why I am so excited about the St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project. It will show scientists things they've never been able to see before about how cancer begins and grows in a child. When I think of the progress St. Jude has made in the last 40 years, I can only imagine the ways this new knowledge can be used to save more children.

Every parent who has ever had a child at St. Jude knows that donors like you help make the remarkable research and loving care possible. There are no words to convey how grateful we are. Parents see the lights in the research buildings burn all through the night at St. Jude, and we know you help keep those lights burning. We believe strongly in the power of that research to one day make it possible to send every child home, cured.

On behalf of all the parents who have faced pediatric cancer, and on behalf of all the parents who will face it in the future, thank you for considering a meaningful gift in support of St. Jude and the Pediatric Cancer Genome Project. Thank you for helping St. Jude begin this incredible journey of discovery that will lead to a better tomorrow for children with cancer.

Sincerely,

Jeff and Janet Carlin

Jeff and Janet Carlin

Perspective

By Dr. William E. Evans

Creating a Better Tomorrow

"We need your continued support as we undertake this project, which is the largest and most powerful single initiative in the history of St. Jude."

or nearly 50 years, families have come to St. Jude Children's Research Hospital because they believe innovative clinical trials and basic science research can create a better tomorrow for children with cancer.

We have made great progress, with cure rates for childhood cancers now pushing about 80 percent. But the advances we have made have been incremental. They have come through finding optimal ways to use anti-cancer drugs that were developed for adult cancers, not for children. We have learned how to combine those drugs better and how to dose them properly for children. The advances we have made have come from better diagnostics, better supportive care, better surgical approaches. And St. Jude has pioneered the use of genetic and pharmacogenetic tests to further optimize treatment.

In spite of this progress, cancer remains the leading cause of death by disease in U.S. children over 1 year of age. If we are going to find cures for all children with cancer, we must



St. Jude patient Ben Sherman visits with Dr. William E. Evans in his office at the hospital. The Pediatric Cancer Genome Project will help children like Ben by advancing scientists' knowledge of what causes cancers and how better to treat them. "The work has already begun," Evans says. "DNA for this project is being sequenced at this moment."

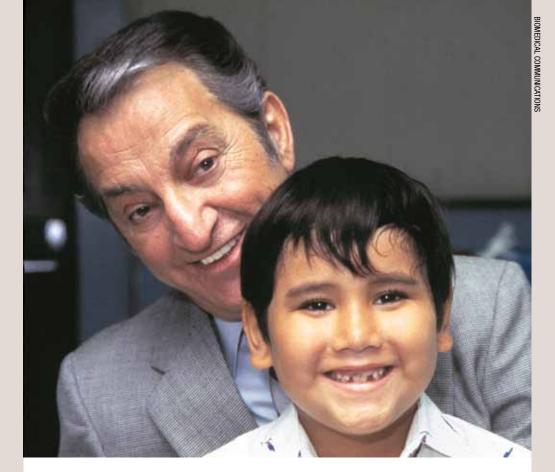
advance our knowledge of what causes a white blood cell to become leukemia; what causes a brain cell to become a brain tumor. Then we must use that knowledge to develop innovative treatments that are more effective and less toxic.

Cancer is a disease of our DNA—of our genome. With the launch of the St. Jude – Washington University Pediatric Cancer Genome Project, we are embarking on a bold initiative designed to identify mutations underlying childhood cancer. This project will advance our knowledge of what causes these cancers and how better to treat them. I am pleased to say that the work has already begun. DNA for this project is being sequenced at this moment.

As data from our work are validated and published, we will make all of the data publicly available to investigators around the world. We anticipate that this will spawn projects and lead to discoveries that build upon the work coming from our project and will lead to studies to fully elucidate the precise mechanisms by which these mutations lead to the development of cancer. We will be fulfilling our mission at St. Jude as well as our responsibility to lead. And we will do so by sharing freely with the world what we discover.

St. Jude is financially supported by thousands of individuals, organizations and corporations, without whom our work simply wouldn't be possible. We need your continued support as we undertake this project, which is the largest and most powerful single initiative in the history of St. Jude. This is an exciting time for St. Jude. But it's an even more exciting time for children worldwide.

Dr. William E. Evans is director and CEO of St. Jude, a position he has held since 2004. During this time, St. Jude has been consistently ranked among the top places to work in academia by The Scientist magazine, and remains the only National Cancer Institute—designated Comprehensive Cancer Center devoted solely to children. Last year, Parents magazine ranked St. Jude as the nation's top children's cancer hospital.



A message from the Thomas family

Dear Friends:

Since our doors opened in 1962, St. Jude Children's Research Hospital has pioneered treatments that have transformed the way pediatric cancer is treated. And in the 48 years since our founding, the world has come to look to us to discover new ways to overcome the deadly diseases that threaten children's lives.

That's why we have embarked on an exciting and pioneering program joining forces with Washington University, a world leader in genomic research, to take cancer research and treatment to the next level. The St. Jude Children's Research Hospital – Washington University Pediatric Cancer Genome Project aims to harness the very latest in technology to unlock the genetic mysteries of childhood cancer, offering great promise for developing powerful new approaches to diagnose and treat young cancer patients in the future.

We learned many valuable lessons from our father, Danny Thomas, but none more important than his conviction that success is measured not by what we accomplish for ourselves but the difference we make in the lives of others. How we wish he were here today to be a part of this amazing quest he could hardly have dreamed possible. We can only imagine his enthusiasm at the start of this journey of discovery that holds such promise for children with cancer.

We hope you will share with us the excitement in learning about this unprecedented project, because you have played a significant role in getting St. Jude to this special place in our history—one that we are confident could be a major milestone for St. Jude and the world of science as we continue our efforts to advance pediatric cancer research.

We know we speak for everyone at St. Jude—the children and their families, the doctors and researchers—when we say thank you for all that you do for St. Jude. Your commitment to our mission makes this exciting work and all of our world-class research and treatment programs possible.

God bless you and your families,

Marlo, Terre and Tony Thomas



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