St. Jude Children’s Research Hospital was founded by the late entertainer Danny Thomas. It opened February 4, 1962. The institution was created because of a promise Danny made during the depression era to St. Jude Thaddeus, the patron saint of the hopeless.

“Show me my way in life,” Danny prayed. In return, Danny promised to build St. Jude Thaddeus a shrine. That shrine became a world-class research institution that treats children regardless of race, color, creed or their ability to pay. This remarkable event also inspired the name of this magazine,

Promise.
Avian flu
For the second winter in a row, the world's medical and scientific communities turned to experts at St. Jude for help during a global crisis. Robert Webster, PhD, and his colleagues at St. Jude spent several months studying the H5N1 "bird flu" outbreak in Asia. Webster worked with officials there to make recommendations about stopping the spread of this disease, which sickened thousands of birds and killed individuals in Thailand and Vietnam.

In late January 2004, the World Health Organization (WHO) sent samples of the avian flu virus from Vietnam to St. Jude, where scientists began creating a vaccine against this strain of the bird flu. Webster directs WHO's U.S. Collaborating Center at St. Jude. Using a reverse genetics system devised at St. Jude, scientists in Webster’s laboratory began creating a new strain that could be used as the master seed for vaccine manufacturing.

In response to the crisis, Webster and Richard Webbly, PhD, both of St. Jude Infectious Diseases, were interviewed by reporters from major media outlets, including Time and Newsweek magazines, NBC Nightly News, ABC World News Tonight, BBC (London), The Discovery Channel, The New York Times, The Wall Street Journal and The Washington Post.

Vinculin and cancer cells
St. Jude scientists have discovered how a protein called vinculin undergoes complex functions of neurons, such as signaling, according to Suzanne Baker, PhD, of St. Jude Developmental Neurobiology. Baker is senior author of a report on this study that appeared in Proceedings of the National Academy of Sciences.

The anti-cancer drug, CCI-779, is undergoing clinical trials for the treatment of cancer. Baker says the findings have direct relevance to understanding the biological basis of a variety of human disorders caused by Pten deficiency.

Poisoning cancer cells
St. Jude investigators have discovered how an enzyme crucial to the cell’s ability to decode genes and duplicate chromosomes can be turned into a poison inside cancer cells.

The discovery is an important step toward designing a new class of anti-cancer drugs. Such drugs might be given with an existing agent that targets this enzyme, creating a one-two punch against solid tumors and leukemia. The enzyme, topoisomerase 1 (Top 1), is crucial to the cell’s ability to unwind the DNA of chromosomes and separate the two strands making up a giant molecule.

This activity permits the cell to decode specific genes or to make a copy of the entire chromosome.

“We showed that modifying Top 1 so it became locked onto the DNA molecule is enough to cause cell death,” said Mary-Ann Bjornsti, PhD, of St. Jude Molecular Pharmacology. Bjornsti is senior author of the report, which was published in the November 2003 Proceedings of the National Academy of Sciences.

These recent news items reflect only a handful of the lifesaving projects occurring at St. Jude. For information about other recent discoveries, visit the St. Jude Web site at www.stjude.org/media.

New drug and Pten
Investigators at St. Jude used an experimental anti-cancer drug to prevent or reverse abnormal brain cell growth that is caused by lack of the anti-cancer gene Pten. The study demonstrated that the runaway cell growth in the absence of Pten is triggered by a second gene called mTor.

The findings show that mTor plays multiple roles in the brain from regulating the size of individual cells to more complex functions of neurons, such as signaling, according to Suzanne Baker, PhD, of St. Jude Molecular Pharmacology. Baker is senior author of a report on this study, which was published in the November 2003 Proceedings of the National Academy of Sciences.

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Windows of Opportunity
BY ALCIA H. MATTHEWS

From washing panes to alleviating pain—Mike and Mary Gurnick are now using their talents and resources to help the children of St. Jude.

Mike W. Gurnick is a man who commits to whatever task he decides to accomplish, including a 58-year span as an industrial window washer. What began as a part-time job turned into a lucrative career, and at the age of 84, Mike is still proudly working a few days each week.

But that’s not where his work ends. Although Mike’s job keeps him busy, he and his wife, Mary, also make time to help improve the lives of others. Married for more than 50 years, the Gurnicks hold a special place in their hearts for children. Mike is a member of the American Legion, a community service organization that supports many causes that assist disadvantaged children. He and Mary are also involved in their church and with a local camp for underprivileged children. In addition, they are longtime supporters of St. Jude Children’s Research Hospital and have donated to the hospital for almost 10 years.

The Gurnicks were donors to St. Jude before ever visiting the hospital, but it was during one special visit that they met Peter Doherty, PhD, a St. Jude immunologist who won the Nobel Prize for Medicine. Impressed with that experience, the Gurnicks decided to increase their donation through a charitable gift annuity.

“We started out sending monthly donations and decided to do more after we made a visit to the hospital,” Mike says. “It was more than we expected of a children’s hospital. To meet the staff and see the kids in person convinced me that our donations were meaningful.”

The Gurnicks are proud of what they are doing to help the children at St. Jude, and they encourage others to do the same.

“St. Jude takes patients whether they can pay or not,” says Mike. “If the families have insurance, they’ll take it, but if not, they take care of the children anyway.

“It’s a good feeling when you know you are helping kids get well.”

A charitable gift annuity allows donors to receive a fixed income for life in exchange for the transfer of cash or marketable securities. The fixed payment rate is based solely on the age of the beneficiary. With a charitable gift annuity, the donor may specify whether to receive an immediate annuity, with payment to begin not later than one year from the date of the gift, or a deferred gift annuity, from which payments are not to begin before a specified future date.

To learn more about charitable gift annuities and other ways to give, call the St. Jude Gift Planning department toll-free at (800) 830-8119 ext. 2081.
By Elizabeth Jane Walker

Jacob Simons may have lost his sight, but not his vision.

Jacob Simons’ days shimmer with the bright colors and perpetual motion of childhood. Pedaling a shiny red bike through his suburban neighborhood, he grins with delight as the breeze caresses his face. Sometimes he vaults toward the heavens on his trampoline or motors around the yard on a green, battery-powered tractor. Occasionally he tests his coordination—and his mother’s nerves—by hopping on a silver and purple pogo stick. But the first-grader is happiest when he’s headed for the ballpark, dressed in the sky-blue uniform of the Marlins, his T-ball team. “Blue is my favorite color,” he says. That observation might seem peculiar, coming from a boy who lost his sight four years ago. But though cancer ravaged Jacob’s eyes, it could not ravage his spirit. “I’ve been doing this for about 25 years, and Jacob was one of the most aggressive cases that I’ve seen,” says Haik. The doctors used chemotherapy, radiation therapy, lasers, freezing treatments and radioactive implants. Nothing seemed to work. “It was like the tumor cells were immortal,” Haik recalls. Fearing that the cancer might spread to Jacob’s brain, Haik removed the boy’s right eye in November of 1999, the left eye 14 months later. Jessica says she will never forget the day when Haik told her he needed to remove Jacob’s other eye. “He came out of the operating room and told me, ‘If I don’t take his eye out, I’m going to risk his life.’”

Through her tears, Jessica replied, “I’d rather have my son here and blind than not have him at all. He’s there in the operating room; you know what you have to do. Go save my child.” Jacob recovered quickly, but his mom mourned for him. “Everything that he would never be able to do just flashed before my eyes,” she says, her voice cracking with emotion. “He would never see his little brother, Kaleb, again. He would never be able to play baseball or do other things that he enjoyed. And he would never see what his mommy looked like again.”

“Did you hear me hit the ball?” —Jacob Simons

In April of 2003, Jessica discussed Jacob’s experiences on the air during a St. Jude radiothon on WKSJ 95.1. Electrician Buddy Young was listening. “I was trying to work with tears just rolling down my face,” Young says. “At the end of Jessica’s story, she said she regretted that she’d never get to see Jacob play baseball.”

That comment haunted Young, a T-ball coach. “I’m not a real emotional guy,” he says, “but all I thought about for three days was Jacob’s story. I didn’t see any reason why he couldn’t play ball.”

When Young invited Jacob to join his team, Jessica was thrilled but skeptical. “How exactly is Jacob going to do this?” she asked.

“You don’t worry about anything. You just bring him,” Young responded. Because Jacob joined the team mid-season, he was unable to attend practice before his first game. When he arrived at the ballpark, “Coach Buddy” explained how the game would work: After hitting the ball off the tee, Jacob would hold a coach’s hand to run the bases. When the Marlins were outfield, Jacob would serve as catcher; a teammate would catch the ball and give it to Jacob, who would then hand it to the umpire.

“His very first game, he hit the ball and ran to first base with a big smile on his face,” Jessica says. “I cried so hard, because I was watching my child do something that I never thought I would see him do.”

A couple of weeks later, Jacob made his mommy cry again.

“The hilltop hour would not be half so wonderful if there were no dark valleys to traverse.” —Helen Keller

One autumn evening in 1998, Jessica Wickel knelt by the bathtub, drying her toddler’s wet body. Gazing into his eyes, she noticed an unusual glare. As she changed his diaper, she again glimpsed a shadow within his pupil. The next day a pediatrician examined Jacob and suggested that he go to St. Jude Children’s Research Hospital. “The doctor never told me that it was cancer,” Jessica says. “But I knew exactly what St. Jude was, because I’d done a Math-a-Thon when I was in school. Then it hit me: ‘He’s got cancer!’”

“And so I passed out in the doctor’s office.”

Jacob had retinoblastoma—a malignant tumor of the retina—in both eyes. At St. Jude, Jessica and Jacob met Barrett Haik, MD, chief of the St. Jude Ophthalmology division, who put the family at ease.

“I thank God for Dr. Haik every day,” says Jessica. “He’s a doctor who will sit down and talk on your level. And he’ll actually sit there and cry with you. He cares just as much for these kids as their own parents do.”

Haik, the late Charles Pratt, MD; Carlos Rodriguez-Galindo, MD; and Matt Wilson, MD, led the team that treated Jacob.

“I’ve been doing this for about 25 years, and Jacob was one of the most aggressive cases that I’ve seen,” says Haik. The doctors used chemotherapy, radiation therapy, lasers, freezing treatments and radioactive implants. Nothing seemed to work.

“It was like the tumor cells were immortal,” Haik recalls. Fearing that the cancer might spread to Jacob’s brain, Haik removed the boy’s right eye in November of 1999, the left eye 14 months later. Jessica says she will never forget the

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The bases were loaded when Jacob came up to bat. He hit the ball so far that he knocked all the runners home. As he sprinted for first base, Jessica went ballistic. “I was screaming; I was jumping up and down; I was on the fence,” she says. “It was just amazing. Even the opposing team was hollering for Jacob.”

“Last year, Young’s baseball league created an annual award for the player who exhibits the best attitude and the most courage and love for the game. Jacob was the first recipient of this honor, which has been named the Jacob Simons Heart Award.”

“TV crews and journalists have chronicled Jacob’s exploits. Jessica even received a phone call from the Florida governor’s office asking for her address. Jeb Bush wanted to write Jacob a letter. ‘I was sorry to learn that you have lost both of your eyes to cancer,’ Bush wrote. ‘I do not think that will stand in the way of your dreams and plans.’”

“I can see everything!” – Jacob Simons

Jacob is an independent and confident 7-year-old. “I don’t need that stick,” he said, when presented with a cane. “I don’t have to learn these dots,” he pronounced, when encouraged to learn Braille. Jacob finally agreed to study Braille, but still disdains the cane.

To avoid curbs and obstacles when riding a bicycle, Jacob listens carefully to his mom’s verbal directions. In addition to having a keen sense of balance, an inquisitive nature and a healthy dose of courage, he is also observant.

“Jacob knows the voices of the people he knows and cares about,” says Mindy Lipson, RN, a certified nurse practitioner in St. Jude Hematology-Oncology. “He’s very brave, perceptive and pretty amazing.”

One day, when riding in the car, Jacob commented, “Look, Mommy, there’s Burger King.” Jessica did a double-take. Sure enough, Jacob had correctly distinguished the brand of hamburger by the scent.

“My son could almost to have another perception that allows him to judge distance and space. ‘I know he doesn’t have eyes, but God bless him, I’m glad he can see. I just don’t know how he does it.’”

“Mommy, I know my eyes were sick, and I know that I can’t see. But it’s okay. Don’t be sad.”

“Now I know that God did listen to me,” Jessica says. “Jacob’s got a great attitude. He’s playing T-ball. He’s happy and he’s healthy and he’s alive. God’s not letting Jacob suffer.”

“So every day I say, ‘Thank you, God.’ Every day. And I know that He listened to me.”

“Please, dear lord, I always pray that you’ll keep me cancer free for the rest of my life and let me live to be a hundred.”

– Jacob’s bedtime prayer
Fifteen-year-old Antwoine has the kind of gentle grin that would make female classmates blush. His tall frame, trim, dark hair and glasses lend a studious air that is offset by typical youth fashion: untucked, red plaid button-down and white T-shirt hanging over baggy jeans. CD headphones peep out from under his collar. It’s a look that teens carefully plan to look not-so-carefully planned. And like most teenagers, Antwoine roots his identity in his clothes, music and hobbies—not in the human immunodeficiency virus (HIV) he acquired at birth.

Antwoine is among a growing number of long-term survivors of HIV, the virus that causes AIDS. The five-pill-a-day regimen he has followed since diagnosis at age 5 allows Antwoine to live with hope instead of fear.

He doesn’t listen to those who equate HIV and AIDS with an automatic death sentence. “I would tell people who choose to believe that a different story,” says the ninth-grader who dreams of playing baseball for the Yankees. “Yes, I do have HIV, but I take my meds every day and do right for myself. No one knows when it’s going to be their time, so I concentrate on the future.”

The opportunity to focus on the long-term aspects of surviving with HIV is also welcomed by the caregivers and researchers who treat Antwoine and hundreds of other HIV/AIDS patients each year at St. Jude Children’s Research Hospital.

Yet, with 40 million people infected with HIV and 15,000 new infections occurring daily, the search for a cure continues so that this preventable disease can finally be stopped.

Patricia Flynn, MD, of St. Jude Infectious Diseases believes Antwoine has every reason to feel optimistic. Treatment has improved dramatically since the early 1980s when the AIDS epidemic was identified. “Between 1987 and 1995, we were all focused on single-drug therapies,” she says. “It wasn’t until 1997, when we finally learned that many drugs acting against the same target are going to be more effective, that we came up with highly active antiretroviral therapy, or HAART.”

A three-drug cocktail now considered standard therapy, HAART allows people with HIV to manage the illness as a chronic condition much like diabetes. The drug combo has shown remarkable success in stemming the transfer of HIV from...
mothers to their babies, which is the most common way children under age 13 are infected with the virus.

As a member of the Pediatric AIDS Clinical Trials Group (PACTG), St. Jude played a significant role in a successful 1992 study—the first randomized clinical trial to test the drug zidovudine in pregnant women. “We’re proud to say that we contributed a large number of women to this revolutionary study,” says Flynn, who holds the Arthur Ashe Chair in Pediatric AIDS Research at St. Jude. “By 1994, we saw a dramatic drop-off in the number of infants and children with HIV. Taking a clinical research finding and seeing its impact in the general population has been very exciting.” The study led to therapies that have reduced the rate of mother-to-infant HIV transmission from as high as 25 percent to below 2 percent in North America and Europe. Yet, all women do not obtain treatment; in the United States 300 to 400 new babies are born with HIV infections each year. Flynn says contributing factors include a lack of prenatal care and women unaware of their HIV/AIDS status. According to Flynn, 15 percent of HIV-infected women learn about their condition during labor. She also points to a lack of universal HIV screening of pregnant women and growing rates of HIV infection among women of childbearing age as additional problems.

Currently, the biggest challenge Flynn sees is a mushroom in the number of adolescent HIV cases, which largely result from risky behaviors. Half of the nation’s new HIV cases occur in youth aged 13 to 24. A Centers for Disease Control and Prevention survey of 15,000 high school students found that about half had unprotected sex and more than 250 injected illegal drugs despite the fact that nearly all the students had been exposed to HIV/AIDS education. Already struggling to promote prevention tactics, caregivers have their work cut out for them as they attempt to convince teens that following strict therapies could lead to longer, productive lives.

“We’re working on it”

St. Jude pediatric nurse practitioner Marion Donohoe, RN, prays for an AIDS cure if for no other reason than to stop her heart from breaking every time one certain patient comes for follow-up visits. “She is the most precious young girl, very quiet, healthy, an honor-roll student.” Donohoe says. “She looks up at me and asks the same question every time: ‘Did you find the cure yet?’ All I can do is smile and hug her and tell her, ‘No, but we’re working on it, sweetie.’”

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Since birth, Patel says. “She adds that many St. Jude patients have been able to use single sets of drugs for five years or more simply because they are disciplined about taking their pills.

St. Jude patients never have to carry the burden of treatment by themselves. The hospital offers a multi-disciplinary team of doctors, nurses, social workers, pharmacists, nutritionists, psychologists, chaplains and psychiatrists to tackle all aspects of the disease. “Our approach is family-centered, comprehensive and coordinated, and we treat families as partners,” says Donohoe. “If you ignore any aspect there would be guaranteed failure because the kids have different needs every time they visit.”

The smallest silver

One of the most devastating aspects of the disease is the stigma attached to being HIV positive. While more and more teens understand they can live long lives with the virus, they are still hesitant to tell even their best friends. St. Jude created a special weekly support group for teen patients so they can talk about the issues they face in a safe, non-judgmental environment. “You’d be amazed at how many brave, courageous teens are out there who choose not to be defined by their disease,” Donohoe says. In a study where teens were asked to divide their lives into pie pieces with slices for school, family, friends, hobbies and HIV, Donohoe says most made HIV the smallest slice. “They go through different stages of how ‘big’ HIV is in their lives, but they all want to be more than the disease. They want to lead healthy lives.”

Pat Flynn, MD, of St. Jude Infectious Diseases and NBA legend Magic Johnson participate in an AIDS awareness event.

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St. Jude researchers can study late effects of disease and treatment such as why some patients experience metabolic bone disease, abnormal build-up of fat in the gut and upper body, and issues that affect adherence patterns throughout life. St. Jude investigators are studying how children metabolize HIV/AIDS drugs in order to develop tailored dosages, and the hospital has begun a process to help patients transition to adulthood with information on insurance, employment and public assistance programs.

Researchers at St. Jude are also conducting safety trials for an AIDS vaccine designed to overcome the various strains of HIV. St. Jude is continually involved in community outreach efforts, both in the United States and around the world. Patel says there can never be enough education because even though more people seem aware of how AIDS is transmitted, the stigma is still present. “The more people know about the problem, get tested and learn about the disease, the less stigma the disease will have, and people won’t have to live in fear all the time,” Patel says. “I, of course, hope for a cure. But I would also like to see the day when HIV is treated as a chronic illness, so that kids with HIV can be liked those who have sickle cell disease and sit in a classroom without being afraid.”

Holding out hope

Antwoine can’t help but dream of the day scientists invent a magic tablet that will rid him of HIV. “That would be the greatest,” he says. Yet, he keeps a positive outlook on his life, his pills and his regular check-ups at St. Jude. “I don’t see those as things that limit me,” he says, flashing his grim again. “They are the things that keep me alive so I can do what I want to do.” His mother echoes her son’s enthusiasm. “He is a miracle,” she says. “He’s going to make it.”

The HIV Alphabet

A is for Aches that you have all the time
B is for Bad to get sick all the time
C is for Coughing
D is for Drugs that you have to take
E is for Effort for fighting your disease
F is for Fighting the bad virus you have
G is for the Good cells to fight the bad virus
H is for HIV
I is for the Immune System
J is for “Jump” for taking your medicine
K is for Keeping us healthy
L is for Long-lasting life
M is for Many, many medications
N is for Nothing can put you down
O is for Opposite people who don’t take all their medicines
P is for People with HIV
Q is for Quality of life
R is for Research to find a cure
S is for Standing out in a crowd
T is for Terrible, terrible disease to have
U is for Unique children
V is for Virus
W is for Wise kids with HIV who take their meds
X is for X-traordinary kids with HIV
Y is for Youth
Z is for Zinging through life with zero illness

By St. Jude kids
Imagine having the power of 280 personal computers at your fingertips. Researchers at St. Jude Children’s Research Hospital do not have to imagine it—they have it.

St. Jude has joined the ranks of world-class supercomputer users with the installation and successful testing of an IBM BladeServer system, which can perform more than 600 billion operations per second. The supercomputer, about the size of two household refrigerators, will speed research by reducing the time it takes for scientists to move from data collection to discovery of important new findings.

“This system really gives us the opportunity to do research that we couldn’t conceive of doing without having this kind of horsepower,” says Clayton Naeve, PhD, chief research information officer and director of the Hartwell Center for Bioinformatics and Biotechnology at St. Jude. “It makes it possible for us to do more things more quickly.”

Bioinformatics is an entirely new discipline merging molecular biology and computer sciences and makes computing critical to current biomedical research. St. Jude has eight doctoral-level bioinformaticists working in the Hartwell Center who provide expertise in mining genome data, gene expression data, proteomics data and other kinds of information. The supercomputer is being used by the Bioinformatics group and researchers in the Structural Biology department for many projects at St. Jude.

“We used to do large database searches against the Genbank, which contains all the human genome data and all the DNA sequence data from every organism that has ever been studied. It used to take us 11 days of computing time to do a particular kind of search. With the new BladeServer, we can do that in about four hours. It’s a remarkable improvement for us.”

St. Jude ranks among world’s top supercomputer users.

“We used to do large database searches against the Genbank, which contains all the human genome data and all the DNA sequence data from every organism that has ever been studied. It used to take us 11 days of computing time to do a particular kind of search. With the new BladeServer, we can do that in about four hours.”

“Many of the important questions being asked by our researchers require enormous computing power,” says Pat Ford, the supercomputer facility’s operations director. Structural Biology researchers use the supercomputer to conduct studies on proteins that play a critical role in various cancers with the goal of discovering how these proteins work. “These studies include efforts to identify new drugs by screening millions of compounds using computational methods and efforts to understand key proteins in cells involved in tumorogenesis,” Naeve says.

“This is an extremely exciting time to be working at St. Jude,” Ford says. “The more experience we gain with our supercomputer, the more effectively we’ll be able to use it, and the more rapidly we’ll find cures for catastrophic diseases.”

Pat Ford, Clayton Naeve, PhD, and Scott Malone are all part of a team that helps researchers harness the power of the hospital’s new supercomputer. Capable of performing more than 600 billion operations per second, the BladeServer is intended to help St. Jude researchers find cures more rapidly.
Three-year-old Hannah Williams likes to play doctor with her doll, Sweetie. But unlike other girls her age, Hannah knows what her doll is feeling when she administers shots, takes her temperature and gives her “sleep medicine.” She is always gentle with Sweetie, reassuring her that “it will be okay; it won’t hurt,” especially when she has to do something to Sweetie’s eyes.

When Hannah was 13 months old, a swinging door accidentally hit her head. In one day, her parents went from thinking their daughter had a lazy eye to torn retinas to bilateral retinoblastoma, a fast-growing cancer of the retina that can be fatal.

“In all my 38 years, I never could have fathomed what I felt the minute we were told our baby had cancer,” Missy Williams says. “All the breath in my body just fell away.”

Hannah’s family had noticed a strange, white reflection that appeared in one of her eyes in photographs. “Everyone’s eyes would be red from the flash except for that one eye, or there would be a white speck on her eye that we thought was just dust on the lens,” Missy explains. But the healthy, happy little ball of fire seemed to have no vision problems, so her parents had not mentioned the spot to Hannah’s pediatrician.

Unanswered questions

Unilateral retinoblastoma is a malignant tumor that occurs in one eye. The treatment for children with unilateral disease is simple: the eye with the tumor is removed and if the cancer has not spread, the child does not need follow-up treatment. Bilateral retinoblastoma can occur in one or both eyes and can involve one or dozens of tumors. In this kind of retinoblastoma, tumors may break away from the main mass like seeds blown from a dandelion and remain suspended in the fluid of the eye called the vitreous. These tiny tumors, or “vitreous seeds,” can be difficult to treat: in the gel-like vitreous they move and spread the way mercury spilled from an old thermometer divides into countless balls of silver.

Twenty-five percent of children diagnosed with bilateral retinoblastoma inherit the mutated gene from their parents. The other 75 percent develop it before birth. Although treatments for the disease have improved tenfold in the last several decades, many unanswered questions remain.

Hannah Williams did not inherit bilateral retinoblastoma from her parents; she developed it in utero. If she has children, they will have a 50 percent chance of developing the disease. Sadly, children with bilateral retinoblastoma have a 40 percent chance of developing other primary cancers.

“Retinoblastoma is the most clear-cut hereditary cancer in the human body,” explains Barrett Haik, MD, director of the St. Jude Eye Clinic. “Some may ask: Why worry about a disease that only affects 200-300 kids a year? Well, it’s the only tumor where you have such a clear genetic predisposition. It was one of the first cancer genes cloned, and if there is ever going to be gene therapy, retinoblastoma is going to be the disease that’s going to be well suited for it.”

Seeking answers

Carlos Rodriguez-Galindo, MD, of Hematology-Oncology is leading a multidisciplinary team that is developing a retinoblastoma protocol slated to begin this summer. The study is designed to determine the best treatment for children with the disease, to further study the biology of the disease, to discover why some children develop the disease in utero and to determine how children with retinoblastoma think and learn.

For decades, retinoblastoma was treated primarily with enucleation (eye removal) or radiation. The new protocol will test the chemotherapy drugs topotecan and vincristine, which are often used in conjunction with lasers, freezing techniques and implantation of radioactive seeds, especially for cases of more advanced disease.

The goal is to prevent enucleation and to avoid or delay radiation therapy, which has many negative side effects for children who are growing and developing.

A new St. Jude protocol will address the best treatment for children with retinoblastoma, study the biology of the disease, investigate why some children develop it in utero and explore how children with retinoblastoma think and learn. Nurse Terry Deaton, a member of the multidisciplinary team, talks with 3-year-old Jalen Edwards.

Unilateral retinoblastoma is a malignant tumor that occurs in one eye. The treatment for children with unilateral disease is simple: the eye with the tumor is removed and if the cancer has not spread, the child does not need follow-up treatment. Bilateral retinoblastoma can occur in one or both eyes and can involve one or dozens of tumors. In this kind of retinoblastoma, tumors may break away from the main mass like seeds blown from a dandelion and remain suspended in the fluid of the eye called the vitreous. These tiny tumors, or “vitreous seeds,” can be difficult to treat: in the gel-like vitreous they move and spread the way mercury spilled from an old thermometer divides into countless balls of silver.

St. Jude focuses on finding new treatments for retinoblastoma

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Twenty-five percent of children diagnosed with bilateral retinoblastoma inherit the mutated gene from their parents. The other 75 percent develop it before birth. Although treatments for the disease have improved tenfold in the last several decades, many unanswered questions remain.

Hannah Williams did not inherit bilateral retinoblastoma from her parents; she developed it in utero. If she has children, they will have a 50 percent chance of developing the disease. Sadly, children with bilateral retinoblastoma have a 40 percent chance of developing other primary cancers.

“Retinoblastoma is the most clear-cut hereditary cancer in the human body,” explains Barrett Haik, MD, director of the St. Jude Eye Clinic. “Some may ask: Why worry about a disease that only affects 200-300 kids a year? Well, it’s the only tumor where you have such a clear genetic predisposition. It was one of the first cancer genes cloned, and if there is ever going to be gene therapy, retinoblastoma is going to be the disease that’s going to be well suited for it.”

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Early detection can save eyes and lives

Sitting in a St. Jude waiting area with their daughter, Ray Williams pointed to a poster picturing a little girl with curly dark hair and a strange white spot in one of her eyes—bright and reflective. He said to his wife, “Oh, Missy, that’s just like Hannah. If only we’d known what it was so we could have recognized it earlier.”

Since that day, Missy has often thought about that poster. “If we could mail it to every pediatrician’s office it would save so many children,” she says. “It would help their parents notice and act, help them catch the disease early. I’d never heard of retinoblastoma. I didn’t even know there was a cancer of the eye. I wish that we could educate every new parent about retinoblastoma. Education is the key. The earlier you find out, the better. It would save more lives, more eyes…”

Retinoblastoma warning signs

- A white reflex, known as a cat’s eye reflex, appears in a child’s eye. Often this is evident in a photograph taken with a flash. In this age of digital cameras and computer graphics programs, it is easy to touch up a photo and eliminate a “flaw.” Noticing such a flaw can save a child’s life.
- The eyes are crossed or turn in or out slightly.
- A child has different colored irises—for example, one blue eye and one brown eye.
- A child complains of not being able to see or focus, or bumps into things.

“We are concerned about the lack of communication when it comes to retinoblastoma,” says Rodriguez-Galindo. “For example, we recently had two new babies here with retinoblastoma. Both had affected parents. None of them was aware that they would pass it on to their children.

“Maybe people block out this information, or the parents or grandparents die so the later generation never knows about the genetic history. Or maybe parents don’t want to tell their kids, and 20 years later they have forgotten or they think it’s better to forget. These kids need to know their genetic history. They also need to know that they have a 40 percent chance of developing another cancer. Retinoblastoma is the genetic syndrome with the highest risk of cancer.”

Looking ahead

A spunky little preschooler, Hannah Williams looks no different from any other girl her age. Even her hazel-green eyes don’t give her away—one real, the other created just for her. Because Hannah’s disease was advanced at the time of diagnosis, she lost her right eye. She endured two rounds of chemotherapy, and the tumors in her left eye were also treated.

Missy Williams says she will have some serious talks with her daughter when she is older. She will tell Hannah that she has a high chance of developing another cancer or passing the mutation to her own children.

For now, Missy and her husband are concentrating on the present. “Nothing gets in Hannah’s way,” says Missy. “And we try never to hinder her. We always encourage our little angel baby to try anything—to accomplish whatever is in her head and heart.”

Parents of St. Jude patients chronicle their journeys in scrapbooks.
Before May 2002, photographs, drawings and ticket stubs were just bits of paper to Jennifer Farrar. She enjoyed looking at family photos, remembering certain birthday parties or special events. She’d smooth her fingers over the edges, smile at the memories then put them away until another day.

But after her son came to St. Jude Children’s Research Hospital with acute myeloid leukemia, Jennifer started photographing him, his medical team, the hospital, and events of all sizes, even quiet day-to-day moments. She saved newspaper clippings and ticket stubs from the family’s outings—a Memphis Redbirds game, a trip on a Mississippi River boat.

Soon she started putting them in a scrapbook. Like a travel journal that recounts destinations, activities and thoughts, Jennifer’s scrapbook unfolds her son’s St. Jude journey. “Jackson was so little when he was diagnosed, just 2,” says Jennifer. “I hope he doesn’t remember what he has had to go through. I want him to remember. I want him to know that God is good. I want him to know about the disease he beat and what a strong and coura- geous little boy he was to endure all that he had to endure. I want him to remem- ber his doctors and nurses, all his friends at St. Jude; the experience is a part of who he is. I want him to have this scrapbook forever so he can remember what a hero he is and how much his family loves him.”

Although Jennifer had completed the first few pages of her scrapbook, it wasn’t until she joined the “ Scrapbooking Class for Parents” at St. Jude that she truly understood the deep significance of the scrapbook and the process of creating it.

**Start with scissors**

Scrapbooking can be considered a form of narrative therapy, which assumes that people are the experts in their own lives. Jill Sebaugh, a domi- nicipal social worker at St. Jude, and Amy Kennedy and Melinda Hugie, Child Life specialists, started the hospital’s scrapbooking class in January 2002.

“Storytelling can be very power- ful,” Sebaugh says. “Two people may have the same experiences and tell the story very differently. This interpre- tation can influence their lives, influ- ence how they make decisions later in life or, ultimately, how they view themselves as human beings.”

Sebaugh set out to form a group with an activity and no stigma. “Many people believe that if they are in a support group that something is wrong,” she explains. “Some people stay away from support groups because of that reason.” The scrapbooking class offers parents a time to be with other St. Jude parents, to share their stories and to process their emotions. “The two- hour, bimonthly class is really one of the few times parents have to be away from their kids, to have the freedom to talk adult-to-adult,” says Sebaugh. “It’s a time to talk about what their child and their family have been through as well as with others who understand; it’s a time to process grief, anger, sor- row, hope.”

Held at Target and Ronald McDonald Houses, as well as at the hospital for parents whose children are inpatient, the class has also been helpful to parents when the child of another family dies. “They can process their feelings, share their fears, talk about how the death will impact their own child,” says Sebaugh. Narrative therapy provides a context for asking questions about what is not often ques- tioned. For many fami- lies, the book pro- vides a pal- pable way to remem- ber. “A scrapbook helps a fami- ly remember all the details. With it, they don’t have to worry that they will forget,” Sebaugh says. “Especially for families who lose their children, the fear of forgetting can complicate grief. Having the scrapbook helps them heal and remember the joys and sad- nesses, the life.”

**Cutouts and conversations**

Even though her scrapbook is not finished, Tammy Warren likes to flip through its pages and ponder how far her family and her 8-year-old son, Tyler, have come in less than two years. “Already I can’t imagine how we got through everything we have,” she says. “Later, this book will really be something for Tyler to look at. He’ll see how young he was, and how brave. ‘Friends and family back home who look at the scrapbook can’t believe what he went through.’”

Jill Sebaugh explains. “Some- times, I simply identify who and what is going on in the photo, but other times I write a lot,” she says. “The combina- tion of the images and the words can show you how you felt in that moment, the ebb and flow of her feel- ings in that one prick of time.”

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Art therapists say that scrapbooking enables people to express themselves through both words and images, accelerating the process of emotional healing.

“Whenever I look at my scrapbook, I cry,” says Jennifer Farrar. “It makes me grateful, thankful. I know how far we have all come and I thank God that Jackson has done so well.”

“As hard as it’s been, I want to remember everything from this time. God brought us through this for a rea- son and I can’t let that be forgotten. The book is very special to me. I hope Jackson will cherish it, too, when I give it to him when he’s older.”

**Priceless coffee-table book**

Jennifer Farrar keeps her scrap- book-in-progress on the coffee table at home. The book includes hundreds of photos of Jackson, his immediate fami- ly and his St. Jude family. Among the photos, drawings and clips, Jennifer has written facts, thoughts and dreams. One page features a photo of Jackson with singer Amy Grant. Another shows him swinging on the playground behind Target House.

“This picture,” she says, “shows Jackson playing with a toy kitchen in the area where he had his bone marrow transplant. The nurses knew he loved it so they moved it in there for him. I wrote under the picture how much he loved playing with the toy pots, pans and utensils. He’ll probably laugh later, when he’s older, and say: ‘Mom, what a silly toy! I can’t believe I played with that!’”

When Jennifer shows the scrapbook to friends and family, especially those who weren’t able to visit Jackson at St. Jude, the tears flow. “They are okay until they get to the photos of Jackson following his bone marrow transplant, and then the ones of him on a ventila- tor,” Jennifer says. “They cry. I tell them it gets better … like a movie I’ve already seen.” Jackson was given an 8 percent chance to live. He has passed one year without relapse and has another year to go before he is consid- ered cured.

The power of memory

Although many scrapbooks tell visual stories with photographs and art, words play a key role. When Tammy Warren looks at her scrapbook, she can remember an exact moment, the ebb and flow of her feel- ings in that one prick of time. “Sometimes, I simply identify who and what is going on in the photo, but other times I write a lot,” she says. “The combina- tion of the images and the words can show you how you felt in that moment, the ebb and flow of her feel- ings in that one prick of time.”

Art therapists say that scrapbooking enables people to express themselves through both words and images, accelerating the process of emotional healing.
Today many organizations use the term “bench to bedside” to describe their programs. But the concept was born 42 years ago in a tiny hospital in Memphis, Tennessee. There, basic scientists and physicians worked in tandem to translate laboratory discoveries into cures. From its humble beginnings, St. Jude Children’s Research Hospital created a worldwide model for bench-to-bedside research. Nowhere is that success story more evident than in relation to retinoblastoma, a malignant tumor of the retina. When the late Charles Pratt, MD, began treating children in the early 1960s, cancer research was in its infancy. “The drug options were so limited that I carried my medicines around in an old Seagram’s Crown Royal bag,” said Pratt, a St. Jude physician who pioneered many chemotherapy agents used to treat retinoblastoma and other cancers.

Today, St. Jude researchers harness technology and knowledge to give clinicians a vast array of treatment options. Michael Dyer, PhD, an assistant member of Developmental Neurobiology, leads a team that is studying normal development of the retina as well as testing new treatments for retinoblastoma (see related stories, pages 4 and 14). Dyer says the proximity of his lab to the clinic makes research more exciting and relevant to patients. “At other institutions, I might do all the same experiments that I do here, but I would just publish my findings and hope that somebody would actually apply what we have found,” says Dyer, who engages in a nearly constant dialogue with Carlos Rodriguez-Galindo, MD, of Hematology-Oncology and Barrett Haik, MD, of the St. Jude Eye Clinic. “Not only are Carlos and Barrett saying, ‘Hey, Mike, have you thought about trying out this drug?’ but I can give them results before they ever get published,” Dyer says. “Things move much quicker here than they would anywhere else.”

Back to basics

The retinoblastoma gene was the first tumor suppressor gene cloned in humans, and the mutation that causes the disease involves one culprit, the Rb gene. An individual with an Rb mutation is much more likely to develop retinoblastoma than is a person who does not have the mutation. But the disease’s origins remain an enigma. “You would think that we would know a lot about retinoblastoma,” Dyer says. “But the sad thing is that we know very, very little—in fact, I would say almost nothing—about what happens to make these cells become tumor cells.”

Dyer and his colleagues have developed new laboratory models to help them track the genetic changes that occur in cells after Rb is mutated. By studying the basic biology of the tumor cells, Dyer hopes to create cancer therapies that target specific pathways or proteins. Such treatments would eliminate the sickness and side effects that accompany general chemotherapy. Many scientists believe that the vast majority of cancers may involve a mutation in the Rb pathway. That’s why many retinoblastoma patients have an increased chance of developing other types of cancer, as well.

By studying the molecular changes that give rise to retinoblastoma, St. Jude scientists hope to broaden their understanding of normal retinal development and of developmental tumors of the central nervous system.

By Elizabeth Jane Walker

Seeking a magic combination

Although doctors have been treating retinoblastoma for more than a century, no one has yet pinpointed a definitive treatment. The laboratory models created in Dyer’s lab will help St. Jude scientists test chemotherapy drugs for retinoblastoma. To speed the process, the researchers are testing drugs that have already been successfully used to treat other kinds of childhood cancers. Methodically, the scientists try different dosages, various combinations and different lengths of treatment. Then they test whether or not the drug actually travels to the tumor in the eye.

“Before we began this project, nobody had systematically tried drug after drug in combination to figure out which are the best ways to go,” says Dyer. Many drugs that might work for medulloblastoma or neuroblastoma are perfect candidates for retinoblastoma because these cancers have many similarities. St. Jude clinicians help basic scientists factor in the possible side effects of drugs. “There might be a fabulous drug for treating and killing these tumor cells but the child can’t tolerate it,” Dyer says. “So in those cases, it just gets cleared off the slate; we don’t end up wasting our time.”

When Dyer finds a promising drug combination, an interdisciplinary team considers its inclusion in upcoming treatment plans for St. Jude patients. The new retinoblastoma protocol slated to begin in the summer of 2004 incorporates topotecan and vincristine, two drugs that underwent extensive testing in Dyer’s laboratory. But Dyer is also hoping to continue screening 12 or more drug combinations per year, in a constant search for the ultimate treatment.

“Before this, Carlos and Barrett would look through the literature and make a best estimate on what might work,” Dyer says. “Now they’re going to have a huge amount of data to base that on, and we’re going to closely follow the children. Do they respond the same way that cells do in culture? We can go from a dish with tumor cells in it to a laboratory model to a patient and back again; I don’t know of anywhere else where that happens in such an efficient way. Without that connection, we would just be doing this blind, and we wouldn’t have that important feedback.”

“St. Jude provides a wonderful sort of environment to do these kinds of things,” Dyer continues. “It’s an amazing place; it really is.”

Discoveries made in the laboratory of Michael Dyer, PhD (above), are quickly translated into treatments that help patients such as Hannah Williams, pictured here with Carlos Rodriguez-Galindo, MD. (See related stories, pages 4 and 14.)
**Promesa y Esperanza:... a SOUND Contribution**

**Spanish-format radio listeners raise millions for St. Jude Children’s Research Hospital.**

“The Hispanic community has enthusiastically embraced the dream of Danny Thomas that ‘no child should die in the dawn of life.’ With the help of Promesa stations and their listeners, St. Jude continues to lead the battle against childhood catastrophic diseases.”

In the early 1990s, this new radio format erupted across the airwaves of the broadcasting industry, pushing what had been a sporadic radio genre into a phenomenon that can claim at least one station in almost every major U.S. city, including each of the nation’s top 20 radio markets. But Spanish radio isn’t just a format to be lumped into categories such as hard rock, easy listening or sports talk; Spanish radio is also an important medium for delivering cultural messages. Recognizing the philanthropic potential in the Hispanic community, ALSAC, the hospital’s fund-raising arm, launched a Spanish radiothon program. In September 1997, Promesa y Esperanza (Promise and Hope) was introduced at KXEK-AM in Fresno, California. “We realized that it was very important to get the message of St. Jude out to the community at the local level, and radio allowed us that great opportunity,” says Lucia Heros, of ALSAC Hispanic Marketing. “We needed to educate the community about St. Jude, raise money and create a way that made it easy for people to give.”

Since then, 79 stations have become members of the Promesa family that stretches from Los Angeles, California, to Miami, Florida. Working together, the stations have raised more than $12 million in pledges to help los niños del St. Jude. And the numbers continue to grow. WADO-AM 1280 in New York joined with St. Jude three years ago to help, in the words of Danny Ortiz, “the most helpless and innocent victims of all children with catastrophic diseases.” Ortiz, program director for WADO, says the message of St. Jude resonates with the values of his station’s listeners. “Hispanics are passionate, empathetic and very loyal toward issues that really matter, like education, family, health and childhood diseases,” he says. “These important issues definitely strike the emotional chord and make listeners want to pick up the phone and help make a difference.”

Although they knew that their listeners would support St. Jude, many broadcast representatives were surprised by the amount of giving they have seen. “We were initially overwhelmed by the support that we received from our listeners,” Ortiz says. “It is unbelievable that in the past three years we have raised more than $2.1 million in cash and pledges for the kids of St. Jude.” Ortiz’s station raised $832,066 during its latest radiothon in February 2004. Modeled after the Country Cares for St. Jude Kids radiothons, Promesa provides stations with everything they need for successful two-day radiothons, from brochures to volunteer phone operators to Spanish-speaking St. Jude families who can give listeners first-hand accounts of what the hospital means to them. “St. Jude had pioneered radio fund-raising through Country Cares and we tested the formula with Spanish-language radio—and it worked,” Heros says. “The phones rang and the community came out to support the kids, and their generosity was overwhelming.”

That generosity continues to grow. In December 2003, the Hispanic community in Chicago showed its generosity by pledging $936,135 during the first radiothons hosted by stations La Ley and Onda. “We are truly grateful for the commitment and support we have seen from our radio stations, La Familia Promesa y Esperanza,” says ALSAC’s Radio and Entertainment Director Teri Watson. “The Hispanic community has enthusiastically embraced the dream of Danny Thomas that ‘no child should die in the dawn of life.’ With the help of Promesa stations and their listeners, St. Jude continues to lead the battle against childhood catastrophic diseases.”

**The Hispanic population in the United States has been booming since the 1980s. According to the latest census, Hispanics are now the largest minority population in America. The popularity of Spanish-format radio has increased as the population has grown.**
As a small child growing up in rural West Tennessee, I first learned from my dad about plans to build a hospital in Memphis dedicated to helping children with catastrophic diseases. This hospital would serve children even if their families did not have the money to pay. The plans and vision for this hospital were those of Danny Thomas, who like my family, was of Lebanese descent. I was proud to know that people of my heritage were giving back to the country that had welcomed us with open arms. In 1962, this vision of a hospital dedicated to children became St. Jude Children’s Research Hospital.

Years ago, there was talk of the hospital being moved to St. Louis. Early one morning, I flew with then-Gov. Lamar Alexander, Lt. Governor John Wilder and Speaker of the House Ned McWherter to a St. Jude Board meeting in Memphis. After that meeting, the Board was invited to Nashville to be honored on the floor of the House of Representatives. Danny Thomas and Ned McWherter exchanged expensive cigars (Danny’s cigar was obviously more expensive than Ned’s). From there, the Board went to a reception at the governor’s residence. Thankfully the state’s cooperation was assured, and St. Jude remained in Memphis.

Since 1985 I have had the honor and privilege of serving as a member of the ALSAC/St. Jude Boards of Directors and Governors. It has been one of the most rewarding and fulfilling experiences any person could ask for.

As I said earlier, St. Jude does not turn children away because their families cannot pay. To do this requires a tremendous focus on fund-raising. Dick Shadyac and the other folks at ALSAC/St. Jude who concentrate on fund-raising do an outstanding job. It is vitally important to support the hospital. I try to do my part. One example is through a golf tournament. In 1993 I approached the Rural West Tennessee House Democratic Caucus with the idea of sponsoring an annual fund-raiser for St. Jude. Representative Randy Rinks (D-Savannah) took up the challenge and, along with the rest of the members of the caucus, we began a golf tournament at Pickwick with proceeds dedicated to St. Jude. We not only raise $60,000 to $80,000 a year at that tournament, but we also raise awareness about the St. Jude mission and the tremendous scope of children served.

There are patients from all parts of the world treated each year, and since it was first established, more than 20,000 children have received services. But in the end, I do not believe that numbers alone are a measure of our success.

In the end, how should we judge success?

Judge success not only by the lives that are saved and the children who are served, but also by the hope we radiate and the promise that someone cares.

Jimmy Naifeh is Speaker of the Tennessee House of Representatives. He was first elected to the House in 1974 and has served as speaker of that body since 1991. He is married and resides in Covington, Tennessee. He has three children and three grandchildren.