On a Roll

Gliding toward a cure for medulloblastoma
St. Jude Children’s Research Hospital was founded by the late entertainer Danny Thomas. It opened February 4, 1962. The hospital 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 hospital that would treat children regardless of race, color, creed or their ability to pay. This remarkable event also inspired the name of this magazine, Promise.
The discovery of the abnormal fusion of two gene segments will help clinicians readily diagnose a rare form of childhood cancer and may help lead to a cure.

The report, published in the July issue of Nature Genetics, identifies RBM15-MKL1, a gene abnormally fused from segments of two previously unidentified genes. Stephan Morris, MD, and Zhigui Ma, MD, PhD, of Pathology at St. Jude Children’s Research Hospital led the study. The work was done in collaboration with Johann Hitzler, MD, a former postdoctoral fellow in Experimental Oncology at St. Jude, who is now at Toronto’s Hospital for Sick Children.

The genetic abnormality is likely a factor leading to the onset of acute megakaryoblastic leukemia, a rare form of acute myeloid leukemia (AML). Clinicians can use the new findings to easily diagnose megakaryoblastic leukemia. This discovery could lead to the development of more effective, less toxic therapies for a cancer that is virtually untreatable. Only about one-quarter of the children with this type of AML respond to available treatments.

In children, megakaryoblastic leukemia most frequently strikes infants and toddlers up to age 4. About 20 percent of all childhood leukemias are of the AML type, of which roughly one-in-ten are megakaryoblastic leukemias.

The scientists found that specific parts of two normal genes break off and then come together to form the new, abnormal fusion gene, RBM15-MKL1, found uniquely in the acute megakaryoblastic leukemias. The normal genes, named by the scientists RNA-binding motif protein-15 (RBM15) and megakaryoblastic leukemia-1 (MKL1), are located respectively on chromosome numbers 1 and 22.

Sometimes epiphanies occur in the most unlikely places. It was outside a bathroom at St. Jude Children’s Research Hospital that Ginny Frattinger gained personal insight into the hospital’s mission. In that corridor, Ginny met one of the most unlikely places. It was when a doctor said [that] he didn’t know what he would have done if he had worked in a hospital where he had to turn a child away because of a parent’s inability to pay.

“It was when we first got here,” Ginny says. “She was sitting in the wagon with a mask on her face, waiting for her mother. She was telling me that she was 3, and she had her little toys.” The wagon struck Ginny as an extra touch that St. Jude provides for patients craving normalcy as they weather the storm of catastrophic disease. “I love the little wagons,” Ginny says. “It is so much better (than wheelchairs).”

“The interchange between visitor and patient occurred when Ginny and her husband, Tom Frattinger, made their first trip to see St. Jude. Tom had become acquainted with the hospital when a friend invited him to play in a 1992 golf tournament. He ended up serving on one of the event’s committees. When Ginny accompanied Tom to a dinner and silent auction following the tournament, she learned that the hospital never turns a child away because of a parent’s inability to pay.

“This is what medicine, I thought, is supposed to be,” she says. With the support of people like the Frattingers, the tiny girl in the wagon—and thousands of other children around the world—will continue finding hope and health at St. Jude.

In Defense of Children
C IDC supporters Tom and Ginny Frattinger

BY JOE HANNA
Throughout his high school football career, quarterback Harris Jones competed in dozens of intense games, demanding determination, ferocity and discipline. But on September 2, 1998, he began the most challenging contest of his life—a game of life and death.

One of the country’s top high school athletes, Harris was accustomed to competition, challenge and accolades. As a high school senior, the quarterback had passed for more than 1,500 yards and 13 touchdowns. He had proven himself in the classroom, graduating with top academic honors. And he had garnered the respect of his peers, who elected him class president for four years and voted him Mr. Milan High School. As runner-up for the national Wendy’s High School Heisman, Harris had appeared on the Today Show, been interviewed on ESPN and traded quips with college Heisman finalists in New York.

Now, the tenacious quarterback faced a foe more ominous than the most musclebound line- man. At 18, in superb physical condition, Harris Jones had acute myeloid leukemia.

The kickoff
A standout in both baseball and football, Harris had experienced extreme fatigue during the spring 1998 baseball season. Doctors prescribed rest for what they believed to be mononucleosis. When Harris reported to Murray State University’s football camp a few months later, his energy level and weight began to plummet, and bruises appeared with alarming frequency. “Harris had just completed a stellar career at Milan (Tennessee) High School, and we were shocked and puzzled as to why he seemed to be struggling so hard physically,” recalls Denver Johnson, former Murray State coach. “At first we dismissed it as freshman jitters, but as training camp went on, it became obvious that something was wrong.”

Tests revealed that Harris’ blood lacked sufficient numbers of platelets, the cells that cause the blood to clot. “Any little blow could have made me bleed to death,” recalls Harris. His doctor immediately sent him to St. Jude Children’s Research Hospital.

When he arrived at the hospital, Harris learned that he must undergo intensive chemotherapy. “I wanted to start treatment as soon as I could,” Harris says. “I was completely focused on getting back on the field again.” But no training regimen had prepared him for the game he was about to play.

For the next eight months, Harris would endure excruciating pain, nausea, diarrhea, rashes, headaches and life-threatening infections. “When Harris started treatment, they listed the side effects that might occur,” says his mother, Rebecca Jones. “He had every single side effect.” The handsome, 218-pound quarterback metamorphosed into a bald, 138-pound invalid. “One week, I was out on the football field playing college ball and living my dream, throwing passes to receivers and calling plays,” says Harris, “a few weeks later, my dad was pushing me in a wheelchair. And then the hair loss started. Most men worry about going bald at 40, and here I was going bald at 18.”

As the days turned into weeks, the bedridden patient began to lose muscle tone. “Physical therapists would bring hand weights to his room, and he was so weak and tired that he couldn’t even use them,” recalls Erika Bernberg, RN, BSN.

The cheerleaders
In spite of his suffering, Harris retained a positive attitude that amazed the nurses and doctors who took care of him. “Even at the worst times, he would look
around and say that he was blessed to be here,” says nurse practitioner Martha May. “He didn’t regret the things that were happening to him, because he felt like they were making him a stronger person.” On days when he felt better, Harris focused his energy on helping others, says Bernberg. “He would go meet new patients and give them little pep talks, telling them to hang in there.”

Harris forged a friendship with John Sandlund, MD, attending physician on the Inpatient unit. The two men shared a passion for football and a deep faith. “Harris was determined to get through the treatment and to beat the leukemia,” says Sandlund. “I’d go see him to encourage him and to let him know that I was praying for him.”

Staff members at St. Jude were not Harris’ only fans. Friends from his hometown and his college rallied to support him. Harris received thousands of cards and hundreds of visitors. Cash-strapped college students pooled their resources to buy gas for road trips to Memphis. More than 200 people donated platelets at the St. Jude Blood Donor Center in his behalf. And Murray State University’s football team wore his initials on their uniforms during each game. Harris’ coach, Denver Johnson, was particularly supportive because he, too, had a tie to St. Jude. His daughter, Kelsey, was receiving treatment for acute lymphoblastic leukemia at the hospital.

“My firm belief is that there are no coincidences in life,” says Harris. “There is no other coach in the country who could have understood better what I was going through.” Realizing that Harris needed inspiration during the long, grueling treatment, the Murray State coaches brought his helmet and practice jersey to St. Jude, where they served as constant symbols of recovery. Every Saturday, Harris held the gear in his lap as he followed the Murray State scores from his hospital bed.

The comeback

In December of 1998, Liberty Bowl officials asked Harris to perform the coin toss at the coin toss at the upcoming bowl game. Frail and weak, he had not walked for months. “I took my first step on Christmas Eve,” says Harris. “If I took even two steps, I was out of breath. That morning, I woke up before my family did, and I practiced. I just wanted to be able to walk as a Christmas gift to my family.” One week later, a pale, but determined figure stood in the middle of a packed stadium and tossed a coin into the air.

In the summer of 1999, Harris was discharged from the hospital. He began training that day to return to the gridiron. He soon found that the goal must be attained in increments of inches instead of yards. “When I came out of the hospital, I thought I was going to be strong again in a couple of months,” he admits. But lifting hand weights in a hospital bed is a far cry from bench pressing hundreds of pounds and running full-tilt down the football field. “The physics of this game are extraordinary, demanding great strength and aerobic conditioning,” says Johnson. “When you knock your body down so far battling cancer, it’s a Herculean task to get back. But I’ve never seen anybody display a better attitude toward adversity than Harris Jones. He met leukemia head-on, with great resolve, anchored in his faith. If anybody is able to return to the game, it will be Harris.”

During his hospitalization, someone had asked Harris what he would like to do more than anything else. “One thing that always meant a lot to me was to run out onto the field with my high school football team and to hear the fans cheer,” said Harris, the team’s former captain. “It was such a rush. I always wanted to be the first one to burst through the banner.” In the fall of 1999, Harris’ wish was granted. Wearing his old high school jersey and pads and serving as honorary captain, he led the team once more. Just before Harris charged onto the field, he was astounded to see a group of people step forward, cheering and applauding loudly.

It was his doctor, pharmacist and nurses from St. Jude. They had traveled more than 100 miles to celebrate Harris’ triumphant return to the field.

Touchdown

Today, the patient who once struggled to lift hand weights can bench press 325 pounds and is planning to play college baseball, as well as football. “I’m stronger now than I was before I got sick,” says Harris, a dedicated business administration student on a full athletic scholarship.

Although he still works to regain his endurance, Harris’ drive, determination and perspective are healthier than ever.

“Forget it. I approached the chemotherapy and leukemia as another game: like it was the fourth quarter and fourth and one on the goal line and we had to score. I did score, but the stakes were higher than the ones in a football game.”

“I think God puts things in your life that make you grow,” continues Harris. “Now, even if it’s raining outside, the sun’s still shining. I know what it’s like to be in a wheelchair. It’s a feeling that people just take for granted, but I don’t. I almost lost it all.”
LIKE most St. Jude patients, Leo wakes each morning knowing he has a disease that he must beat. Leo follows a very strict medical regimen: He takes a pill each morning at 11 and takes more pills each night at 11. He has a support group that lends an ear.

Leo knows a team of medical professionals who help him each day while they try to find a cure for his disease. This young man is HIV positive.

Some 36 million people are infected with the human immunodeficiency virus (HIV), the retrovirus that causes acquired immune deficiency syndrome (AIDS). About 14,500 people become new victims of HIV daily.

Although most people associate St. Jude with its remarkable track record for fighting childhood leukemia, the institution focuses on numerous childhood catastrophic diseases. So when AIDS began claiming the lives of infants and children in the 1980s, St. Jude was there. In 1987, St. Jude founder Danny Thomas and HIV research pioneer Walter Hughes, MD, announced that the hospital would enroll children with AIDS. The institution quickly became a leader in the fight against the disease.

Today, investigators in the St. Jude AIDS program have designed a novel HIV vaccine and are studying the newest antiviral therapy drugs. The hospital’s HIV/AIDS program is one of the most active pediatric clinical research centers in the nation.

Researchers in Infectious Diseases and Immunology collaborate on human clinical trials for an HIV vaccine that is both formulated and manufactured at St. Jude. They have worked collaboratively for more than a decade.

St. Jude is also the primary center caring for children and adolescents who are infected with HIV in the Memphis area. The local health department and hospitals refer their young patients with the virus to St. Jude, which has 12 active HIV protocols, 11 of which enroll toddlers and teens.

**Meeting the needs of teens**

In the past, most children with HIV were infected through blood transfusions or mother-to-infant transmission. Today, most of the 50 HIV-infected patients at St. Jude are teen-agers who were infected through sexual transmission.

Leo is 18, and, if he is found for HIV, he will likely spend the rest of his life taking medications at precise daily intervals.

**Rising to the challenge**

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potent antiviral drugs—have been linked to the development of lipid metabolism disorders. Preliminary studies are showing that cardiac disease rates are five times higher than normal in adults who have used these medications for a number of years. “We’re looking at starting young infants at about 2 months of age on these medicati-
ons,” Flynn explains. “We have a lot to learn about whether or not we are seeing the same sort of lipid profile abnormalities. Are these kids going to be having [heart attacks] at the age of 20?”

Questions like these will drive St. Jude investigations during the next few years.

Helping moms and babies

To decrease the virus’ transmission from pregnant mothers to children, St. Jude began administering AZT as part of the national Pediatric AIDS Clinical Trials Unit in 1994. The success rate has been startling. Today, the transmission rate is below 5 percent, compared to a 25 percent rate before the use of AZT.

The hospital’s early success in stemming transmission of the virus from pregnant mothers to their children has allowed St. Jude to add a new focus to the teen epi-
demic. Each year, five to 10 teen mothers are added to St. Jude pro-
tocols, which include medicines to keep their HIV infections in check and to help protect the health of their unborn children. Close collab-
oration with University of Tennessee clinical investigators in the department of Obstetrics and Gynecology allows seamless transi-
tions of patient care. “We have a circle of people, no one knows Leo is HIV positive. In fact, if you were to meet Leo in the hospital and ask why he is here, he would most likely tell you he has “a blood dis-
ease.”

Christine Sinnock is a social worker who works with HIV-infected patients at St. Jude. She knows firsthand of the public rela-
tions battle these young patients face. “Up until now, we have not been able to raise awareness about their dis-
ease,” says Sinnock. “But society has preconceptions about people infected with HIV. AIDS has come at a high price in a world where privacy can be stolen through the snap of a camera shut-
ter, the click of a computer key, or the chime from a beeper when they have a new message. There’s a belief that the vaccine will prevent your immune system from being infected by the virus and that any infection that does occur will be mild and harmless.”

Defending against the invader

L

ike an enemy soldier trained in guerilla warfare, the human immunodeficiency virus (HIV) evades the body by disguising itself and ambushing unsuspect-

ing cells. Within the next five years, St. Jude researchers hope to have successfully produced a vaccine capable of defending chil-
dren against this virus, which has created the AIDS pandemic.

“Our goal would be to immu-
nize young children 5 years of age or less, before they are at the age of contracting the virus,” says Julia Hurwitz, PhD, Immunology, St. Jude vaccine will consist of three shots, which target as many as 100 envelopes, or dis-
guises, used by the virus. “We suggest that many of the other strategies are missing the target, because they are not addressing the diversity of the virus,” Hurwitz says. “By representing the diversi-
ty of HIV in a vaccine, we argue that we can better arm the immune system to prevent infec-
tion. We therefore designed a vaccine cocktail incorporating multiple, distinct HIV envelope proteins.”

Researchers have shown that the St. Jude vaccine, in develop-
ment since 1993, can trigger the production of antibodies able to neutralize HIV in a culture dish. The three-shot vaccine will work by waking up the immune system and helping it identify the virus’ many different disguises. “It’s as if you have an army in your body ready to battle HIV, but all the soldiers are asleep,” Hurwitz explains. “These three shots will awaken the soldiers. The vaccine will prepare your immune system for battle by showing your white blood cells what to look for.”

Each injection will target different white blood cell subsets, arming several distinct immune system populations. “After vacci-
nation, individuals will produce strong antibody and T-cell responses that should prevent infection if there is a later expo-
sure to HIV,” Hurwitz says.

Currently, one shot of the three-part vaccine has already been produced and is being test-
ed in a clinical trial to confirm safety. Material for the other two parts of the vaccine is now in pro-
duction for similar safety testing. The vaccine will undergo many testing stages during the next few years. Once safety trials of all the components are complete, researchers will combine the three parts and move into trials designed to determine whether the vaccine can produce the immune response needed to pre-
vent HIV infection.

Production and testing of a complicated biological material like the HIV vaccine takes many years to complete, but with steady progress, this team of St. Jude soldiers plans to win the war against a worldwide killer.

The human immuno

deficiency virus (HIV) is responsible for the world AIDS pandemic.
races down the sidewalk at warp speed. Arms pumping, inline skates a blur, the 11-year-old flashes a triumphant smile at his mother. “Slow down!” she urges. With a sidelong glance under luxuriant, dark eyelashes, Carlos executes an effortless stop, leaving a trail of skid marks in his wake.

Few fifth-graders could match Carlos’ prowess on inline skates. Gliding at these blistering speeds demands skill, strength and a delicate sense of balance. What the casual observer would never guess is that this youngster once had a tumor in his cerebellum, the part of the brain that controls coordination. Five years ago, Carlos could neither walk nor talk. Today, his parents have to sprint to keep up with him.

Inline treatment plan

In the fall of 1996, Carlos underwent two operations in New Jersey and New York to remove a tumor in his posterior fossa, the lower, rear portion of the brain that houses the cerebellum and the brain stem. But surgeons were unable to remove the
entire tumor, which was classified as medulloblastoma, the most common malignant brain tumor in childhood. “They only gave Carlos a 40 percent chance of living,” recalls his mother, Linda Tomassoso-Saavedra. When she began to investigate treatment options, Linda turned to Carlos’ doctor for advice. “Okay, assume this is not Carlos; this is your son,” said Linda. “Where are you going to send him?” The physician replied, “The best hospital in the world is St. Jude Children’s Research Hospital... it has the most innovative protocols. That’s where I would send my son.”

When Carlos and his parents arrived at St. Jude, he was enrolled in SJMB96, a new protocol, or specific treatment plan, designed for patients between the ages of 3 and 21 who had medulloblastoma or supratentorial primitive neuroectodermal tumors. The study also involved children at institutions in Texas and Australia. Because part of Carlos’ tumor was still present, he was assigned to the high-risk group, which received the protocol’s most aggressive therapy. The treatment consisted of three main kinds of radiation and therapies that would eventually be used in his treatment. A diverse group of physicians, scientists, nurses and support personnel had pooled their talents and skills to address the array of challenges inherent in such a project. “That’s the neat thing about the way this place operates, says Clinton Stewart, PhD, of Pharmaceutical Sciences. “The clinicians and the clinical scientists and the basic scientists all talk and work together to come up with better protocols for the kids. A huge crowd of folks is involved in putting something like this together.”

In 1992, Stewart and St. Jude pediatric oncologist Charles Pratt, MD, had conducted the world’s first pediatric clinical trial of topotecan, the drug that would be given to Carlos. In ensuing years, researchers learned that topotecan could kill medulloblastoma cells and that it could effectively penetrate the cerebrospinal fluid (CSF), the fluid that flows through the brain and spinal column. The challenge Stewart faced was adjusting Carlos’ dose of topotecan so that the drug would travel through the bloodstream and into his CSF at exactly the right levels. Investigators found that they could apply radiation to a smaller area of the brain and still destroy the tumor. Carlos’ boost dose targeted the tumor bed instead of the entire region. Using conformal radiation therapy, radiologists could focus intense radiation on a specific location, killing Carlos’ cancer cells while reducing damage to healthy cells.

Topotecan. “From a pharmacokinetic standpoint, the clinical trial worked beautifully,” observes Stewart, who is also one of several St. Jude investigators studying a drug that may help patients who experience hearing loss from medulloblastoma treatment. Spokes on the wheel After six weeks of topotecan, Carlos began radiation therapy. The protocol offered the first systematic introduction of 3-D conformal radiation to target a smaller area than had traditionally been treated for medulloblastoma. Radiation therapy for medulloblastoma has long included treatment of the whole brain and spine, with a boost dose of radiation to the entire posterior fossa. As radiation destroys the tumor cells, it can also damage nearby normal tissues, causing learning problems, hearing loss, and growth and development problems. Investigators found that they could apply radiation to a smaller area of the brain and still destroy the tumor. Carlos’ boost dose targeted the tumor bed instead of the entire region. Using conformal radiation therapy, radiologists could focus intense radiation on a specific location, killing Carlos’ cancer cells while reducing damage to healthy cells. When radiation is applied to a child’s head and spine, almost 40 percent of the patient’s bone marrow is affected, reducing the bone marrow’s function for many months. Anticipating that side effect, clinicians had already collected and stored Carlos’ stem cells. During the final phase of treatment, he received four intensive courses of chemotherapy. To help his system fight infection, the healthy stem cells were reinfused after each course. In this manner, Carlos was able to tolerate a much higher dose of chemotherapy than is normally given. “By giving the stem cells back, the patients recovered more quickly without the long-term side effects of prolonged marrow suppression and increased chance of infection,” explains Gajjar.

Patients completing the protocol were offered the opportunity to participate in cognitive testing to evaluate any changes in intellectual functioning that had occurred as a result of treatment. Children who needed help in this area could receive intervention through behavioral modification training or methylphenidate drug therapy. “The most significant and behavioral modification projects are the first two studies of their kind in the world,” says Raymond Mulhern, PhD, chief of Behavioral Medicine. Carlos underwent psychological testing to determine the severity of his attention problems and then began taking methylphenidate. “It absolutely has helped him, says First, Carlos’ schoolwork,” says his mother. “He can focus better, attend to tasks longer, and he feels better about himself.”

Midpoint results of the SJMB96 protocol indicate that survival rates could increase dramatically for children like Carlos—as high as 80 percent for high-risk patients and 90 percent for standard-risk patients. Current survival rates range from 55 to 65 percent for...
high-risk patients and from 70 to 80 percent for standard-risk patients. “The early outcome results of this approach are very encouraging,” says Gaigal, who is currently designing another study based on results from the protocol.

Like SJMB96, the new protocol will involve staff from many different areas of the hospital. “We see a moderately large number of kids with medulloblastoma, and everybody basically relates like spokes on a wheel to the given protocol that’s in development,” says Larry Kun, MD, who heads the St. Jude Brain Tumor Program.

What’s next?

One of the most exciting additions to the next medulloblastoma protocol will likely come from the laboratory of Richard Gilbertson, MD, PhD. A faculty member in Hematology-Oncology and Developmental Neurobiology, Gilbertson came to St. Jude last year after winning the Schweiguth Prize, a prestigious international research award. He is investigating the function of a group of cellular proteins called ErbB2 receptors. Involved in the development of many brain tissues, ErbB2 receptors can also make cells grow abnormally and form tumors. “We have found that children who have high levels of ErbB2 in their tumors do not fare as well as those who have lower levels of the receptor. This marker may be used to determine which patients should receive more aggressive therapy for medulloblastoma.”

In SJMB96, patients were assigned to standard-risk or high-risk categories by determining whether the cancer had spread or the entire tumor had been removed. But sometimes the tumors of “standard-risk” patients do not respond well to therapy. Why not? Gilbertson says the answer may lie in the ErbB2 receptor. He proposes looking at the tumor cells of newly diagnosed medulloblastoma patients and evaluating the amount of ErbB2 receptor that is present. Children who have excessive levels of ErbB2 will be assigned to “high-risk” categories, regardless of clinical findings, and will receive aggressive therapy. “Nobody has ever used a so-called biological marker to try and guide therapy in this disease,” says Gilbertson.

Gliming toward a cure

Tom Curran, PhD, chair of Developmental Neurobiology, is involved in several other studies that may shed light on medulloblastoma. He and his colleagues study the fundamental biology of the brain, a structure that consists of billions of cells. “The brain,” Curran says, “is like the most complicated jigsaw puzzle you could ever imagine.” Curran has been studying a gene called reelin since he discovered it in 1995. Reelin controls the process that causes newly generated cells to move to their appropriate positions in the cerebellum. When reelin is mutated, cells in the cerebellum do not migrate properly, resulting in a defective brain structure. Mice and humans with reelin mutations cannot move around properly. This is the same brain structure in which medulloblastomas arise.

Another project in Curran’s department involves the patched gene, which is mutated in a rare form of medulloblastoma. Normally, patched serves as a braking mechanism to slow down cell growth. When one of these genes is lost, cells grow with abandon, forming tumors. By learning more about the patched gene, Curran’s team hopes to find new ways of stopping tumor growth. “If you can really understand the genes that cause tumors, then you will be able to make much better drugs,” says Curran. “But it takes a very long time to do that. This is, in part, a reason St. Jude is successful. We take on difficult problems and know it’s going to take a long time to solve them, but we build toward that because of the resources that are provided by ALSAC.”

Curran’s interest in medulloblastoma began six years ago when he arrived at St. Jude and spent a week in the clinic. “I met a medulloblastoma patient who had been cured, but he was still having trouble walking and learning,” says Curran. “I realized then that this was a tumor that I needed to work on. St. Jude is the best place to do that. Here, there is an integration of clinical science with basic research, and I have an opportunity to make an impact on these very difficult problems.”

“When you work at St. Jude, you see every day the reason that you’re here—you see the patients in the corridors,” Curran concludes.

Linda Tomasso-Savvedra says the proximity of labs and clinics means that children like Carlos obtain the best possible care. “This hospital is really comprehensive,” she says. “With the most innovative protocols and the most sophisticated equipment, it’s the best in the industry. And there’s a lot of love here.”

“Besides,” she says, as her son whizzes by on skates, “where else can you go where you can actually sit down and talk with the doctor who wrote the protocol?”

More Than Medulloblastoma

Any types of brain tumors exist. The St. Jude Brain Tumor Program has active protocols for most of them.

The Brain Tumor Program collaborates directly with the Developmental Neurobiology department, which researches brain development and function.

The extent to which the Brain Tumor Program is integrated with other hospital areas is unique. The clinical program is a partnership among the Radiation Oncology, Hematology-Oncology, Developmental Neurobiology, Pathology, Behavioral Medicine and Pharmaceutical Sciences departments and is supported by other services including the Hartwell Center for Bioinformatics and Biotechnology, Neurology, Nursing and Rehabilitation.

St. Jude was chosen by the National Cancer Institute (NCI) as one of nine centers to form a Pediatric Brain Tumor Consortium, which develops innovative therapies and makes them available to children with brain tumors. This new consortium allows our patients to get the most advanced therapy available for brain tumors.

St. Jude is the only pediatric research hospital that has been awarded an NCI cancer center support grant.

St. Jude is the only private cancer center in the United States committed to caring for and supporting children with cancer regardless of families’ financial or health care resources.
More than 400 runners are going the distance for St. Jude in this year’s Marine Corps Marathon.

On a Sunday in October, David Scanlan will run. He will run to show that he can do it again, having recovered from injuries when a car struck him during an evening jog last year. He will run for his son, who suffered from cancer back in 1986.

But most importantly, he will run for the children of St. Jude Children’s Research Hospital. And he will not be alone. On October 28, Scanlan will join 16,000 other athletes participating in the 26th annual Marine Corps Marathon, a 26.2-mile test of endurance and stamina through the streets of Washington, D.C. Scanlan and 400 other competitors from 28 states will run on a team that is raising money for St. Jude. For Scanlan and several others, the run is
personal. Scanlan is not just a St. Jude supporter; he is a St. Jude parent. In 1986, his son was suffering from non-Hodgkin lymphoma and a fungal infection. At one point, doctors told Scanlan and his wife that their son might not make it through the weekend. The couple spent days in the St. Jude Intensive Care Unit while their child fought for his life.

Scanlan knew that St. Jude was his son’s best hope. That is why he runs in the marathon today; to make sure that the work at St. Jude never stops.

In 1998, three women decided to enter the marathon to challenge themselves and to raise money for St. Jude. Those women were WMZQ radio personality Jessica Cash, station intern Cheryl Conner and Julie Butler, senior director in the DC-area regional office of the American Lebanese Syrian Associated Charities (ALSAC), St. Jude’s fund-raising arm. The following year, St. Jude officially fielded a team of dedicated runners. Team members have raised more than $600,000 for the hospital through the marathons. Each runner must raise at least $1,000 to participate. Cash’s radio station has topped the $1 million mark during its Country Cares radiothon for two years in a row, thanks in part to fund-raising events such as the Marine Corps Marathon.

Hearing Cash talk about the marathon inspired Rick Runner to join. “I was driving to work listening to the radio,” recalls Runner, a 19-year Army veteran. “I thought it would be a neat way to do the marathon. And it is hard not to adopt the St. Jude cause the more you hear about it.”

When Runner walked into the tent during the first group meeting last year, he found that his arrival was highly anticipated. “They thought it was a joke,” Runner said, referring to his last name. It didn’t help that his home address contained the word “homestretch,” as well.

Runner enjoyed the camaraderie at the event, and he was moved to discover that by running he could help a child. The 2000 squad raised about $250,000. During their post-race meeting, team members learned that the amount they had raised would pay for treatment for a child with acute lymphoblastic leukemia, the most common form of childhood cancer. “I was stunned,” Runner says. “Just by running and raising a few dollars, we had saved a life.”

But the Marine Corps Marathon is not really “just running.” It is a grueling test of endurance that requires intensive preparation and commitment.

When the runners feel like they can’t make the next leg of the marathon, they think of the children at St. Jude. That is what Scanlan does. He thinks of the children he met in 1986, and he thinks of the children today who are fighting for their lives. Suddenly, making the next corner isn’t so difficult.

Scanlan has one other bit of motivation that keeps him running.

He knows that when he reaches the finish line, he will receive a big hug from 26-year-old David III—now a survivor of childhood cancer, thanks to St. Jude.
focused much on skin cancer, but Children's Research Hospital. Vinzent Kidd, PhD, a member of soon you are dealing with another sunburn at a later date that chromosome abnormalities or muta-

UV radiation from the sun causes protect itself against skin cancer. The sunburn is a way for your body to that is usually correct. Essentially, a have our own shape and structure because certain cells die to create that 11 weeks of development, these skin digits of the hands and feet. At about development, and it is a process that programmed cell death.

“It's a normal process that's been going on for hundreds of millions of years,” says John Cleveland, PhD, a member of the St. Jude Biochemistry department. “Organisms need a way to find better treatments.”

In fact, cell death is such a neces-
tage of to find better treatments.”

Cleveland and other basic science researchers might not result in treat-

They discovered that the gene for the protein caspase 8 is frequently silenced in a certain form of neuroblastoma. The caspase 8 protein is a crucial player in many cell death processes. Children with this tumor have a particularly poor prognosis. The Kidd and Lahti team found that a large proportion of the neuroblastoma tumors with more than two copies of MYCN lack the caspase 8 protein. In these tumors the caspase 8 gene was shut down by a chemical modification involving the addition of methyl groups to the gene. By reintroducing the caspase 8 gene into deficient neuroblastoma cells the researchers restored the cells’ ability to undergo cell death in response to the chemotherapy drug doxorubicin.

The team also found that the cas-
pase 8 deficit can be corrected using demethylating agents. This corrective action will be tested in a clinical trial, using a demethylating compound—decitabine—that has been approved by the Food and Drug Administration. St. Jude researchers are collaborating with the Harvard School of Medicine in Boston.

“The Harvard investigators will treat the patients with decitabine for a few days; then those patients will receive a round of chemotherapy,” Kidd explains. “We will receive the cell samples from the patients, and we will analyze them to determine the methylation status of the caspase 8 gene.” Lahti adds, “It will tell us whether the drug is turning the gene back on and how well it’s working.”

Kidd and Lahti agreed that they would never have been involved in this discovery if they had not come to St. Jude. “We couldn't afford to, Kidd says. “It's all made possible by a line; research scientists are limited by what funding they have.” Lahti adds, “You can find something that looks very significant, but if you don't have the data to back it up, nobody wants to fund it. Getting that necessary data can be very expensive.”

Kidd says, “ALASC funding allowed us to...” “spend enough time on the caspase 8 story to bring it to the point where it was clearly fundable and we knew it was potentially impor-
tant,” Lahti says, finishing his sen-
tence. Kidd added, “That’s a real dis-
tinction about this institution. We've been here 10 years, and we enjoy it because we have the opportunity to do things we might not be able to do at other research centers.” Finishing each other’s sentences is common for Kidd and Lahti, who are not only research partners but also husband and wife.

“We have a 17-year-old son, and he’s now ready to go to college,” Kidd says. “When we first arrived at St. Jude he was only 7, and we real-
ized, seeing the kids here, how very lucky we are to have a healthy child.”

Lahti added, “We’ve told our son, ‘If you can make just a small impact somewhere in the world during your lifetime then you will have been a suc-
cess. As scientists, that’s all we can hope to do. It’s nice to know that our research here can provide some insight into something that might help treat children with specific tumors.”

Both agree that the fact that the demethylating agents will help make patients more responsive to therapy, but if not, other options are in the works. “We have nobody at St. Jude to continue to discover new knowledge of important biological functions. They know that finding the answers to “why cells commit suicide” and other basic science questions will eventually lead to cures for childhood catastrophic diseases.”

Surrounded by healthy cells, a damaged cell (center) activates its own death.
On March 10, 1993, only two months away from my eighth birthday, my family and I received information that would change our lives forever. I was told that I had non-Hodgkin lymphoma.

My first reaction was, “Oh, how could this happen to me? I didn’t even know that kids could get cancer!” Until then, I had thought that only adults could get cancer. It was a shocking and scary thought that I could have this. I thought, “Will they cure me? Will I die?” At 7 years old, the last thing you’re thinking about is dying, but I had to.

My bout with cancer was very hard on my friends, but they stuck with me and I could never have gotten through it without them. They had no idea what cancer was and what could happen, but they were always there for me. I had to receive chemotherapy every Thursday for two-and-a-half years. I have learned that through God, my family and my friends I can handle anything.

I don’t regret that my illness happened, because there are too many good things that have come out of it. Everyday problems don’t bother me, because compared to battling cancer, they are insignificant. I have learned that I am a lot stronger than I had realized. I have learned who my true friends are and who means the most to me. There are many friends I would never have met if I had not gone to St. Jude. I lost some friends I made there, but the short time I had with them has changed my life in ways that I can’t explain.

It is eight years later, and I am a healthy 16-year-old living a normal life. I love hanging out with my friends, shopping and working on St. Jude fund-raisers. Someday I hope to be a public relations director of a Nashville record company. But for now, I am thankful that I can just be a normal kid. Thank you, St. Jude!

Danielle Truxillo

“I thought, ‘Will they cure me? Will I die?’ At 7 years old, the last thing you’re thinking about is dying, but I had to.”

Danielle enjoys drama and public speaking. She has been involved with the St. Jude Dream Home in Lafayette, Louisiana, and has worked with radio stations in several states during Country Cares for St. Jude Kids®.