

Promise

SPRING 2008



THE Tie THAT BINDS
A gift of life spans
three generations

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is a quarterly publication of the
Department of Public Relations
St. Jude Children's Research Hospital
332 N. Lauderdale St.
Memphis, Tennessee 38105

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

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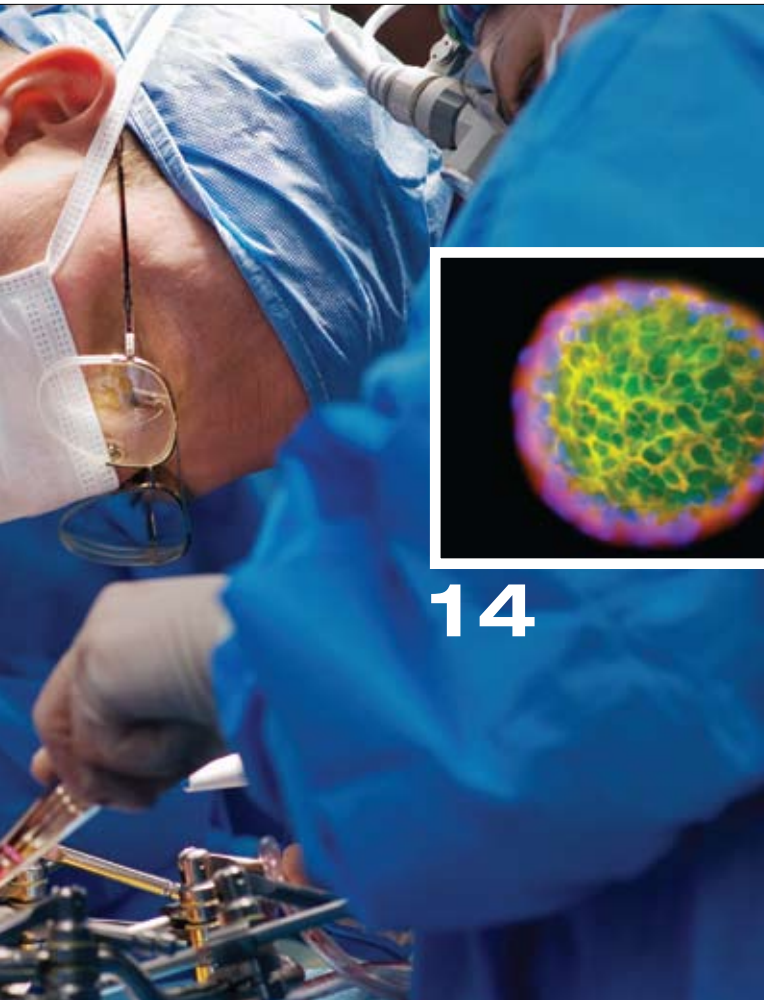
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A publication of St. Jude Children's Research Hospital Spring 2008

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On the cover: photo by Peter Barta.

Highlights

Discovery sheds light on immune response

St. Jude investigators have discovered that a common housekeeping mechanism most cells use to keep their interiors healthy also helps immune system cells engulf and destroy germs. This finding may help researchers understand how the body defends itself against infections and how cancer cells can resist chemotherapy drugs.

Researchers at St. Jude discovered a link between the two mechanisms—phagocytosis (engulfing germs) and autophagy (housekeeping). The discovery suggests that once they are triggered they share a common mechanism to enhance the elimination of germs that cause diseases.

“Autophagy is a cell-survival jack-of-all-trades, and we’re trying to understand the signals that trigger its onset,” said the paper’s senior author, Douglas Green, PhD, St. Jude Immunology chair. “We want to know how invading microorganisms avoid being destroyed by autophagy and learn how cancer cells use autophagy to resist chemotherapy drugs before they have a chance to work.”

A report on this discovery appears in the December 20, 2007, issue of the journal *Nature*.



Few existing medicines have a proven ability to prevent cancer. Chloroquine may be one that does.

Anti-malarial drug may prevent cancer

Physicians might one day be able to prevent certain cancers by using an anti-malarial drug that largely ignores healthy cells and targets cells that are becoming cancerous, according to results of studies at St. Jude.

In the lab, St. Jude investigators found that the anti-malarial drug chloroquine disrupts the development of lymphomas when in the presence of an overactive cancer-causing gene called *Myc*. The finding is important because few medicines have a proven ability to prevent cancer, said Michael Kastan, MD, PhD, St. Jude Cancer Center director. Kastan is senior author of a report on this work, which appears in the January 2008 issue of *Journal of Clinical Investigation*.

Since DNA damage helps transform normal cells to cancer cells, the St. Jude team reasoned that an agent that bolsters the cell’s DNA repair response might help prevent cancer.

“We focused our attention on chloroquine since we had previously discovered that the drug activates the damage-responsive genes, *Atm* and *p53*, even in the absence of DNA damage,” Kastan said. “Because of the long history of using the drug to treat malaria and certain immunologic disorders, we know that most individuals can tolerate long-term treatment with chloroquine with few serious side effects.”



Scientists define eye cancer gene's role



How does a rare pediatric eye cancer progress?

A genetic discovery led by St. Jude scientists helps answer a long-standing mystery about the eyes of vertebrates. The findings may translate into a deeper understanding of how genes coordinate the complex process of eye formation and how a rare pediatric eye cancer progresses.

“A series of complex developmental processes must be carefully orchestrated for the eye to form correctly,” said Michael Dyer, PhD, of Developmental Neurobiology. “One important aspect of this coordination is that retinal thickness be the same, irrespective of eye size. For example, the mouse eye is about 5,000 times smaller than that of the elephant eye, but the retinal thickness in these two species is comparable.”

The researchers found that a gene called *N-myc* coordinates the growth of the retina and other eye structures to ensure the retina has the proper thickness necessary to convert light from the lens into nerve impulses that the brain transforms into images. Until their study, reported in the January 15, 2008, issue of *Genes & Development*, almost nothing was known about the molecular mechanisms responsible for properly sizing the retina. Dyer is the paper's senior author.

Recently, Dyer and his team identified the specific type of cell that gives rise to retinoblastoma, a potentially fatal malignant tumor in the retina that affects about 300 children in the United States annually. “The determination of *N-myc* target genes during retinal development may also contribute to the current understanding of retinoblastoma progression,” he said.

St. Jude launches smoking cessation program

Eighteen percent of childhood cancer survivors are smokers—a number that St. Jude investigators say is too high to ignore. To help lower that percentage, the hospital has launched a new smoking cessation program designed just for childhood cancer survivors. It's just one more way that St. Jude is improving the quality of life for cancer survivors.

Robert Klesges, PhD, Epidemiology and Cancer Control, and other St. Jude faculty have received a grant from the National Cancer Institute to establish the St. Jude Cancer Survivors Tobacco Quit Line. This program aims to assist cancer survivors in their smoking cessation efforts.

“Having cancer survivors call in to individuals who know the unique problems they face—not only medically, but psychologically—will give them some comfort and assistance in their cessation efforts,” Klesges said. “In addition to being confidential, it is convenient, because they can call from anywhere.”

The toll-free number for the St. Jude Cancer Survivors Tobacco Quit Line is 877-4SJ-QUIT.

Highlights



Robert Webster, PhD (at left)
and Richard Webby, PhD.

Webby takes helm of WHO lab

Richard Webby, PhD, of St. Jude Infectious Diseases, has been named director of the World Health Organization (WHO) Collaborating Center for Studies on the Ecology of Influenza Viruses in Lower Animals and Birds.

Robert Webster, PhD, who headed the lab since 1975, recommended to the WHO that the position be transferred to Webby. Webster and Webby have worked together at St. Jude since 1999.

Of the five WHO collaborating centers, the St. Jude center is the only one that focuses on the transmission of animal viruses to humans. The other laboratories, located in Atlanta, Georgia; Tokyo, Japan; London, England; and Melbourne, Australia, deal primarily with human influenza.

"It's time to hand the torch to the next generation to continue this important role of St. Jude in the international community," said Webster, who holds the hospital's Rose Marie Thomas Chair in Infectious Diseases.

In recent years, with the assistance of employees in the Children's GMP, LLC, the St. Jude collaborating center has produced seed strains for H5N1 viruses. Webby used reverse genetics to make the first such seed strain.

"I will serve as the liaison between our lab and the World Health Organization, providing WHO with any information they need on outbreaks in animals and the characterization of viruses from those outbreaks," Webby said. "If these animal viruses do move into humans, understanding the characteristics of those viruses will certainly help WHO respond."

Antibody approved for use in clinical trials

The first therapeutic monoclonal antibody produced by the Children's GMP, LLC, has been approved for use in trials by the Food and Drug Administration (FDA). The antibody was primarily produced to treat neuroblastoma, a childhood cancer that arises in immature nerve cells.

Fariba Navid, MD, and Raymond Barfield, MD, PhD, both from Oncology, will head the St. Jude clinical trials that use the antibody, which targets GD-2, a molecule expressed on the surface of neuroblastoma cells. GD-2 is also expressed on melanoma, a type of skin cancer. Children with melanoma and neuroblastoma will be eligible for treatment in the proposed clinical trial.

Detailed documentation of each step of the production process is required to demonstrate to the FDA that the process is controlled and reproducible. This documentation represents a significant part of the production process unique to the GMP facility. At several key steps of the purification process, the antibody was analyzed using tests developed by the GMP's Quality Control unit and the St. Jude Hartwell Center for Bioinformatics and Biotechnology. This process ensures that sufficient quantities of highly purified monoclonal antibody are produced.

The Children's GMP, LLC, leases, manages and operates a facility that engages in the production of biologics and drugs under current Good Manufacturing Practices regulations at the request of St. Jude. The biologics and drugs will be used in research by St. Jude and other leading biomedical research institutions for clinical trials in collaborative studies with St. Jude.

Investigators find way to identify kids at risk for RSV

St. Jude investigators and collaborators have shown how to predict if a child who is infected with respiratory syncytial virus (RSV) while being treated for cancer or another catastrophic disease is at high risk for developing severe infection. The finding will help clinicians improve guidelines for managing the treatment of these children.

RSV is a common cause of pneumonia during winter, frequently causing fever, runny nose and coughs. It can be much more severe in patients who are undergoing cancer treatments and whose immune systems are suppressed. Clinicians have had difficulty predicting the severity of the illness in individual patients.

The scientists found that if children infected with RSV are under 2 years old or have very low levels of immune system cells in their blood called lymphocytes, they are at a higher risk for the RSV infection to move into the lung. Such infections are especially dangerous because they can be fatal in some immunocompromised children, and there is no standard effective treatment for these infections. The researchers also found that neutropenia (low levels of immune system cells called neutrophils), was not a risk factor for severe RSV infection. A report on the findings appears in the February 2008 issue of the journal *Pediatrics*.

“The new information is important because it helps identify children who are most at risk for severe disease using easily available clinical information,” said the paper’s senior author, Aditya Gaur, MD, of Infectious Diseases. “This narrows down the patient population who needs to be considered for antiviral therapy, which is costly and often inconvenient to receive from a child’s perspective.”

St. Jude shares discoveries, saves lives



St. Jude spreads hope to kids in Chile

St. Jude prides itself on sharing scientific discoveries with the world. But when St. Jude shares clinical trials internationally, there is much more involved than just sending a set of directions to clinicians in another nation. That’s especially true when those countries have limited resources.

A “twinning” strategy is a program designed to improve cure rates for specific diseases through partnerships between established medical research institutions in the developed world and selected institutions in developing countries. The St. Jude International Outreach Program (IOP) reported results of a successful twinning with an institution in Santiago, Chile, for a complex clinical trial of a treatment for the bone cancer osteosarcoma.

During the clinical trial, the principal investigators in Memphis and Santiago communicated regularly by telephone and e-mail, as did orthopedic surgeons, radiologists and pathologists. Multidisciplinary teams met by videoconference to discuss the trial. St. Jude made sure that the Chilean site had adequate personnel, equipment and training for the project. St. Jude also helped provide the prostheses that were implanted during limb-salvage surgeries and secured a drug to enhance blood count recovery.

“Our report reflects how successful St. Jude has become at designing and conducting even complex clinical trials for twinning through IOP,” said Najat Daw, MD, Oncology. Daw is senior author of a report on this clinical trial, which appears in the December 2007 online issue of *Pediatric Blood and Cancer*.

Protein disposal discovery could yield new treatments

St. Jude scientists have gained new insights into how myeloma cells dispose of defective or excess proteins. Myeloma is a cancer of plasma cells.

The researchers identified key cellular components that carry out protein disposal. The finding helps explain how cancer drugs called proteasome inhibitors interfere with this process. The discovery is important because the newly identified components of the protein disposal mechanism could be targets for novel cancer drugs. Such drugs would kill the cell by blocking protein disposal.

A report on this work appears in the November 30, 2007, issue of *Molecular Cell*.

“Proteasome inhibitors are currently being used to treat some types of cancer, including multiple myelomas, although many aspects of this cellular process remain poorly understood,” said Linda Hendershot, PhD, of Genetics and Tumor Cell Biology. “Our study sheds new light on how that process works.”

TrueValue

BY LYNDA NANCE

She sought a cause that was
worthy of her support.
Mary Wardrop found a mission
of value at St. Jude.

Finding value has always been important to Mary Wardrop. During World War II, she conserved resources by riding her horse to school every day. As a professor and researcher, she found fulfillment in helping students embrace the wonders of mathematics. And as a dedicated supporter of St. Jude Children's Research Hospital, she has found value in supporting the work of physicians and researchers who are fighting to save young lives.

St. Jude has been a part of Mary's life for decades. She first heard of the hospital when she attended school in Memphis, Tennessee, at Southwestern (now Rhodes College).

After earning master's and doctoral degrees, she embarked on a career in teaching and research. She and her husband, Robert, taught mathematics until their retirement in 1990. Since that time, Mary has established two charitable gift annuities through St. Jude and has included the hospital in her estate plans.

"The more I've learned about St. Jude and what's done for the patients," she says, "the more enthusiastic I've become."

Her first visit to the hospital occurred many years ago. "Once I visited the hospital, I knew I wanted to do something that would help the children," Mary says, noting that she wanted to be sure her estate would benefit "an institution that would affect so many people."

She returned to the hospital in 2005 for a visit that coincided with a college reunion.

"Each time I walk the halls, I'm impressed with what St. Jude provides for the patients, and with the fact that St. Jude doesn't charge families beyond what insurance



THOMAS TOOHEY BROWN

"The more I've learned about St. Jude and what's done for the patients, the more enthusiastic I've become," Mary Wardrop says.

covers," Mary says. "I particularly appreciate that most children are seen as outpatients so they can maintain more normal family lives, and that St. Jude pays for their lodging, food and travel."

In October 2007, Mary made a third trip to the hospital to attend a scientific symposium, where she was introduced to some of the lifesaving research occurring at St. Jude. In the lab of biochemist Gerard Zambetti, PhD, Mary learned about the *p53* gene and how it affects tumor suppression and formation. She also learned about Zambetti's studies on the regulation of the cell cycle, cell survival and differentiation. "He was fascinating," she says. "He could explain his work in terms we could understand."

Even after undergoing surgery for a benign tumor and enduring the loss of her husband after 30 years of marriage, Mary expresses gratitude for "an interesting and wonderful life" filled with opportunities for teaching and giving.

Through her legacy to St. Jude, those opportunities to give will continue. Mary knows that by supporting a hospital that does so much good for so many children, she adds value to an already rich life. ●

To learn more about making a gift to St. Jude or other planned giving opportunities, call ALSAC Gift Planning at (800) 395-1087 or e-mail giftplanning@stjude.org.

Eagles Are Landing for St. Jude

By TARA MILLIGAN

Vijay Singh and Stanford Financial Group team up to help St. Jude kids.

He has won three major golf championships and is a member of the Golf Hall of Fame, but professional golfer Vijay Singh described his visit to St. Jude Children's Research Hospital as the "most emotional day I've ever had."

Singh visited the hospital to help Stanford Financial Group present funds raised from the 2007 Stanford St. Jude Championship. His visit also recognized Stanford's successful first year as the title sponsor of the premier PGA TOUR event held annually in Memphis, Tennessee. The tournament made a historic donation of \$1.76 million to St. Jude last year.

As the new title sponsor, Stanford made significant enhancements to the golf tournament, but the increased donation is primarily the result of a pledge by Stanford to donate \$1,000 to St. Jude for each eagle carded during the 2007 PGA TOUR through the Eagles for St. Jude program. Stanford also invited the public to donate to St. Jude and track eagles made through www.eaglesforstjude.com.

The PGA TOUR golfers made a total of 1,222 eagles in 2007. Singh, who serves as the ambassador for Eagles for St. Jude, personally pledged to donate \$1,000 for every eagle he carded during the TOUR.

But after visiting the hospital, Singh said the 12 eagles he made in 2007 weren't nearly enough for the kids of St. Jude. He has increased his pledge for every eagle to \$5,000 this year. Singh also made a personal donation of \$50,000 to the hospital.

"I know my accomplishments help St. Jude achieve its mission to find cures for these special children," Singh says. "It makes me feel proud every time I make an eagle, and it gives me added drive and passion to play my best golf."

Singh made another personal promise to St. Jude patient Brandon "Tyler" Whaley. During his tour of the hospital, Singh chatted with Tyler in his hospital room. Sadly, Tyler lost his battle with acute lymphoblastic leukemia shortly after the visit.

This experience touched Singh deeply. Singh dedicated his first eagle of 2008 to Tyler.

"I've been to a lot of places in the world and seen a lot of things, but St. Jude has probably been the most wonderful place I have been," Singh says.

The 2008 Eagles for St. Jude program is well under way, and other golfers are following Singh's lead.

Camilo Villegas has announced his participation in the program, pledging a personal donation of \$3,000 for every eagle he makes this year.

Eagles have become even more valuable to St. Jude thanks to Stanford partnering with the women's professional golf organization, LPGA, to include their tour in the campaign. LPGA favorite Morgan Pressel has committed to donate \$1,000 for each eagle she makes in 2008.

For Singh, making as many eagles as possible is a professional and personal goal. "Eagles for St. Jude allows me to share that good feeling that I have on the golf course and turn it into something truly lasting and meaningful off the golf course," he says.

The 2008 Stanford St. Jude Championship will be held June 2-8 at TPC Southwind in Memphis.

For more information, visit www.stanfordstjude.com. ●

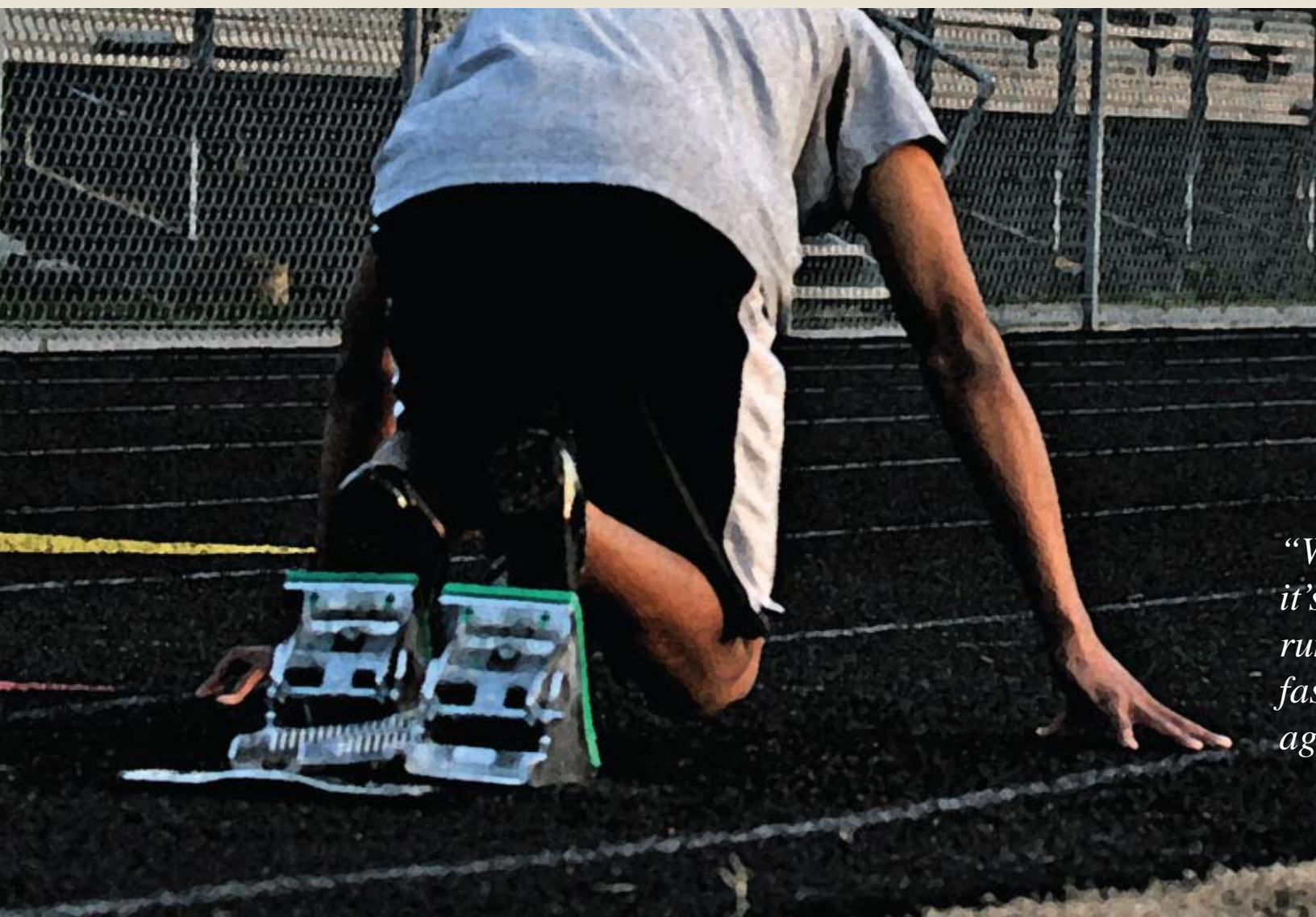


PETER BARTA

Singh puts aside his golf clubs for a different kind of game during a visit with St. Jude patient Bryce Norwood.

WINNING THE RACE AGAINST WILMS

BY ELIZABETH JANE WALKER



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At the moment of diagnosis, Wilms tumor already has the lead in a life-or-death race. But kids with cancer in both kidneys are sprinting ahead and vanquishing their adversary, thanks to St. Jude.

Some people compare it to a roller coaster ride. Others liken it to an interminable nightmare. But Tony McMorris describes his son's journey through cancer treatment as an exhausting sprint with life-or-death odds. When doctors discovered softball-sized tumors on the kidneys of 1-year-old

Brock McMorris, the race was on.

"When cancer comes into your life, it's like a track meet where you're running a 100-yard dash and the fastest person in the world is running against you with a head start," Tony says. "By the time you figure out what's going on, the cancer's already ahead of you, and it's not waiting around."

Tony and Lisa McMorris learned

in 2001 that Brock had a rare type of kidney cancer called Wilms tumor. In the United States, approximately 500 children are found to have Wilms tumor each year. But only 5 to 7 percent of those children will have tumors in both kidneys—that's about 25 kids in a nation of more than 300 million people. Brock was one of those 25. He had five tumors on his right kidney and many more on his left.

"I want to take him to the best place in the world," Tony said.

"I've got kids myself," Brock's pediatrician replied. "You say you want to go to the best place in the world? If it were my son, I'd take him to St. Jude Children's Research Hospital in Memphis, Tennessee."

On your mark ...

Three days after the diagnosis, Tony, Lisa, Brock and his sister, Anna, arrived at St. Jude and met the team of medical professionals who would take care of Brock. "It was like a puzzle," Tony recalls. "You had your oncologist, you had your radiologist and then you had your surgeon. For our surgeon, we were assigned to Dr. Davidoff."

Andrew Davidoff, MD, and his colleagues have extensive experience treating children with bilateral Wilms tumor, or cancer on both kidneys. In most hospitals, patients such as Brock would have one or both kidneys removed in an attempt to eradicate the cancer. But St. Jude has adopted a different—and extraordinarily successful—approach. Since 1999, every St. Jude patient with bilateral



ELIZABETH J. WALKER

When cancer comes into your life, it's like a track meet where you're running a 100-yard dash and the fastest person in the world is running against you with a head start."

Wilms tumor exhibiting favorable histology (cell characteristics) has undergone bilateral nephron-sparing surgery. This procedure is designed to remove the malignant tumor, sparing healthy kidney tissue.

If one kidney is removed and the cancer recurs in the other one, the possibility of losing renal (kidney) function is high. If both kidneys are removed, the child must endure dialysis and a possible kidney transplant. So the best scenario for the child is to retain as much healthy kidney tissue as possible.

Get set...

Surgeons traditionally hesitated to perform bilateral nephron-sparing surgery because the tumors appear to be inoperable on preoperative scans. Nephron-saving surgery is a more complex procedure than a complete nephrectomy, or kidney removal.

"Sometimes things may look scary on preoperative scans, making surgeons think that there is nothing to save," says Davidoff, division chief of St. Jude General Pediatric Surgery. "But in our experience, we have always been able to save normal kidney on both sides. We've learned not to make preconceived judgments based on imaging alone."

"The incidence of renal failure in kids with bilateral Wilms is significant," Davidoff says. "We want

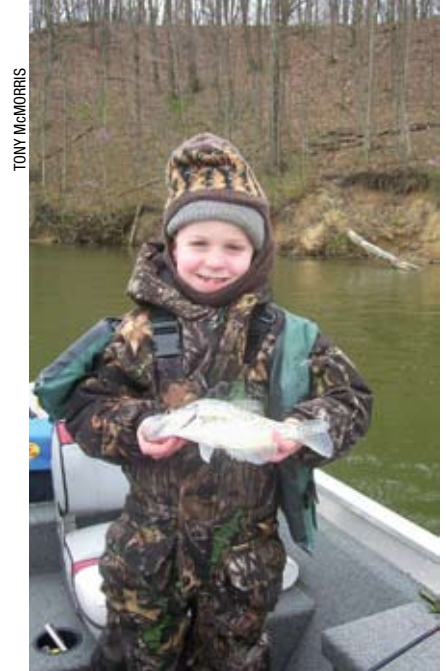
to save these kids from renal failure by saving as much kidney, on both sides, as possible." St. Jude accepts a high number of children with bilateral or surgically difficult cases. Several patients have come to the hospital in the past few years after being told elsewhere that they should have both kidneys removed. All of those children underwent successful nephron-sparing surgery at St. Jude.

St. Jude patients with bilateral Wilms tumor generally receive chemotherapy followed by bilateral nephron-sparing surgery within 12 weeks of the initiation of therapy. This approach has allowed surgeons to preserve the renal function of children while winning the race against the cancer. Since St. Jude began using this process, all children who exhibited favorable histology Wilms tumor and underwent nephron-sparing surgery are still alive.

Davidoff and his St. Jude colleagues recently authored an article about their experiences treating patients with bilateral Wilms tumor. The findings were published in the prestigious journal *Cancer* (April 1, 2008 issue). Editors of the journal deemed the study so important that they included an editorial highlighting its significance.

The finish line

Davidoff was able to remove all of the tumors on Brock's kidneys, saving 30 percent of one kidney and half of the other. Nuclear medicine tests have indicated that the 7-year-old has normal kidney function. "If you take 100 normal kids off the street and give the test to them, Brock's kidney function would be within the realm of their normal," Tony marvels. "That's



As Brock McMorris proudly displays his catch, his dad breathes a prayer of thanks. "Every time I look at Brock," Tony says, "I see a boy who's living because of God, because of that team of doctors and because of the research that's happening at St. Jude."

simply amazing, considering what he's had to live through."

When Brock's physician told him that football might be too dangerous a sport for someone who has undergone kidney surgery, the boy inquired whether bull riding might be a good alternative. He finally agreed that fishing would be acceptable. Today, Brock is an avid fisherman who insists on baiting his hook every January 1 to usher in the New Year.

In 2007, the wind was howling and the temperature was in the single digits when he and his dad headed to a lake near their home in Illinois. Tony gladly took his son on the traditional outing, breathing a prayer of thanks that their race against cancer has been successful.

"Every time I look at Brock," Tony says, "I see a boy who's living because of God, because of that team of doctors and because of the research that's happening at St. Jude." ●



Andrew Davidoff, MD, and his colleagues have been able to save part of each kidney in kids with bilateral Wilms tumor.

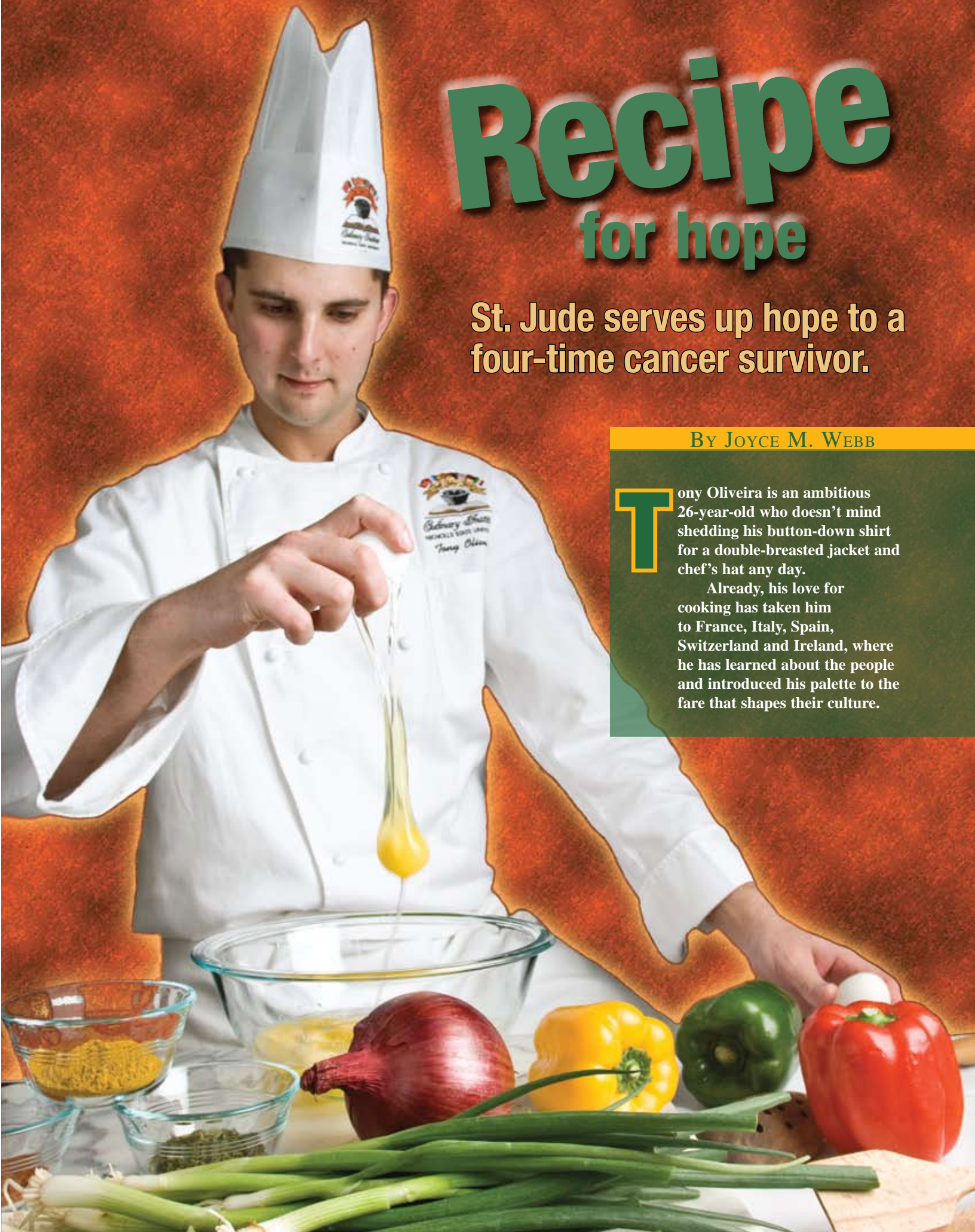
Recipe for hope

St. Jude serves up hope to a four-time cancer survivor.

BY JOYCE M. WEBB

Tony Oliveira is an ambitious 26-year-old who doesn't mind shedding his button-down shirt for a double-breasted jacket and chef's hat any day.

Already, his love for cooking has taken him to France, Italy, Spain, Switzerland and Ireland, where he has learned about the people and introduced his palette to the fare that shapes their culture.



He enjoys spending time in the kitchen among the sound of clattering pots and pans, carefully planning his meals—slicing, dicing, braising and searing until he comes up with entrées that satisfy the taste buds of those around him.

“I like making people smile, and I do that through food,” Tony says. “Some people make others happy by singing; others do it with their artwork. Cooking is my way of making people happy.”

After surviving cancer four times during his teen and young adult years, Tony has found that his passion for cooking has grown just as intense as his will to live.

Competitive side

At an early age, Tony fed his competitive nature by playing baseball, football and participating in local triathlons. One summer while running and training for a triathlon, the 11-year-old fell to the ground without warning. He sat there for a minute, trying to make sense of what had just transpired.

A few days later, Tony had trouble walking and his parents took him to an orthopedic specialist for X-rays. When the X-rays turned up nothing, Cody and Linda Oliveira took their son to the pediatrician for lab work. Then the family headed to Kiawah Island, South Carolina, to soak up the sun. It seemed like the perfect summer getaway, but Tony could not muster enough strength to climb stairs or sink his toes into the warm, white sand. He felt miserable and found comfort on the couch for the entire vacation.

When the family returned home, Tony’s pediatrician referred him to St. Jude Children’s Research Hospital. Tony had seen TV specials about the hospital but never dreamed that he and his family would find themselves looking to St. Jude researchers and physicians for hope.

“Once they told us where we were going, my parents realized that we were lucky to have the best place in the country to take care of me,” he says.

St. Jude physicians determined that Tony had large cell lymphoma, a cancer of the lymph glands. Since he was unable to compete in sports while undergoing eight months of chemotherapy, he shifted his attention to cooking competitions. He didn’t have to go far to learn the tricks of the trade.

Tony recently won the 2008 S. Pellegrino™ Almost Famous Chef regional competition in Houston, Texas, subsequently placing fourth in the national contest. Celebrity chefs and judges loved his entry: pomegranate-lacquered duck breast served with candied turnips and roasted ruby red beet risotto.

Birth of a chef

Tony relied on his father’s years of cooking experience and Cajun roots in Houma, Louisiana, to get him started. At 12 years old, he tagged along with his father to chili-cooking competitions and barbecue cooking contests, including the Memphis in May World Championship Barbecue Cooking Contest, which takes place annually just a few miles from the St. Jude campus.

“They’d sneak me in as a cook under somebody else’s name. I’d cook as a lady one week and as a man another week,” Tony recalls. “I started beating all these adults and thought, ‘Wow, I guess I’m getting kind of good at this.’”

With his cancer in remission, Tony established a junior chili-cooking category at a regional fair and was thrilled about the opportunity to compete in his own league. But before the competition could begin, his cancer recurred. Just seven months after completing cancer treatment, Tony learned that he had recurrent lymphoma that had spread to his hip, bone marrow, lung, spleen and kidney. Tony knew the news was devastating, but his innocence and limited knowledge of cancer allowed him





Tony Oliveira visits with Dale June, RN (at left), and Ben Stanford, RN, in the medicine room at St. Jude. Tony has grown to know the clinical staff like family throughout his 14 years of treatment at St. Jude. "Tony is like the ever-running bunny that never gives up," June says.

to keep a positive attitude and focus on getting better.

He talked a friend into filling in for him at the competition while he received chemotherapy, radiation therapy and a bone marrow transplant to treat his recurrent lymphoma. Tony was especially motivated to get well when his friend took home the winning trophy.

For the next several years, Tony's cancer was in remission. He went on to win the junior category at the fair for three consecutive years. He also established his own barbeque team at the Memphis in May World Championship Barbecue Cooking Contest.

In August 1998, at age 17, his lymphoma recurred again—this time in the lymph nodes located in the central part of Tony's chest. The teenager underwent six more months of chemotherapy and radiation therapy.

Melissa Hudson, MD, director of the St. Jude Cancer Survivorship Division, says Tony always maintained an upbeat attitude throughout his treatment.

"His story is a good message for adolescents and young adults in particular," she says. "The kids we see who are most resilient are those who say, 'I am going to maintain any sense of normalcy and continue with my plans. I'll deal with the cancer issues as I have to, but I'm not going to put my life on hold.' Tony always had a goal and was very positive, even in the face of cancer. He wasn't going to miss a minute of having a good life."

Bon attitude

In 2004, Tony took a break from his busy schedule as a part-time student, landscaping business owner and night-shift restaurant manager to vacation on the snow-covered slopes of Colorado. After skiing with his family and friends, he reported to St. Jude for his annual checkup. There, he learned that after five years in remission, he had developed another cancer—a high-grade osteosarcoma (malignant bone tumor) in his left hip and pelvis. Physicians explained that Tony could lose his leg. The news hit him like a ton of bricks, because he was old enough to understand the potential ramifications.

That evening, he and his dad discussed the situation. "You know I love skiing," said Tony, eyes brimming with tears. "Let's go to Colorado."

So that night, father and son flew to Colorado. "Nobody knew but my mom, my sister and my girlfriend. That was the last time I skied," Tony says.

After two weeks on the slopes, Tony and his father returned to St. Jude, where Tony underwent a limb-salvage procedure to remove part of his left hip bone and pelvis. He completed chemotherapy in May 2005, and his cancer has been in remission ever since.

"I live every day as if I'm going to get better and better, and I keep pushing," he says.

Well done

After finishing chemotherapy, Tony enrolled in Nicholls State University's Chef John Folse Culinary Institute in Thibodaux, Louisiana.

John Folse is the only U.S. culinary program to participate in the prestigious Institut Paul Bocuse Worldwide Alliance in France. This program brings together top culinary students from the United States, Canada, Brazil, Peru, Japan, Taiwan, Greece and Finland. In May 2007, Tony was one of three students from his school invited to participate in the 14-week, intense culinary program in France. He and his peers ran a fine-dining restaurant, serving entrées such as veal, lamb and choice-cut beef. They also planned the menu and learned about restaurant management.

Shortly after his return to the United States, Tony served as executive sous chef for the school's largest fundraising event. He and some classmates joined the dean of the culinary school on a 12-day leadership seminar in Michigan to discuss the program's future plans and opportunities.

After graduation in May 2008, Tony plans to work at an exclusive country club in Houston, Texas. His St. Jude oncologists say the future looks bright.

"Here's a kid who has seen his life limited for many years. During that time, he did not go to bed one single day feeling he was a normal, healthy person," says Carlos Rodriguez-Galindo, MD, of St. Jude Oncology.

"He could have been content with people feeling sorry for him. Not Tony; he would not allow that. He's a great person and an example of how fighting cancer can be a lesson for us all."●

"My parents realized that we were lucky to have the best place in the country to take care of me."

Collaboration for a Cure

BY ELIZABETH JANE WALKER

The world's top experts in pediatric and adult cancer are uniting to eradicate a rare cancer that kills both children and adults.

What's the best way to find a cure for a vicious cancer that kills both children and adults? The answer seems obvious: Assemble the world's top experts on adult and pediatric cancer. Encourage them to focus their intellect, energy and creativity on curing that disease.

It sounds simple, doesn't it? But it has never been done before. *Until now.*

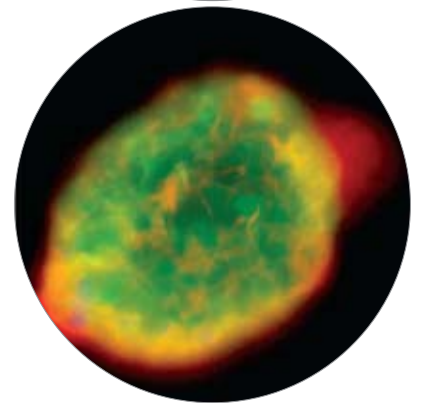
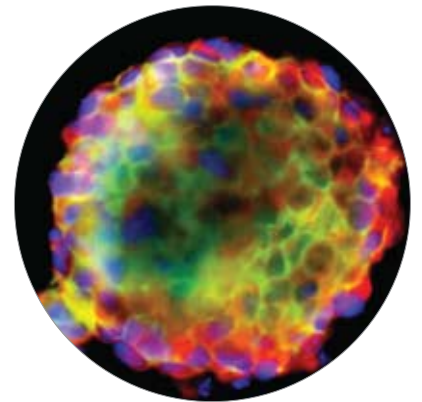
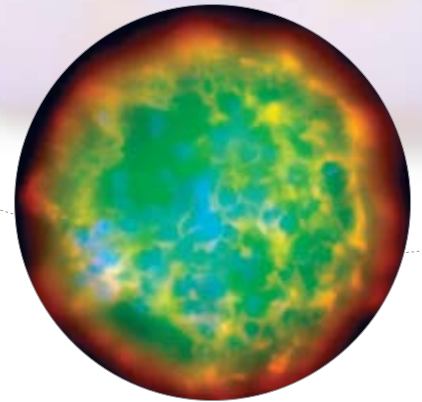
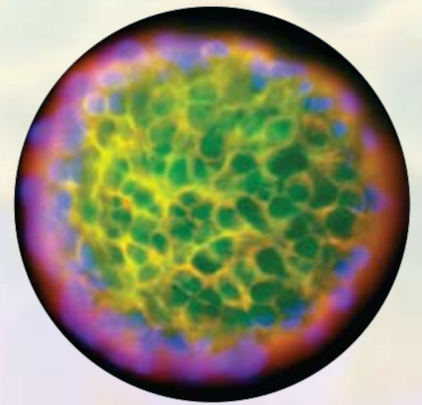
Recently, two groups of brilliant scientists embarked on the first direct collaboration to find a cure for ependymoma, a rare central nervous system tumor that affects people of all ages.

Ependymoma arises from cells located within the ventricles of the brain and spinal cord. In children, the tumors usually appear in the brain; in adolescents and adults, the tumors generally form along the spinal cord.

Treatment for ependymoma usually consists of surgery to remove the tumor, followed by radiation therapy. Unfortunately, scientists have no other weapons against this deadly cancer. Chemotherapy is not highly effective, so patients rarely survive if the cancer is not completely removed or if it recurs.

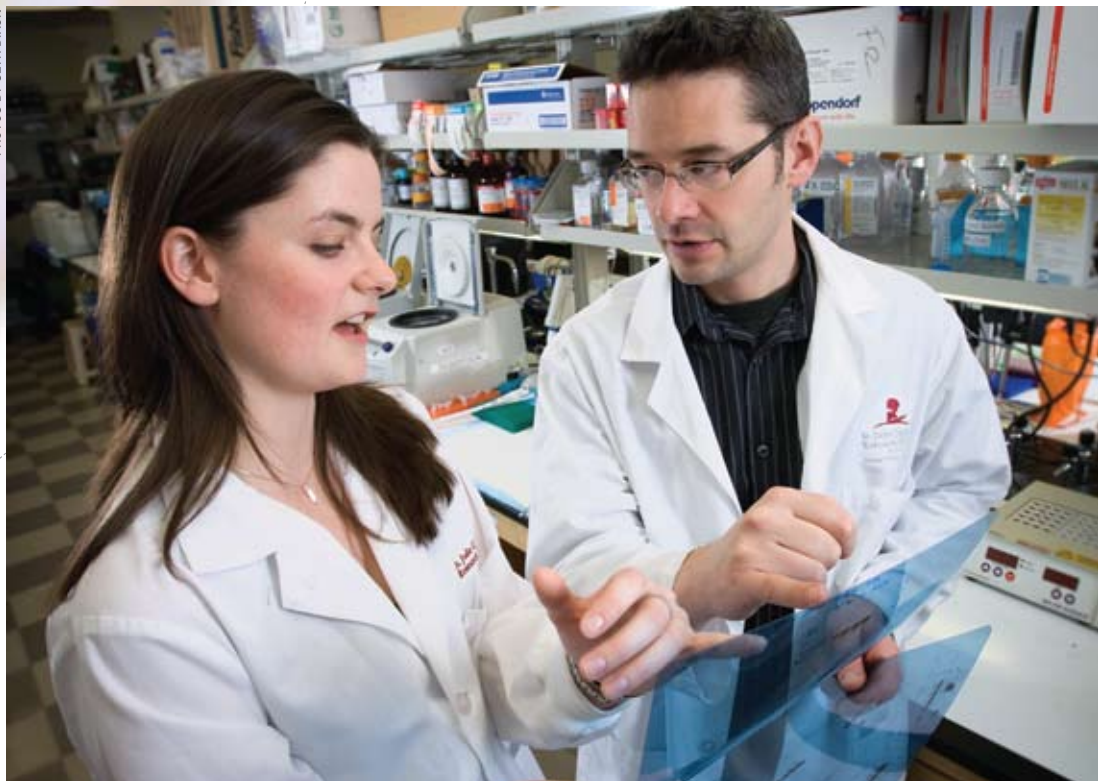
Researchers at St. Jude Children's Research Hospital are working with colleagues at MD Anderson Cancer Center in Texas to increase the odds for all patients who develop ependymoma. The Collaborative Ependymoma Research Network consists of two teams with one common goal: the St. Jude group studies the pediatric form of the disease, while the MD Anderson team addresses the adult form. Investigators hope that this collaboration will mean the difference between life and death for patients around the world.

The St. Jude efforts are headed by Richard Gilbertson, MD, PhD, co-leader of the St. Jude Neurobiology and Brain Tumor Program. "This initiative is exciting because it's the first time that clinical trials will occur for children and adults with the same disease," he says. The St. Jude portion of the project consists of four components: cancer stem cell research, pathology and genomics, drug development and clinical trials.



Gilbertson's lab discovered that radial glial cells may give rise to ependymoma. Scientists create clusters of these cells (shown above) to test drugs that may be used to treat ependymoma.

Richard Gilbertson, MD, PhD, of St. Jude Developmental Neurobiology works with postdoctoral research associate Jennifer Atkinson, PhD, in the lab. Gilbertson heads the St. Jude component of the Collaborative Ependymoma Research Network. Atkinson works in both the stem cell and the drug development portions of the project.



Cancer stem cell research

In his St. Jude laboratory, Gilbertson is discovering ways to determine which genetic mutations are required to transform a stem cell into a cancer stem cell. His laboratory was the first in the world to isolate cancer stem cells for ependymoma.

“We have already developed the first models of the disease in the laboratory, and we think we have found a cell in the nervous system that goes wrong to make an ependymoma,” Gilbertson says. He and his colleagues also discovered that ependymomas from different parts of the nervous system contain distinct groups of genetic alterations.

“If you’re looking at tumors in the front of the brain, one from a 6-month-old child will look almost exactly the same as one from a 71-year-old man,” Gilbertson says. “Actually, that child’s tumor would look quite different from a tumor that might occur in the back of a 6-month-old’s brain. This tells us that ependymoma is not age-dependent; it is site dependent. I think that is because the tumors are dictated right from the beginning from the cell type.

“We have been doing a lot of work to understand those cells,” he continues. “Spinal tumors occur mostly in adults; they are very rare in children. Ependymomas in children occur mainly in the brain. We think the reason why spinal ependymomas occur in adults and the intracranial tumors occur in children is because the population of that cell type changes with age.”

For the past three years, Gilbertson has conducted

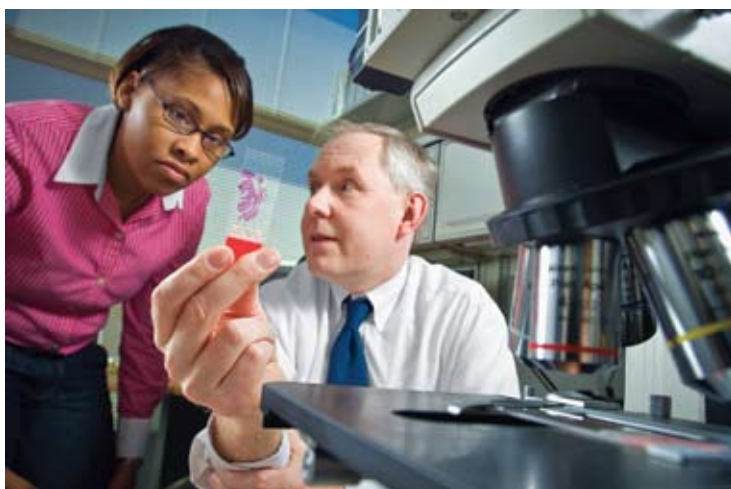
an international study involving 230 samples of ependymoma. St. Jude researchers have used the gene array technology capabilities of the St. Jude Hartwell Center for Bioinformatics and Biotechnology to identify more than 75 genes that may play a part in causing this brain tumor. Gilbertson and his colleagues will continue this project, which promises to uncover more secrets about the cancer.

Pathology and genomics

Meanwhile, pathologists are building on Gilbertson’s recent findings to figure out how to classify ependymoma accurately. “We’re really hopeful that we can get a good understanding of what is a poorly understood disease at the present time by looking at the whole range of tumors, both in kids and adults—taking what we know of pathology at the moment and supplementing it with molecular data that Richard has derived,” says pediatric neuropathologist David Ellison, MD, PhD, of St. Jude Pathology.

Currently, pathologists classify and grade the tumors based solely on their appearance. Even though this system has been refined through the years, it is not clinically and biologically useful.

“There’s a lot of controversy about whether or not the grading of ependymomas really correlates with how the tumors behave in patients,” Ellison explains. “We can identify that a tumor is an ependymoma, but understanding the different types and grades is a gray area. We’re at the point where if we’re going to do



David Ellison, MD, PhD, and Shaundra Glass of St. Jude Pathology discuss their roles in creating a completely new classification for ependymoma. The information will help clinicians as they predict prognosis and treatment response.



Kip Guy, PhD, St. Jude Chemical Biology and Therapeutics chair, confers with Alexander Arnold, PhD, who helps Guy in the project to identify and develop chemicals that will be effective against ependymoma.

something useful with the pathology, we need to have molecular information to supplement what we're looking at down the microscope."

Ellison is spearheading the effort to create a completely new classification for childhood and adult ependymoma. This project will help clinicians understand the diverse biology of the disease, allowing them to better predict prognosis and treatment response.

Ellison and his colleagues at MD Anderson will look at all the different subtypes of ependymoma and analyze them for the presence of the molecular abnormalities that Gilbertson has been identifying in his lab.

"That sort of analysis has never been done with ependymomas before," Ellison says. "We know a certain amount about the molecular abnormalities of ependymomas, but we haven't found anything that's guided treatment. We will be leading this analysis of the pathological subtypes versus the molecular abnormalities. Ependymoma is a tumor that's crying out for a good molecular study that links with what we already know about the pathology to create a combined classification that is biologically and clinically useful."

Drug development

Ependymoma is a wily adversary that has thus far proved resistant to conventional chemotherapy.

"Currently, we have some drugs for ependymoma that cause the disease to respond, but they do not ultimately affect survival," Gilbertson says. "Radiation therapy plays an important role in the treatment of ependymoma, but

basically if you don't take the whole tumor out, the child will have a much reduced chance of surviving. So what this tells us is that conventional treatments aren't working, and we need to have completely new approaches."

Kip Guy, PhD, St. Jude Chemical Biology and Therapeutics chair, is leading the hospital's effort to identify and develop chemicals that will be effective against ependymoma. Faculty and staff in the St. Jude Chemical Biology and Therapeutics department will screen thousands of compounds to pinpoint ones that inhibit cancer stem cells and block tumor formation.

Currently, Guy's team is looking at drugs that already exist, but that may have not been considered for use with ependymoma. "That's about 1,200 existing different drugs," Guy says. "We're also looking at combinations of those drugs. Obviously, that's a way to really jump-start a development program: If you can identify an existing drug, then all you have to do is basically reapply it. That's our first-path strategy."

In the long term, the researchers in Guy's area will concentrate on finding chemicals that might be starting points for new drugs. They will carry them forward through testing and development for use in clinical trials.

Clinical trials

The ultimate destination for these new drugs is the clinic. Because ependymoma is a rare cancer that affects about 140 children in the United States each year, an effective clinical trial would need to enroll patients from several institutions. St. Jude and MD Anderson will serve



Amar Gajjar, MD, visits with 9-year-old Leia Fraley, who is undergoing treatment at St. Jude for ependymoma. Gajjar is heading the clinical portion of the St. Jude project that is focused on finding a cure for ependymoma.

any disease that cancer stem cells are similar to normal stem cells and that the cancer stem cells exist in special environments called niches. The niche is required to protect the stem cell and control it.

“Whereas normal stem cells constantly communicate with the niche to say, ‘Now it’s time to divide; now it is time to stop,’ cancer stem cells say, ‘Now it’s time to divide; now it’s time to divide,’ and they just keep proliferating,” Gilbertson explains.

“The upcoming clinical trial will use a novel combination of drugs,” Gajjar explains. “One drug will target the vascular niche, whereas the other two drugs will actually hit the cancer stem cells. We hope the combination of hitting the stem cells and the vascular niche will kill the tumor.”

The hospital’s participation in the Collaborative Ependymoma Research Network allows pediatric oncologists at St. Jude to take the lead in finding a cure for a cancer that has eluded treatment for years. It’s just one more example of how St. Jude excels in finding ways to move discoveries quickly from the research laboratory to the bedside. ●

“This initiative is exciting because it’s the first time that clinical trials will occur for children and adults with the same disease.”

as hubs for other clinical affiliates that are participating in the project.

The adult and pediatric programs will open joint protocols, with the first one scheduled to start within the next few months. The pediatric and adult trials will run simultaneously and will have many similarities. Amar Gajjar, MD, co-leader of the Neurobiology and Brain Tumor Program, will direct the clinical portion of the St. Jude project. Thomas Merchant, DO, PhD, Radiation Oncology division chief, will lead the radiation oncology portions. Clinton Stewart, PharmD, of Pharmaceutical Sciences, will provide pharmacokinetic and pharmacogenetic support to the pediatric clinical trials.

The first clinical trial will build on discoveries Gilbertson’s lab has made within the past year. He and his colleagues recently demonstrated for the first time in

1st in Experience

St. Jude researchers were the first in the world to isolate cancer stem cells of ependymoma.

St. Jude investigators were the first to discover that ependymomas from different parts of the nervous system contain distinct groups of genetic alterations.

St. Jude is the only NCI-designated pediatric cancer center in North America.

The Neurobiology and Brain Tumor Program at St. Jude runs one of the world’s largest pediatric neuro-oncology programs.

St. Jude and MD Anderson have formed the first, direct collaboration between pediatric and adult oncologists to seek a cure for ependymoma.



The Tie that Binds

BY MIKE O'KELLY

**“My grandfather had helped save the
life the life of his great-granddaughter
whom he had never met.”**



When Chris Dempsey's grandfather died in 2003, each of the grandchildren selected one of his personal belongings to honor his memory.

The lifelong farmer from Missouri had annually donated a portion of the sale of his crops to St. Jude Children's Research Hospital, a place he had never visited. Chris decided to choose a St. Jude necktie as his memento—an item that caught his eye and represented a cause his grandfather had supported.

"I picked that tie never having been inside St. Jude, but I thought, 'That's a pretty tie, and it represents something my grandfather believed in,'" Chris says.

A special bond

Chris and his wife, Monica, have two children of their own, Micah and Morgan, and had served as a foster family for three children when their fourth foster child arrived. Monica felt an instant bond the day she first laid eyes on 8-day-old Taylor.

"I thought it was just me wanting to feel this, but when I saw her for

the first time, I felt something that I had not felt with the other babies that we had fostered," Monica says.

Three years later, in May 2006, Taylor became the fifth member of the Dempsey family when her adoption was finalized. She had already settled in long before that time, thanks to an energetic personality.

Bound for St. Jude

When Taylor became less lively and developed a persistent fever in August of that year, Monica took her to the family's pediatrician. He prescribed an antibiotic and sent Taylor home. After Taylor still felt lethargic for a week, the family's doctor felt a mass in her abdomen and said Taylor would need to undergo a CT scan.

The test revealed that Taylor had Wilms tumor, a cancer of the kidney that primarily occurs in children. Taylor was referred to St. Jude and made her first visit to the hospital a day after receiving the scan results.

Taylor's primary oncologist was Lisa McGregor, MD, PhD. "When she got here, we found that not only



PHOTOS BY PETER BARTA

Wearing the St. Jude tie he received from his grandfather, Chris Dempsey shares a laugh with Taylor in a play area at St. Jude.





Lisa McGregor, MD, PhD, examines Taylor during a recent visit to the hospital. The 4-year-old returns to the hospital every three months for routine checkups.

did she have the kidney tumor, but it extended upward into the inferior vena cava (the large vein that carries deoxygenated blood from the lower half of the body into the heart), and also she had disease in her lungs,” McGregor says.

Since the tumor had spread to her lungs, Taylor had what is called stage IV Wilms tumor.

The Dempseys were told the mass in Taylor’s lungs could be removed with surgery, but that the tumor in her kidney would have to be shrunk with chemotherapy treatment. Based on the way the tumor looked in the microscope, it was classified as favorable.

“We can point to that Friday afternoon when we got the news as being the absolute worst time in our entire lives,” Chris says. “We went home that weekend and had to explain to Micah and Morgan that their little sister had cancer. They couldn’t believe it. They had known people who have had cancer, but it was always adults, never children.”

The Cheetos connection

The tumor in Taylor’s lungs was successfully removed by St. Jude surgeons, and as she recovered in a hospital bed in the Patient Care Center, her personality began to brighten once again.

When asked one afternoon what she would like to eat, Taylor said “Cheetos,” and then requested that everyone entering her room call her by the same moniker.

“From that point on, every nurse who would come in would look at her bracelet and say, ‘Hello, Cheeto,’” Chris says.

While Taylor was going through four weeks of chemotherapy to shrink the tumor after her first surgery, it was commonplace to hear on the hospital intercom, “Cheeto Dempsey to the Medicine Room; Cheeto Dempsey to the Medicine Room,” Monica says.

A month after the initial surgery, physicians successfully removed the tumor in Taylor’s abdomen, and she continued with chemotherapy and radiation treatments to ensure the cancer cells were gone.

“We would have sold everything to save Taylor’s life, but St. Jude didn’t ask us to do that. Though we never received a bill from St. Jude, we feel a tremendous debt to the hospital that helped save her life.”

Celebrating together

In February 2007, the Dempseys received the good news: Taylor was cancer free and would no longer have to undergo chemotherapy, which was celebrated with the traditional “No Mo’ Chemo” celebration at the hospital. With family, friends and St. Jude staff cheering amid a shower of confetti, the 4-year-old enjoyed the experience without quite comprehending what it meant.

Taylor was extremely proud of the T-shirt that came with the event, Monica jokes. “She wore that T-shirt for weeks on end. She wore it to bed

and during the day,” Monica says. “She thought it was the best T-shirt she had ever had.”

Taylor now visits St. Jude every three months for routine check-ups.

“Everybody at St. Jude always welcomed her with open arms, begged for her hugs and couldn’t wait to see her,” Monica says. “They miss her now because we don’t go back very often. It’s like a celebration every time she has a check up.”

Following each checkup, the Dempseys fill out a form provided by St. Jude. “On that sheet of paper, there are several medical terms,” Chris says. “But we look for the part that says, ‘No sign of recurring cancer.’ That’s the sentence we look for.”

Hooked on St. Jude

Chris and Monica have each spoken at St. Jude events to let others know Taylor’s story and to give back to the hospital that was so gracious to them in their time of utmost need.

“We would have sold everything to save Taylor’s life, but St. Jude didn’t ask us to do that,” Chris says. “Though we never received a bill from St. Jude, both of us feel a tremendous debt to the hospital that helped save her life. Anything we can do to help serve the hospital is something that we want to do.”

Chris reflects on his grandfather’s contributions to the hospital, tells the story about the necktie and also speaks about Taylor when he gives a speech on behalf of the hospital. He admits there is a unique, cyclical nature to Taylor’s illness and her treatment at St. Jude.

“I had one of those experiences when the hair on the back of your neck stands up,” Chris says, referring to a morning when he was getting dressed for church during Taylor’s treatment. “I had that moment where I reached for my tie, and I realized that my grandfather had helped save the life of his great-granddaughter, whom he had never met.” ●

A Closer Look

BY ELIZABETH JANE WALKER

A new electron microscope gives scientists a glimpse into the heart of childhood catastrophic disease.

In the semi-darkness, Sharon Frase peers into what looks like a massive periscope. Computer screens spring to life as she literally gazes deep into the heart of a cancer cell to reveal its inner workings. "Here are the mitochondria," she explains, pointing to the organelle that is the cell's energy source. "This is the nucleus where all of the genetic information is stored." It's difficult to comprehend that these spectacular images originate in a nearly invisible speck of tissue that has been placed on a Lilliputian grid and tucked deep inside a transmission electron microscope.

The instrument that created these images will help scientists at St. Jude Children's Research Hospital better understand cancer and other diseases. Capable of magnifying an object 700,000 times, the hospital's new electron microscope enables investigators to see things they could not see before.

"This technology will allow us to get a better look at cancer and better understand how it grows and spreads and responds to therapy," says Michael Dyer, PhD, Developmental Neurobiology. By comparing images derived from an electron microscope, Dyer and his colleagues have learned how the eye cancer retinoblastoma spreads. "Using the electron microscope, we learned how the cancer cells break away from the tumor and begin to spread throughout the body," he says. "This may allow us to develop new therapies to stop retinoblastoma metastasis."

ANN-MARGARET HEDGES



"This technology will allow us to get a better look at cancer and better understand how it grows and spreads and responds to therapy."

An electron microscope uses a beam of electrons to produce highly detailed images that reveal a specimen's structure and composition. The new instrument, one of only 200 of its type in the world, is the centerpiece of a recent expansion of cellular imaging at St. Jude. Nearly twice as powerful as the hospital's other electron microscope, the 200kV model offers many innovative

features, such as the capacity to provide 3D views. "This scope is like nothing I have ever used in my 35 years of electron microscopy," Frase explains. "It's so sensitive that your voice can disrupt the images."

Preparing specimens for imaging is a tedious and time-consuming process that demands knowledge, patience and a steady hand. The lab's technicians can provide the imaging service or can teach interested faculty, postdoctoral fellows and other scientists how to use the equipment.

Frase, director of the electron microscopy center, pulls out a small block of epoxy resin, in which has been embedded what appears to be a fleck of pepper. "This is a piece of tumor," she says. A technician uses a diamond knife to cut the specimen into whisper-thin slices, manipulating the sections with a brush consisting of a single hair. Sections are placed on tiny copper grids and stained with heavy metals before being loaded into the microscope.

The new electron microscopy center is one more example of how the hospital constantly improves its research capabilities. St. Jude Scientific Director, James Downing, MD, spearheaded the effort to expand the facility, an initiative that is sure to yield scientific discoveries that will save lives. "Our goal is to be the best in the world," Frase says. "St. Jude wants to have everything available that a researcher needs to find cures for devastating childhood illness. That's the bottom line, and that's what St. Jude has done by installing this facility. I feel fortunate to be a part of it."●



Safe and Sound

Some of the most successful cancer-fighting drugs also cause hearing loss in children. In addition to saving lives, St. Jude is actively seeking ways to reduce such side effects.

BY MIKE O'KELLY

Five-year-old Alex Moore waits intently inside a soundproofed booth in the Rehabilitation Services department at St. Jude Children's Research Hospital. As a faint, fleeting "beep" sounds in his left ear, he hurls a toy block in the direction of St. Jude audiologist Johnnie Bass, who monitors an audiometer outside of the booth.

Ricky and Lindsay Moore watch as their son undergoes conditioned play audiometry, a modified version of the standard hearing test used for younger patients. When Alex hears a beep, he throws a block. The process is repeated at gradually higher frequencies.

When he was 3 months old, Alex began undergoing treatment for the eye cancer retinoblastoma. As a result of his exposure to the chemotherapy drug carboplatin, Alex suffered ototoxicity, or hearing loss.

"Learning Alex had suffered hearing loss was almost as surprising to me as his initial diagnosis," Lindsay says. "Although we knew it was a possibility, it was not common." Alex has moderate-to-severe, high frequency hearing loss in both ears.

"He's wearing hearing aids in both ears, and he has adjusted well," Ricky adds.

Scientists at St. Jude are interested in learning what causes such problems. An answer could one day help clinicians offset the hearing loss that occurs in children as a result of treatment with cancer-fighting drugs such as carboplatin and cisplatin.

Catching the wave

As sound waves race into the inner ear at hundreds of miles per hour, their energy generates waves in the fluid-filled part of the inner ear. Within that fluid are rod-shaped cells covered with hair-like cilia. The energy from sound waves causes the hair cell cilia to swing back and forth quickly in a steady rhythm. When the sensory hair cells are damaged in non-mammals, such as fish, chicken and birds, the cells can be regenerated. But when hair cells are damaged in humans, the opposite is true. That causes permanent problems for children whose hearing is damaged during cancer treatment.

Jian Zuo, PhD, of St. Jude Developmental

Five-year-old Alex Moore participates in a hearing test at St. Jude.

Jian Zuo, PhD, oversees the work of graduate student Katie Steigelman and international research scholar Yiling Yu.

Neurobiology, and his team of researchers are comparing the regeneration of hair cells in non-mammals with what happens in the mammalian ear. “When a non-mammal’s sensory, mechanical neurons are destroyed because of ototoxic damage, they are able to regenerate hair cells,” Zuo says. “We are trying to determine how you can make a mammal regenerate hair cells after damage.”

Researchers are trying to determine how the delicate cell system in the ear actually hears sound. Humans and other mammals can detect extremely small vibrations of sound, with a minimum range of one nanometer in amplitude. Most humans do not consciously detect such a faint sound, but the hair cells inside the ear respond with movement.

“It’s quite remarkable that all mammals can distinguish low-frequency and high-frequency sounds,” Zuo says. “The sound can range in magnitude from very low-zero decibels, like a whisper on a quiet, summer night—to 120 decibels—that’s as loud as an airplane taking off.”

In mammals, the rod-shaped body of the hair cell contracts and then vibrates in response to sound waves, amplifying the sound. While both mammals and non-mammals have cilia on their hair cells, only mammals’ hair cells have prestin, a protein motor that drives this cellular contraction.

According to Zuo, when hearing loss occurs, damage is done to the mechanical, sensory neurons in the cochlea, the small organ in the inner ear.

Pinpointing damage

Because of toxicity issues with the chemotherapy drug cisplatin, physicians sometimes use carboplatin as an alternative. But carboplatin may also cause hearing problems.

“Some laboratory studies have shown that carboplatin has caused damage to the outer hair cells of the cochlea, while other studies have shown damage to inner hair cells only and no damage to the outer hair cells,” Bass says.

Outer hair cells receive neural input from the brain, while inner hair cells send neural signals to the brain.

For the past two years, St. Jude has partnered with the University of Memphis in a study concerning sounds produced by healthy ears in response to acoustic

stimulation. The protocol enrolls children with the eye cancer retinoblastoma who are receiving carboplatin.

The procedure involves putting a probe with a soft tip into the child’s ear. A sound stimulates the ear, and the probe measures return vibrations from the hair cells. A decrease in these levels often indicates permanent damage to those cells. St. Jude staff will compare measurements of outer hair cell function and inner hair cell function in patients receiving carboplatin. Clinicians will use that information to determine if changes in cochlear function occur and if damage is occurring to one or both hair cells.

“This will help us come up with better intervention, management and treatment of these patients if they do experience hearing loss because we’ll know better about where the damage is occurring,” Bass says.

Now hear this

To obtain a better understanding of how the entire hearing process works, Zuo’s team is manipulating particular proteins in cells to explain how a specific gene

or cell contributes to the process. When investigators inactivated the protein prestin, Zuo found that the entire hearing process was disrupted.

Recent work by Zuo’s team involves the manipulation of genes in the hair cells. Results on the retinoblastoma gene have indicated that when the hair cells reenter the cell cycle, they cannot complete it and they die. Zuo and

his colleagues are now targeting surrounding cells with the aim of regenerating new cells.

“We hope that further genetic manipulation of genes in those cells would give those cells the ability to reenter the cell cycle and start to proliferate, then try to differentiate into new hair cells—just like they do in birds and fish,” Zuo explains.

Bass says the main goal of the study is to detect hearing loss as early as possible. “Our question was, ‘Can we catch damage before it even shows up as hearing loss?’” Bass says.

While stopping chemotherapy might not be an option, counseling the family about the child’s risk for developing future hearing loss could be helpful. Clinicians will warn Alex Moore’s parents about the dangers of exposure to loud noises or taking other medications that might cause further hearing deficit.

“We’re using all the information that we’re gathering to understand where hearing loss is occurring, how early it is occurring and how we can catch it early,” Bass says. “The outcome of that is being able to counsel patients better and communicate with physicians our concerns with hearing, especially in visually impaired patients.”●

“Our question was, ‘Can we catch damage before it even shows up as hearing loss?’”

Perspective

Saving Lives

"I am involved in saving animal lives because of my passion for wildlife, but I am just as involved in saving human lives."

BY JACK HANNA

At age 2, Julie Hanna began treatment for leukemia at St. Jude. Today, she and her dad, Jack Hanna, travel the world as part of their involvement in the TV series *Jack Hanna's Into the Wild*. "Without St. Jude, Julie would not be here. We owe her life to St. Jude, and we will be eternally grateful," Jack says.



In 1977 my wife, Suzi, and I noticed that our 2-year-old daughter, Julie, was not acting like herself. We took her to a doctor, who said, "Your daughter has leukemia. You need to get to St. Jude Children's Research Hospital very quickly."

Suzi stayed at St. Jude with Julie while I traveled back and forth to work at the zoo and to take care of our other daughters, Kathaleen and Suzanne.

At the hospital, one of the hardest things for me was to meet kids who were not there when I returned. Seeing those parents lose their little children, I told myself I would always help St. Jude.

Hospital founder Danny Thomas once visited Julie when she wasn't doing well. She had staph infection, pneumonia and leukemia—not a good combination. As long as I live, I'll never forget what Danny told me. He said, "You know, Jack, the greatest day in the world would be when we wouldn't have to have this hospital. That means there would no longer be a need for it, because we had found a cure."

In 1995, Julie had a massive brain tumor, which led to brain surgery and a long recovery. The odds were low that anyone who went through that would graduate from college. But Julie returned to college and finished her degree. It was a great feat.

When I help raise money around the country for St. Jude, I often hear people say, "St. Jude is great, but we don't have to do much any more because there's a cure for leukemia." I tell them, "Until the oldest living survivor of childhood cancer lives

a normal life, we have to keep working."

I am involved in saving animal lives because of my passion for wildlife, but I am just as involved in saving human lives. Last year, I helped David Karam with a St. Jude fundraiser at the Columbus Zoo. A son of the late S. Robert Davis came up to me and said, "I want to give you a check." He handed me \$100,000 for the hospital. It was one of the greatest evenings in my life.

Today, Julie is a beautiful 32-year-old. She works at the Columbus Zoo in the Promotions Department and takes our animals to national TV show appearances. Because of what has happened to her, her love for other people and children is beyond measure. She has this caring nature, and it carries over to her work with the animals.

I spend about 240 days a year traveling the world, and I take Julie everywhere I can—places like Africa, Australia, Europe. I remember those young parents back in 1977 who no longer have their children, and I think about what they would give to have their children with them today.

My family truly understands what it means to have your health. Without St. Jude, Julie would not be here. We owe her life to St. Jude, and we will be eternally grateful—it's that simple. ●

The Columbus Zoo's director emeritus, Jack Hanna is host of Jack Hanna's Into the Wild, a nationally syndicated TV series.



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PETER BARTA

Recording star Jewel visits with patient Amanda Jones during the 19th annual Country Cares for St. Jude Kids® radio training seminar in January. During the seminar, country music artists and radio station personnel toured the hospital, met patients and learned how to plan successful radiothons. Country Cares for St. Jude Kids® has raised more than \$315 million since its inception.


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