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The Battle
to Rebuild

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For father and son, the battlefields were different; the challenges were similar.

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A large, vertical, rectangular image with a dark blue and purple color palette. It shows a microscopic view of cells, with several large, irregularly shaped cells visible. The cells have a granular texture and some have prominent nuclei. The background is a deep blue with some lighter, hazy areas. In the bottom right corner, the number '16' is printed in a large, white, sans-serif font.

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On the cover: photo by Ann-Margaret Hedges.

Highlights

Drug combo shows promise

Oncologists frequently use combinations of chemotherapy drugs as a knockout punch against tumors. The strategy has proven successful because it aims to fight cancers more effectively than the individual drugs could alone. St. Jude researchers have reported initial trials of a new drug combination that promises to be a similar treatment for childhood cancers. The initial trials of the drug combination of oxaliplatin and etoposide showed that the combination caused few side effects.

“We saw evidence that the treatment was working in the patients with brain tumors,” said Lisa McGregor, MD, PhD, Oncology, the study’s first author. “One patient with recurrent medulloblastoma had his tumor shrink away, and one patient with pineoblastoma showed significant tumor shrinkage.”

A report on this work appeared in the journal *Cancer* in February 2009.

Dyer receives prestigious award

Michael Dyer, PhD, of St. Jude Developmental Neurobiology, has been selected as a Howard Hughes Medical Institute (HHMI) Early Career Scientist. Dyer is one of 50 scientists selected nationwide for the 2009 HHMI Early Career Scientist program, a competition recognizing outstanding scientists who have demonstrated originality and productivity during the earliest stages of their careers and who show exceptional promise for future research contributions.

“Dr. Dyer is one of our rising stars, and his selection for funding by HHMI is well-earned recognition,” said Dr. William E. Evans, St. Jude director and CEO. “This new funding will allow him to accelerate his research to identify novel targets that will lead to more effective treatments for childhood cancers.”

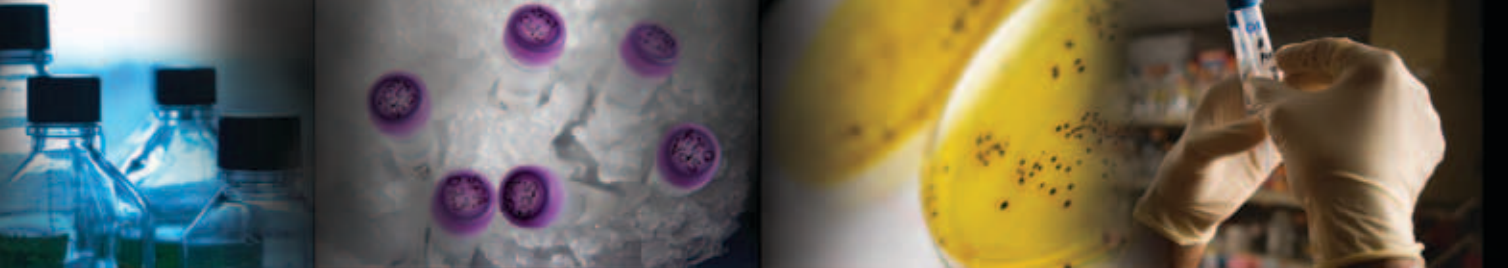
New insights into p53

The p53 protein plays an important role in protecting the body from cancer. This protein is constantly poised to detect potentially tumor-causing DNA damage. When it detects such abnormalities, p53 either arrests cell proliferation or triggers a lethal cell suicide program that rids the body of the malignant cell before it can divide.

St. Jude researchers have discovered important new details about the proteins that control this process. The basic studies could yield treatments that trigger suicide in a broad range of cancer cells.

The studies, led by Richard Kriwacki, PhD, of Structural Biology, explored the function of a key p53 activator. This protein, called p14^{Arf}, was originally discovered in 1995 by Charles Sherr, MD, PhD, a Howard Hughes Medical Institute Investigator and co-chair of St. Jude Genetics and Tumor Cell Biology. Results of Kriwacki’s recent studies were reported in the *Journal of Molecular Biology*.

The p53 machinery is so critical that its breakdown figures in more than half of all cancers.



Learning about chromosomal segregation

Every cell in the body arises from the process of cell division—an intricate molecular process in which a cell precisely copies its gene-containing chromosomes and segregates them into identical parcels that migrate into the two new daughter cells. Malfunction of this process can have profound consequences. The action point in regulating chromosomal segregation is called the centromere.

Janet Partridge, PhD, Biochemistry, and her colleagues are probing the details of centromeres using the yeast strain called *S. pombe*. In their latest work, the researchers have added a significant piece to the biological puzzle that is the centromeric machinery. The scientists published their findings in the journal *Molecular Cell* in April 2009.

“We don’t fully understand the cause-and-effect of how chromosome mis-segregation can contribute to tumor formation because we don’t know enough about the basic mechanics of how chromosomes segregate normally,” said Partridge, the study’s senior author. “But if we can learn how it should work in simple organisms like yeast, and then extrapolate those findings to mammalian cells, it could give us a handle on where to look for the genes that might be mutated in these abnormal cells to drive tumor formation.”

PETER BARTA



Cool science

Through many of its outreach and community education events, St. Jude fosters an interest in science in young people. During a science fair organized this spring by the hospital’s research technologists, Teresa Shakespeare, PhD, of Genetics and Tumor Cell Biology, and eighth-grader Anthony Vaughn II of the St. Jude Adopt-A-School, Bellevue Middle School, observed the extraction of DNA from epithelial cheek cells.

ALL team receives national recognition

St. Jude scientists who represent the interdisciplinary team studying acute lymphoblastic leukemia (ALL) have been recognized by the American Association for Cancer Research with its Team Science Award.

The award acknowledges the importance of interdisciplinary teams to the understanding of cancer and/or the translation of research discoveries into clinical cancer applications.

“The impressive accomplishments of this team have only been possible because they are an extremely interactive, innovative and multidisciplinary translational research team,” said Michael Kastan, MD, PhD, St. Jude Comprehensive Cancer Center director. “Through their teamwork and treatment protocols, they have advanced cure rates in ALL to unsurpassed levels.”

The team includes Dario Campana, MD, PhD, Oncology; Cheng Cheng, PhD, Biostatistics; James Downing, MD, scientific director; William E. Evans, PharmD, St. Jude director and CEO; Melissa Hudson, MD, Oncology; Sima Jeha, MD, Oncology; Charles Mullighan, MD, Pathology; Ching-Hon Pui, MD, Oncology chair; Susana Raimondi, PhD, Pathology; Mary Relling, PharmD, Pharmaceutical Sciences chair; and Raul Ribeiro, MD, Oncology.

Highlights

Spotlight on survivors

In a new study of adults who survived cancer as children, St. Jude researchers have found that many survivors lead sedentary lifestyles and are more likely to be less physically active than their siblings. The study's results appear in the journal *Cancer*, May 2009.

Childhood cancer survivors are at greater risk of obesity, diabetes and heart disease than the rest of the population. "Physical activity is a key step that survivors can take to reduce the health risk of these effects," said Kiri Ness, PhD, Epidemiology and Cancer Control, the study's first author.

The investigators are launching follow-up studies to explore whether energy metabolism in cancer survivors affects their ability to benefit from exercise. Ness and her colleagues also plan to investigate whether programs to encourage exercise can help cancer survivors avoid many of these health problems.

Discovery may improve brain tumor prognosis

A team of researchers have discovered that a set of genetic abnormalities related to a specific cell signaling pathway initiate and drive pilocytic astrocytomas, a common brain tumor most often found in the cerebellum.

A report on this work appears in *The Journal of Pathology* in June 2009.

In the study, scientists analyzed low-grade astrocytomas from 50 patients, searching for common genetic changes. The findings confirmed in pilocytic astrocytomas a high frequency of gene fusions involving *BRAF*, a gene thought to trigger cancer. Another fusion event involved a related gene called *RAF1*. All of the pilocytic astrocytomas tested contained either one of those fusions or a mutation in a gene called *KRAS*, also known to be linked with cancer. These genetic changes permanently activate the MAPK molecular pathway, allowing cells to multiply uncontrollably.

The research could have important therapeutic implications. Drugs specifically inhibiting the MAPK pathway are now being tested in various cancers, such as malignant melanomas.

"Our more detailed molecular understanding of pilocytic astrocytomas will also be useful in diagnosis, enabling pathologists to use genetic tests to distinguish among different types of childhood brain tumors to guide better treatment decisions," said David Ellison, MD, PhD, St. Jude Pathology chair, and the study's co-corresponding author.

JUSTIN VENEMAN



Sharing research

More than 285 postdoctoral fellows from 45 countries are being trained in pediatric-based research or clinical care at St. Jude. The trainees learn from clinical and basic science investigators who work together in the same setting where children benefit from their research. Clinicians work closely with researchers to translate scientific discoveries into improved therapies. Samantha Cicero, PhD, Developmental Neurobiology, explains her poster presentation at the 2009 Postdoctoral Fellow Appreciation Poster Session held this spring in the Danny Thomas/ALSAC Pavilion. The event allowed postdoctoral fellows to showcase their work and learn about the research of their peers.

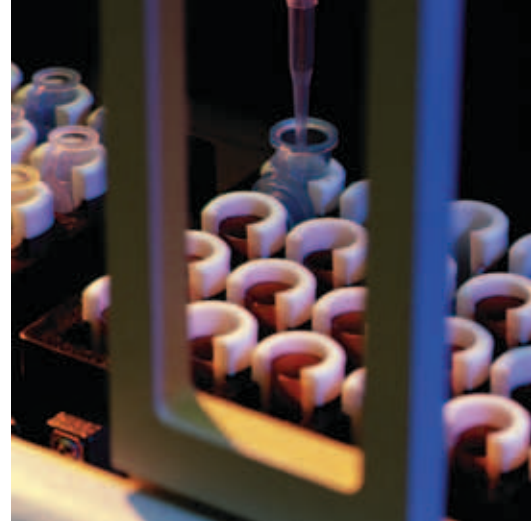
Taming dangerous lung inflammation

One of the most threatening complications of influenza stems not from the virus itself, but from the overreaction of the immune system. A group of researchers has uncovered new clues that could lead to drugs to suppress influenza-triggered inflammation. A key target of exploration is a protein complex called the cryopyrin inflammasome, which switches on an enzyme called caspase-1; this, in turn, activates other proteins called cytokines that launch the innate immune response.

“Our findings about the role of cryopyrin inflammasome show that these molecules could be important targets for drugs or vaccines to treat the complications of influenza,” said the study’s senior author, Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology.

The scientists reported the findings in the journal *Immunity* in April 2009. The findings may also have implications for such disorders as rheumatoid arthritis and Crohn’s disease.

For more information about influenza research at St. Jude, turn to page 6 of this issue.



New insights into engineering immune cells

Immunologists have made great strides in enlisting the body’s own immune cells to fight cancers and infections. These scientists have developed techniques to extract so-called killer T cells from the blood, re-engineer them by providing new T cell receptors that allow them to target tumors or microbes, and re-introduce them into the body.

Now, St. Jude researchers led by Terrence Geiger, MD, PhD, Pathology, have developed a new technique to enhance target recognition by the therapeutic T cells; modifications of their T cell receptors can dramatically boost target recognition. The scientists also discovered subtle side effects of such T cell engineering that they say raise questions in the field. Even small changes in the T cell receptor that targets T cells against cancer or other cell types can in some circumstances also aim it at brand new targets, including the body’s own tissues. Thus, although T cell engineering remains highly promising, such immunotherapies must be extensively tested to avoid hitting the wrong targets.

Geiger and his colleagues published an article on this topic in *The Journal of Immunology* in April 2009.

ICU wins prestigious national award

Nurses and staff in the St. Jude Intensive Care Unit (ICU) have been recognized by the American Association of Critical-Care Nurses (AACN) with the Beacon Award for Critical Care Excellence. The award salutes the nation’s top adult critical care, pediatric critical care and progressive care units.

The St. Jude ICU is fully dedicated to acute-phase care of the pediatric oncologic and/or post-hematopoietic stem cell transplant population, making it the only one of its kind in the country. Less than 3 percent of the estimated 6,000 ICUs in the United States have been given the Beacon Award.

Scientists identify crucial eye cells

St. Jude investigators recently discovered that eye cells many scientists believed were retinal stem cells are, in fact, normal adult cells. If retinal stem cells could be obtained, they might provide the basis for treatments to restore sight to millions of people with blindness caused by retinal degeneration.

The new findings suggest that research on cell therapies to restore blindness should not concentrate on the eye cells previously believed to be retinal stem cells. More promising, the scientists said, is research aimed at re-engineering stem cells to develop into the light-sensitive photoreceptor cells that are lost as a result of retinal degeneration. Such studies could lead to implantation of such engineered photoreceptor cells into the eye to restore sight.

Led by Michael Dyer, PhD, Developmental Neurobiology, the team published their findings in *Proceedings of the National Academy of Sciences*, March 2009.

Keeping WATCH

BY SUMMER FREEMAN

As home to the only World Health Organization collaborating center focusing on the transmission of animal influenza viruses to humans, St. Jude is closely monitoring the H1N1 pandemic.



In late April 2009, a mounting threat moved swiftly through communities worldwide. Newspaper headlines and 24-hour cable news anchors speculated about problems of pandemic proportion. Each day, the World Health Organization (WHO) added dots to a map, signifying the menacing spread of influenza A (H1N1), originally called swine flu.

The St. Jude Children's Research Hospital Infectious Diseases department has a long and storied history with influenza research. For faculty and staff in that department, it seemed that the moment they had been preparing for had come.

"In the beginning stages, there were more things that we didn't know about this virus than what we did know," says Richard Webby, PhD, director of the WHO laboratory at St. Jude. "We have not seen this particular combination of genes in the same virus."

Seeking answers

At the pandemic's start, St. Jude received samples of the virus for testing from the Centers for Disease Control and Prevention (CDC). At press time, the WHO states that more than 94,500 cases of H1N1 infection have been reported worldwide,

including 429 deaths. Thus far the virus, although contagious, typically does not cause severe illness and manifests as a mild case of the flu. Symptoms are similar to regular human flu and include fever, cough, sore throat, body aches, headache, chills and fatigue.

While there is a sense of relief that the H1N1 strain is not as virulent as some influenza virus outbreaks of the past century, St. Jude researchers are as busy as ever. A team of 50 St. Jude faculty and staff, specializing in different areas of study, have assembled to investigate the new strain.

Top: Richard Webby, PhD, (center) is director of the World Health Organization's Collaborating Center for Studies on the Ecology of Influenza Viruses in Lower Animals and Birds—the only such laboratory in the world.

Bottom: Jon McCullers, MD, of Infectious Diseases, speaks to media during a press conference about the H1N1 pandemic.

The virus' emergence raises many questions that have yet to be answered. And the size of the threat H1N1 poses cannot be determined yet. By their very nature, viruses are crafty organisms, ever changing and evolving. Scientists agree that of the many unknowns, perhaps the biggest is how deadly H1N1 could become.

"With the H1N1 swine influenza spreading, we are in a situation where we must prepare with maximum urgency for the worst-case scenario—keeping in mind that the virus may wither and wane by this fall and become a wimp or become a monster," says Robert Webster, PhD, who holds the hospital's Rose Marie Thomas Chair in Infectious Diseases.

Drawing on experience

St. Jude, home to some of the world's most renowned scientists studying infectious diseases, is one of the five WHO collaborating centers across the world and the only one that focuses solely on the transmission of animal viruses to humans. In 2007, St. Jude was named one of six Centers of Excellence for Influenza Research and Surveillance funded by the National Institute of Allergy and Infectious Diseases, a part of the National Institutes of Health.

Along with its work in monitoring the highly virulent H5N1 strain, as well as studying influenza pandemics of the past, St. Jude has researched H1N1 strains for years.

"We know the biology of this group of viruses," Webby says. "At least one of the parents of this virus has unique characteristics and has done exceptionally well in terms of adapting and growing in swine, and now it's doing the same thing in humans."

Influenza viruses are seemingly simple organisms—segments of RNA, enclosed in protein capsules surrounded by a globular envelope of proteins. The uncomplicated structure makes it especially flexible and able to mutate as it moves from host to host. This constant evolution is why scientists have to create new vaccines for human flu every winter.

Given the opportunity and time, some flu viruses learn to hop from one species to another—and that's where the scenario becomes more complicated.

"There is an enormous diversity of influenza viruses of all shapes and all different flavors," Webby says. "When viruses get into hosts, such as humans, pigs and certain birds, they evolve along with these hosts, picking up genetic signatures. We can look at an influenza virus and, through genetic sequencing, determine what hosts that virus came out of."

Looking back, planning ahead

Four main influenza type A virus subtypes have been isolated in pigs: H1N1, H1N2, H3N2 and H3N1. The current H1N1 outbreak combines strains of human, avian and swine flu, with pigs serving as the mixing vessel for the viruses.

The most deadly outbreak caused by an influenza virus was the 1918 pandemic of Spanish flu, which killed more than 40 million people worldwide, about 2.5 percent of Earth's population at the time.

St. Jude researchers have long looked at past outbreaks to understand the factors that contribute to influenza's spread and severity as well as to sequence the viruses'

genomes to identify the mutations that can signal pandemics.

At the first signs of the current outbreak, scientists were tempted to draw parallels between the 1918 pandemic and the most recent H1N1 infections. In both cases, the virus strikes healthy, younger groups rather than older populations who are normally at risk for the flu. Timing of the two viruses is also worrying. Both surfaced in the spring, rather than during the winter, when flu viruses usually thrive. The 1918 strain, like the new H1N1 virus, originally manifested with mild sickness, but returned in the fall with a vengeance.

Webby believes it is too early to speculate on a repeat performance. "There is nothing yet to suggest that this would do the same," he says. "And there is nothing yet to suggest that it would do anything different."

The race for researchers now is to find answers.

"We are continuing to monitor these strains to see if there is any evidence of them changing," Webby says. "We are becoming particularly interested in the virus' epidemiology. It looks like there is pre-existing immunity within the human population and particularity in older people. The older population has had more exposure to the H1 viruses. This one virus has a cousin in the human population now."

St. Jude scientists are working on genome sequencing for the virus and vaccine development. They are also researching the effectiveness of seasonal vaccines and are continuing their surveillance of the disease's spread.

"It is coming up to the winter season in the Southern Hemisphere," Webby says. "H1N1 is exploding through Australia, and we'll be able to get a better feel for what it's going to do in the next few months." ●

Scholastic Helps Kids Do the



Scholastic Inc. teams with Math-A-Thon to reinforce crucial math skills while helping children raise funds for St. Jude.

BY JOE HANNA

For 30 years, the St. Jude Children's Research Hospital Math-A-Thon® program has successfully helped children improve their math skills and helped raise millions of dollars in the fight against childhood cancer.

But now Math-A-Thon can do even more—not only to help the children of St. Jude, but also to help a new generation of students develop the critical math skills they will need in their adult lives.

How do you improve on such a good thing? By joining forces with

the most trusted name in learning.

St. Jude recently announced that Scholastic Inc. has teamed with Math-A-Thon to elevate the educational and fundraising program to a new and exciting level for the 2009–10 school year. For decades, teachers and school administrators nationwide have relied on Scholastic for quality educational tools and trusted resources.

"Each year, the money raised by Math-A-Thon helps St. Jude doctors and researchers as they work to unlock the mysteries of

childhood cancer and other deadly diseases," said David L. McKee, chief operating officer and interim CEO of ALSAC, the fundraising organization for St. Jude. "We are thrilled to partner with Scholastic, a company that shares our focus on improving the lives of children. With Scholastic's help, the Math-A-Thon program will reach new levels as an educational tool for teachers and a fundraising tool for St. Jude."

Under the direction of Scholastic, the Math-A-Thon Funbook features a new curriculum of math activities to meet national standards in education and challenge today's K–8 students with age-appropriate math problems. The work the students will do as part of Math-A-Thon will also involve subjects that must be covered before students

leave particular grade levels. The subjects are broken down into focal points, which will be covered in the new Funbook.

The new addition expands the benefits of the Math-A-Thon program from the St. Jude campus to the classroom to school districts themselves. Not only does the new Funbook allow students to raise funds for St. Jude while practicing their math skills, but it also helps them prepare for the standardized tests that are held toward the end of the school year.

"Scholastic is delighted to partner with St. Jude on their Math-A-Thon program," said Jennifer Prescott, Scholastic professional media editorial director of Custom Media. "Our team of expert curriculum developers is inspired by the opportunity to deliver quality, standards-based activities that will help thousands of students build and practice essential math skills, while helping to raise critical funds for the patients of St. Jude."

More than 10,000 schools and 300,000 students across the country take part in Math-A-Thon each year. To participate, students obtain donations by asking family and friends for pledges to solve math problems in the Math-A-Thon Funbook. All donations benefit St. Jude. ●

To learn more about this new chapter in the Math-A-Thon program, visit www.mathathon.org or call (800) FUNBOOK.



Blessed To Be a Blessing

One couple's legacy benefits the children of St. Jude.

BY JANICE HILL

Esther and Norman “Chad” Chadwick were never blessed with children of their own, but the late couple continues to bless children around the world through their legacy to St. Jude Children’s Research Hospital.

Esther’s decision to leave a portion of their estate to St. Jude has generated more than \$7 million for brain tumor research, the neuro-oncology clinic and the Child Life program. Esther, who died in July 2007, was preceded in death by her husband approximately 20 years earlier.

“One of the amazing things about her gift is that she made it without ever seeing the hospital and without having a personal connection—no family member had cancer as a child,” says Marisa Intile, Esther’s niece. “But she read extensively, and she knew St. Jude was a wonderful charity.”

As co-executor of the Chadwick’s estate, Intile toured the hospital her aunt was never able to visit.

“Seeing the children’s faces, the size and extent of the hospital and the cheerfulness of the hospital is life changing,” Intile says. “You can actually see the hope—it’s clear the patients feel it, the families feel it, and the staff is devoted to it.”

Because Intile and co-executor Ida Tufo had both lost family members to brain cancer, they decided that the largest portion of the Chadwicks’ gift would support brain tumor research and care. Intile’s father passed away 32 years ago, and Tufo lost a son five years ago. The



JUSTIN VENEMAN

A gift by Esther and Norman Chadwick (at right) benefits children such as Yun Jin Lee (pictured with Child Life Specialist Clare Grode during a recent Child Life activity). The Chadwicks’ gift benefits the hospital’s brain tumor research and neuro-oncology clinic as well as the Child Life program.



co-executors also earmarked \$1 million of the estate to serve as a matching gift challenge for St. Jude donors.

Although the Chadwicks’ gift was remarkable, the couple came from humble beginnings. One of seven children born to Italian immigrants, Esther followed her dream of a career in New York and became an executive assistant for Avon Products Inc. There she met Chad, who had begun working in the company’s mail room at age 15. He attended night school; after a stint in the military, he worked his way up to become executive vice president of Avon’s sales and marketing.

“Uncle Chad was very smart, but he was always interested in others and made everyone feel at ease,” Intile recalls. “Aunt Esther was a beautiful, meticulous, well-read woman who loved to travel with Uncle Chad.”

Esther’s many interests in later life included the children of St. Jude. “She would often say, ‘I got a letter from Marlo’ and would tell us about it. And when she received a video about St. Jude, she would pass it around the family,” Intile says.

“I would love to be able to sit down and tell Aunt Esther what I saw at St. Jude,” Intile continues. “Everything there is made possible because so many give out of the goodness of their hearts. I came away with a renewed belief in the genuine goodness of people and what they can achieve.”

To learn more about making a legacy gift to St. Jude, call (800) 395-1087 or e-mail giftplanning@stjude.org. ●

The Battle to

Lance Fletcher and his dad fought a war on two fronts. Now that their family is reunited and Lance's osteosarcoma is in remission, the Fletchers concentrate on constructing a future.

BY ELIZABETH JANE WALKER

When Joe Fletcher left home to serve his country in Afghanistan, he knew all too well that he would be living in a dangerous environment far from his wife, Carol, and his children, Lindsey and Lance. But never in his wildest dreams did Joe envision that his son would soon be waging his own private war.

After having served 18 years in the Army National Guard, the longtime school teacher had been unsurprised when his third deployment order arrived. This time, he would command a mentoring team that would provide training to the Afghan National Police.

Situated on a flat plain surrounded by craggy peaks, the terrain of Mazir-e-Sharif, Afghanistan, reminded Joe of the American West. But the comparisons ended there. Clad in 60 pounds of body armor, Joe traversed an alien landscape of unfamiliar customs, language and culture; a place where deadly explosive devices could lurk just beneath the dust and where many citizens lived in mud huts with dirt floors. When an explosion killed two members of another team in July of 2008, Joe pondered:

"I've always believed that the choices you make in life determine what happens in your future. At times though, I have to admit that there are times when life takes a detour that is beyond your control. Tragedy often strikes when we least expect it, whether it's a fatal accident two blocks from home or a chronic disease."

Ironically, more than 7,600 miles away, stealthy cancer cells were multiplying in the leg of Joe's 8-year-old son.



During breaks from treatment, Lance makes stop-motion animation films with characters and vehicles he has built. Joe Fletcher (below), now home from Afghanistan, assists his son with the projects' video aspects.

PETER BARTA



Trouble on the home front

At home in New Mexico, Lance was making the most of his summer vacation. He tossed balls with his cousins, attended church camp and played outside with his best friend, David. Occasionally, Lance mentioned an ache in his leg. Carol chalked it up to growing pains. After taking a mild pain reliever, Lance would drift off to sleep, dreaming of more summertime adventures.

The night before the family left for a trip to Pennsylvania, Carol noticed a swelling in Lance's left leg. She applied ice to the area and limited her son's activities for several days. "He's wrenched his knee or stretched

some ligaments," Carol thought, and made a mental note to visit the pediatrician upon their return home.

Two weeks later, an X-ray revealed the unthinkable—a mass above Lance's left knee. Carol immediately knew the diagnosis.

"We're dealing with osteosarcoma," she thought.

Most parents have never heard of the bone cancer called osteosarcoma, but the Fletchers were all too familiar with the disease. Long ago, Joe's 27-year-old sister had died of that kind of cancer, after receiving what Joe believed to be less-than-optimal care at a regional hospital.

Only a few hours after Lance's X-ray, doctors confirmed that he did, indeed, have osteosarcoma.

When the physician asked Carol where she would like to take her son for treatment, she named a medical facility in the region. "I chose that hospital because it was only two hours away from our home. But I wasn't at peace about my decision," Carol recalls.

Divided by miles, united in spirit

In Mazir-e-Sharif, Joe checked his e-mail and found a cryptic message from his wife. "Give me a call no matter what time it is," she wrote.

"I immediately knew something was wrong," he says.

As Joe talked with Carol, images of his sister and his beloved son rolled through his mind like tanks on a battlefield. "When you go to Afghanistan, you're mentally prepared that you may come back hurt or harmed," he says. "But you never expect something life threatening to happen to one of your kids. It's a devastating feeling."

Because of his sister's experience, Joe knew the importance of beginning treatment as quickly as possible. Like Carol, he was uncomfortable obtaining treatment at the local hospital. "I want the best for Lance," he said.

The couple immediately began researching osteosarcoma treatments online and through conversations with friends.

Carol first learned about St. Jude Children's Research Hospital through her aunt. The mother of one of Lance's classmates also told Carol about the hospital's new osteosarcoma study. But before the Fletchers could make a final decision, Carol knew she needed some quiet time.

"That weekend, I spent a lot of time in prayer," she says. "I asked for a bit of guidance and for the right doors to be opened."

The first thing Monday morning, Carol called the pediatrician's office and asked if Lance could obtain a referral to St. Jude. "I prayed, 'Lord, if this is not it, please close that door,'" Carol recalls. "And every door opened; everything went through. It was amazing."

The next morning, she and Lance were on a plane to Memphis, Tennessee.

When the duo walked through the doors of the St. Jude Patient Care Center, Carol breathed a sigh of relief. "Oh, we're gonna be OK," she thought. "Things are gonna be fine."

The best medicine

When Lance arrived at St. Jude, doctors immediately noticed a small spot on his lung. Sometimes lung scans show spots that indicate harmless scar tissue from past infections. But the physicians wanted to check out this spot. "Carol and I discussed whether we should let them

biopsy Lance's lung, because it was probably nothing," Joe recalls. Today, the Fletchers are relieved that they agreed to the biopsy. The cancer had, indeed, spread to that area. After the cancerous tissue was removed, Lance began treatment on a new protocol, or scientific treatment plan, led by St. Jude oncologist Najat Daw, MD.

"The outcome of patients with osteosarcoma has reached a plateau, and we need a novel strategy to improve it," Daw says. "We hope the new trial will help us increase survival rates for children with this disease."

The protocol combines standard chemotherapy with therapy designed to target the tumor's blood vessels and enhance the tumor-killing ability of the chemotherapy. Clinicians are studying whether a monoclonal antibody called bevacizumab inhibits a protein that stimulates blood vessel formation in osteosarcoma tumors. Bevacizumab has already been used in adult patients with cancer to improve the efficacy of standard chemotherapy.

As part of his treatment, Lance also underwent a limb-sparing operation, in which part of his diseased femur was replaced with a prosthesis that can be extended as he grows. When the time comes to lengthen the bone, a donut-shaped coil emitting an electromagnetic field will be placed around Lance's leg. The magnetic field heats a plastic tube within the prosthesis. As part of the tube melts, an internal spring uncoils and the prosthesis lengthens. When Lance reaches his full height, surgeons will replace this prosthesis with an extremely strong permanent prosthesis.

"If we had stayed in our area and gone to one of the hospitals in the region, the odds that Lance would have kept his leg are pretty slim," Carol observes. "They would have probably done an amputation, because that's the easiest thing for them to do."

"Lance initially had some trouble with the chemo," recalls Kerri Nottage, MD, an Oncology fellow. "I would walk into his exam room and he would just be lying on the table. Then one day, I walked into his room and he was sitting up. I was shocked and thrilled. It was nice to walk in and get that surprise. Now, when I walk in, he is usually playing. That's great to see."

Nottage has also been an enthusiastic victim of Lance's practical jokes. One memorable prank involved a whoopy cushion he placed below the paper on the examination table. When she asked him to roll over during the exam, the cushion made its noise. Nottage played along. "I thought it was hysterical," she says.

Friends through the seasons

Although the chemotherapy treatments have been brutal, Lance has coped with the help of his close-knit

family, his friends and his increasingly varied interests. “He’s very, very smart, and he’s a self-motivated learner,” observes Michaela Shurden, Lance’s third-grade teacher in the St. Jude School Program.

“I like to draw landscapes; I like to build. I think I’m going to go to school to be an engineer,” Lance recently announced.

Shurden encourages Lance in his aspirations. “He’s extremely good at math, and he has begun constructing electrical circuits using a kit we have in the classroom,” she says. “He could be an engineer for sure.”

Child Life Specialist Jessika Morris also has a special bond with Lance. “He’s a deep thinker,” she says, noting that the 9-year-old is creative and perceptive, upbeat and cheerful. She is helping Lance create a book that chronicles his experiences at the hospital. “The project is completely led by Lance,” Morris explains. Lance has photographed hospital places and people who are important to his story and has divided the book into seasons. “Since he has been here for nearly a year, he wanted to use ‘the seasons of St. Jude’ as a theme,” Morris says. “When he returns home, he can use the book to help his family and friends understand his journey.”

One of Lance’s chief interests recently has been the

small, knobbed building blocks called Legos.

“He’s a regular Lego maniac,” says Joe, as his son climbs into his lap.

“I built a Republic gun ship from Star Wars that had 1,043 pieces,” Lance explains.

Lego instructions encourage users to separate the Legos by colors before beginning construction. But the budding engineer scoffs at the thought. “I don’t do that,” he says. “I like a challenge.”

Carol and Joe bought a tripod and camera so that their son can make stop-motion animation films with his Lego creations. Lance takes a photo of a character or vehicle, moves the item slightly and takes another photo. It’s a meticulous and time-consuming process. When the hundreds of photos are eventually assembled, the characters seem to move. “I’ve got one of my movies on YouTube,” he explains. “It’s a light saber duel.”

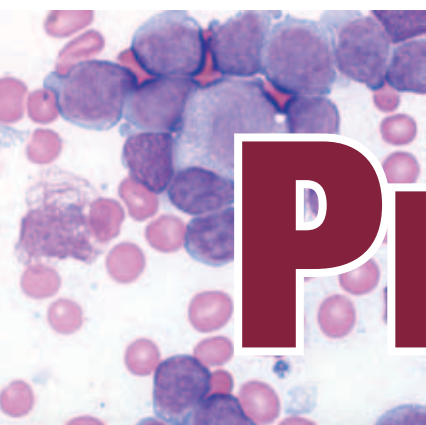
Now that his dad is home, Lance is building more than Lego creations. He and his family are constructing a future. They can see it now, just ahead. And incoming patients at St. Jude can glimpse the excitement shining in the faces of the Fletcher family. Joe summed it up in a May 2009 entry to his online journal:

“There are always new children arriving at St. Jude for treatment. The new ones are usually easy to spot because they’re the ones that still have their hair. I feel a little tug in my heart when I see them because I remember when we first arrived. I remember that feeling of despair of not knowing what will happen to your child. St. Jude helped us get through that time, and everything is going well.

I smile once again as I think about Lance being down to his last three chemo treatments. We’ve come a long way. I’m enjoying each and every day with my little man and looking forward to the day when we go home and live together as a family.” ●

Lance is treated on a new protocol led by St. Jude oncologist Najat Daw, MD. “The outcome of patients with osteosarcoma has reached a plateau, and we need a novel strategy to improve it,” she says. “We hope the new trial will help us increase survival rates for children with this disease.”





PERILOUS Precursors

BY ELIZABETH JANE WALKER

St. Jude scientists identify a completely new and deadly subtype of leukemia that arises from early T-cell precursors. The discovery allows early detection and therapeutic intervention to improve the outcome for children with this form of drug-resistant leukemia.

Upon discovering their child has leukemia, parents tumble into a dizzying vortex of emotions. For one agonizing heartbeat, the sun ceases to shine; the atmosphere loses its oxygen; the world tilts on its axis. The universe narrows down to one overwhelming question: “Will our child survive?”

If the child has acute lymphoblastic leukemia, the most common

form of cancer in children, the answer is most likely “yes.” But if the patient has T-cell acute lymphoblastic leukemia (T-ALL), that question is more difficult to answer.

T-ALL is a type of leukemia in which immature white blood cells called T cells proliferate in the child’s blood and bone marrow. Normally, T cells are an important component of the human immune system. Their job is to seek out and destroy invaders. But when these cells run awry, they crowd out normal blood cells, wreaking havoc and—if unchecked—causing death. In fact, about one in five children with T-ALL die of the disease.

In 1973, researchers at St. Jude Children’s Research Hospital were the first scientists to identify T-ALL as a distinct subtype of acute lymphoblastic leukemia. Since that time, research on this disease has continued at the hospital, as investigators work to unlock its mysteries and to determine how to save the lives of more children.

“The survival rate for ALL now exceeds 90 percent,” explains Dario Campana, MD, PhD, of St. Jude Oncology. “It is extremely important that we identify the small subset of patients who cannot be cured with traditional therapy.”

A dangerous subtype

Campana and his colleagues recently identified an aggressive subtype of T-ALL that is resistant to standard chemotherapy. They dubbed the new subtype ETP-ALL, since it arises from early T-cell precursors (ETPs). Children with this new subtype account for many of the deaths attributed to T-ALL. Because of this discovery, clinicians worldwide will now be better able to identify and treat children with this disease.

“One of the principles of modern leukemia treatment is to avoid over-treatment or under-treatment,” Campana explains. “It is extremely important to identify immediately which patients have a higher risk of relapse and need to be treated with aggressive chemotherapy or transplant. It is equally important to determine who can be successfully cured with much less-intensive and less-toxic treatment. Until now, we didn’t have solid classifications that would allow us to make these kinds of decisions for patients with T-ALL, so they were all treated in the same way.”

Like blood stem cells, ETPs are immature cells that have the ability to differentiate into several kinds of cells. Elaine Coustan-Smith of

St. Jude Oncology suggested that leukemia originating from ETP cells might be more resistant to therapy than other kinds of leukemia. She and her colleagues then used genetic and immune screening to examine 139 cases of T-ALL that occurred at St. Jude within a 15-year period. The team discovered that 17 of those children had the ETP signature.

“For many years, we have stored samples from our patients,” Coustan-Smith explains. “Fifteen years ago, the technology was not sophisticated enough to allow this kind of analysis. Fortunately, we had samples that were in such good shape that we could thaw them out and analyze them.”

The scientists found that less than one-fifth of St. Jude patients with the ETP signature had survived the disease. The children who did survive had undergone bone marrow transplantation. To validate these findings, the researchers also analyzed records and samples from 100 children treated in the Italian national study Associazione Italiana Ematologia Oncologia Pediatrica. Thirteen patients had the cell marker profile that indicated ETP-ALL. Of those children, the two-year survival rate was zero.

Because of this discovery, St. Jude will recommend bone marrow transplantation to any patient who is found to have ETP-ALL, according to Ching-Hon Pui, MD, St. Jude Oncology chair.

“The vast majority of ETP-ALL patients treated with the best-available chemotherapy would still relapse,” Pui explains. Children exhibiting ETP-ALL will receive irradiation and drugs to eradicate their residual leukemic cells and bone marrow cells. The patients will then receive new blood-forming stem cells.

The research continues

Armed with information from this study, other institutions will also be able to screen their patients for the new subtype. A report on the research was published earlier this year in *The Lancet Oncology*.

“The markers that we use to identify ETP-ALL are used routinely by everyone who does immunophenotyping of leukemia,” Campana says. “People never noticed this subset of leukemia before because they never came across the right combination of markers.”

What’s the next step?

First, the scientists want to find ways to make the cancerous cells sensitive to treatment or to identify new drugs that would target those cells. “Maybe there are ways to manipulate these cells in such a way that they become more responsive to conventional chemotherapy,” Campana says.

The investigators are also interested in more closely analyzing the molecular features of ETP-ALL. Charles Mullighan, MD, PhD, of St. Jude Pathology played an important role in characterizing the ETP-ALL subtype for the project.

“We examined gains and losses of DNA across the genome and found that there was a lot of genomic instability in this subgroup,” Mullighan says. “However, at present we have not identified a genetic change common to all patients with this type of leukemia. We plan to apply new methodologies and sequencing techniques to identify the genetic basis of this disease.”

“We also want to see whether transplantation is really an effective curative option and whether cell therapy strategies can be applied to ETP-ALL,” Campana adds.

“There is still a lot for us to do.”●

ANN-MARGARET HEDGES



Dario Campana, MD, PhD, Elaine Coustan-Smith and their colleagues have identified an aggressive subtype of T-ALL that is resistant to standard chemotherapy. Armed with information gleaned from the research, clinicians will be better prepared to identify and treat children with this disease.

The Final FRONTIER

For some, space may be the final frontier. But strange new worlds can also be found on a molecular level.

BY CARRIE L. STREHLAU

The battle of battles has begun. Starship *Neutrophil* pulls alongside starship *Macrophage*. The first in a galaxy of defenders, each ship is poised to defend the universe against attack. After successfully fulfilling their quest, the starships self-destruct, leaving tranquility in their wake.

White blood cells called neutrophils and macrophages are the first responders of the immune system. They serve as the initial line of defense against invading microbes—identifying, engulfing and eliminating the enemy. When these protective cells have obliterated their attackers, they must quickly destroy themselves so the immune system can return to normal and the body can dispose of the toxic microbial waste and damaged cells.

Scientists at St. Jude Children's Research Hospital have discovered a regulator for this process that might yield insights into diseases like sepsis and some leukemias.

To explore strange, new worlds

St. Jude researchers recently found that a gene called *MCL-1* produces a protein that protects neutrophils from self-destructing as these white blood cells mature in the



bone marrow. The MCL-1 protein also helps macrophages survive while they do their job of eliminating extracellular microbes.

"The fine-tuned balance mediated by MCL-1 is critical because you want to protect the macrophages when they encounter a pathogen and allow them to do their job," says Joseph Opferman, PhD, of St. Jude Biochemistry. "After clearance of the microbe, the body needs to rapidly downregulate the immune response by eliminating the cells that have been recruited to the infection site and return the immune system to normal. Otherwise, an accumulation of active inflammatory cells can lead to tissue destruction."

The researchers' basic findings of MCL-1's function could yield insights into its role in such disorders as sepsis, an often lethal inflammation in which the immune system goes out of control. Also, the finding could give insight into leukemias in which MCL-1 levels are known to increase, contributing to the abnormally prolonged life of the malignant cells.

"Myeloid cells are very important to the body," Opferman says. "We are trying to understand what regulates their development, survival and function. The most important finding of this research was an unexpected difference in the molecules used for promoting the survival of the neutrophils versus macrophages."

"This is a molecule that is essential for a variety of different cell types' survival. What we are trying to do is assess whether it is playing another role in a very important type of blood cell that is in essence the first line of defense in the immune system."

To seek new information

Trying to understand that role is significant because it can teach researchers about when these blood cells are deregulated and how that might lead to cancer.

"MCL-1 happens to be a molecule that promotes cell survival," Opferman says. "Therefore, it needs to be tightly regulated. We are trying to understand how to take advantage of its normal regulation in order to foster the elimination of unwanted, damaged or obsolete cells."

MCL-1 had been shown to be important in a variety of other blood cell lineages. Previously, Opferman showed that the molecule was necessary for the survival of lymphocytes, blood stem cells and a variety of different early blood cell progenitor populations in the bone marrow.

"Starting this study, there was a common implication that this pro-survival molecule was essential for all blood cell lineages," he says. "And, some people in the field

suggested that no matter what lineage you knock MCL-1 out in, it's going to be lethal. That was not what we found in this study."

In studies with macrophages, the researchers found that while MCL-1 was not necessary for development and basic function, its loss rendered the macrophages sensitive to elimination when they ingested microbes.

"This is one of the most striking findings," Opferman says. "In all other blood cell lineages, if you delete MCL-1, those cells are basically gone. But macrophages survive, and we want to find out why they survive, and why losing MCL-1 only makes them more susceptible to apoptosis."

To boldly go

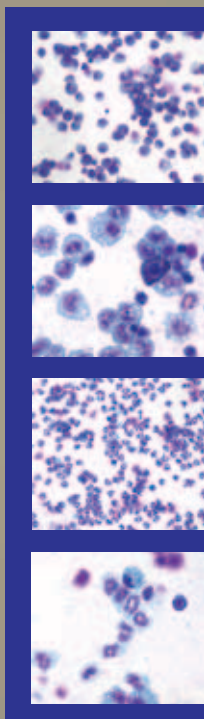
Besides yielding insights into inflammation, a deeper understanding of MCL-1's normal role might also help in developing treatment strategies for myeloid leukemia.

"MCL-1 is highly expressed in several different leukemias and lymphomas, and many groups are developing treatments to antagonize MCL-1 function in order to eliminate cancer cells," Opferman says. "As we come to understand the primary, normal functions of MCL-1, we appreciate that simply eliminating its function might have significant detrimental side effects. Our findings suggest that treatment strategies should aim at modulating MCL-1 protein levels without completely blocking its function."

The other important finding was that the macrophages, which normally express this protein, were not eliminated but instead had some functionality. That was also not previously observed in the literature.

"The real question I am interested in is how MCL-1 affects cell survival and function *in vivo*," Opferman says. "We are trying to find what role MCL-1 plays in normal cell development and understand how it is regulated. One of the lessons that can be learned from these studies is that, if we can understand its normal regulation, we might be able to take advantage of these normal regulatory pathways. Instead of causing a full elimination of the protein, which would have dramatic side effects, we might be able to turn it down in situations where you want to promote blood cell elimination. In other cases, you might be able to turn up MCL-1 expression when you want to prevent elimination of blood cells. That is the way I see our role."

For children who might one day benefit from this research, the exploration is far more exciting than mapping stars or studying nebula. For them, the possibilities are as wide as the universe. ●



A young boy, Evan Pertile, is smiling from inside a red play tunnel. He is wearing a pink polo shirt, colorful plaid shorts, a blue baseball cap, and a blue wristband. The tunnel has red handles and a green interior. The background shows a playground with other equipment and a paved area.

Where would two physicians turn if their son had a brain tumor?
One couple found world-class treatment—
as well as their son's trademark smile—at St. Jude.

A REASON TO *Smile*

BY MIKE O'KELLY

Six-year-old Evan Pertile has a bright, cheerful countenance that usually shines through in his family's holiday photos. But something wasn't right as he, his parents and three brothers posed on Thanksgiving Day 2008 for the annual snapshot.

"I don't think Evan smiled once," says his mother, Rachel. "He just wasn't feeling well."

The day before, Evan had awakened with an unusual headache that concerned Rachel and her husband, Alex, who are both physicians. After the headache subsided, the couple agreed that if it returned, Evan would go to the hospital for an imaging scan.

On Thanksgiving night, the family drove to their vacation home to relax and spend a long, holiday weekend. When Evan awoke the next morning crying,

Alex immediately took him to the emergency room. Hospital staff there said Evan had a bad sinus infection. Unconvinced, Alex demanded that the ER physician perform a CT scan.

Since it was a holiday weekend and no one was available to interpret the results, Alex, a radiologist, read the scan, which confirmed his suspicions—a 4-centimeter tumor was lodged in Evan's cerebellum.

"It was a shocking moment, but being a father helped me pull together," Alex says. "It crossed my mind that I have to be the strong one and take him through this."

After a moment of consolation with his son, Alex left the hospital to pick up Rachel and his other sons, William, Jonathan and Xander, while Evan waited in a patient room.

It was the beginning of a journey that would lead the family to the world-renowned pediatric brain tumor program at St. Jude Children's Research Hospital.

Confirming the worst

Alex refused to answer the phone on the drive home, even though Rachel called numerous times. He wanted to inform her face to face. Rachel had already assumed the worst.

"I called my sister, and I said, 'Rebecca, Evan has a brain tumor. I just know. It's the second severe headache he's had, and it's atypical,'" Rachel says.

As Alex backed their vehicle into the driveway, Rachel knew something was wrong. When Alex got out of the car without Evan, it was confirmed.

"I said, 'We need to pack; we need to take Evan to a major center,'" Alex recalls.

A familiar ray of hope

Evan was found to have medulloblastoma, the most common malignant brain tumor in children.

The couple asked their pediatric oncologist to recommend the best place for Evan to undergo therapy. The answer was St. Jude.

Two days later, a neurosurgeon removed the tumor from Evan's brain. Specialists said the tumor's pathology revealed a rare form of the tumor, which St. Jude physicians later determined was inaccurate. The couple asked their pediatric oncologist to recommend the best place for Evan to undergo therapy. The answer was St. Jude.

"It was not even a moment's hesitation. As soon as she said 'St. Jude,' we said, 'That's where we are going,'" Rachel says.

Alex and Rachel were familiar with St. Jude. They had donated money in the past and had seen the hospital's TV and print advertisements. Alex recalled taking note of one magazine advertisement in which a St. Jude patient with a brain tumor was featured.

"I thought that was a unique ad, and then a week later, Evan had a brain tumor," Alex says. "I remember being in the waiting room during his first surgery, and I kept running into that ad over and over again in different magazines."

Coming to St. Jude

Although the Pertiles knew about the remarkable work occurring at St. Jude, they were surprised to find that important issues such as travel, lodging, food and mental well-being are also handled. Rachel was relieved to know St. Jude had staff to take care of these matters and to make the first day at the hospital less stressful.

"The security guard at the front desk held my hand and helped us. She was so welcoming. I felt a little calmer, and I knew we had done the right thing," Rachel says. "I was overwhelmed with the organization and the care. Every single person is there for the children."

After a second brain surgery to remove additional tumor cells, Evan began the other components of treatment, which include radiation therapy to his head and spine and four rounds of chemotherapy. The day after his second surgery, Evan was back to his cheerful self, running around the hospital.

Before beginning six weeks of radiation therapy, Evan's stem cells were removed in a process known as an autologous blood stem cell harvest. After each round of chemotherapy, he receives a transfusion of these cells to boost his weakened immune system.

"We try to minimize the volume of high-dose radiation to the tumor bed to avoid the long-term, late side effects," says Amar Gajjar, MD, who heads the St. Jude Neuro-Oncology Division.

Traditional therapy usually involves one year of chemotherapy for patients, but the St. Jude protocol calls for a reduction in the duration of treatment, and instead delivers the chemotherapy in monthly cycles of high-dose chemotherapy for four months total duration.

"We cut short the intensive



(Above) Radiologist Alex Pertile, MD, and family practitioner Rachel Pertile, MD, spend time with their son in the Danny Thomas Research Center.

(At right) Evan visits with Larry Kun, MD, Radiological Sciences chair, during a recent checkup. "At St. Jude we have the foremost medulloblastoma physician in the world, Dr. [Amar] Gajjar, whom we adore, as well as Dr. Kun, the radiation oncologist, who is like Evan's best friend," says Rachel.

chemotherapy, which gets very good results and gets the children back into a normal routine more quickly and with much less toxicity," Gajjar says.

Making new friends

After his first round of chemotherapy, Evan surprised his caretakers with his rapidly improving white blood cell counts and a voracious appetite that suddenly reappeared. Evan credits his renewed appetite to the encouragement from his new friends in the armed forces, who tell him to eat so he can become a strong soldier someday.

Shortly after Evan's first radiation treatment, Rachel met a woman on a plane who worked at the Fort Leavenworth military base in Kansas. After hearing Evan's story, the woman spread the word to her colleagues. In the weeks and months

since, military personnel from all branches in different parts of the world have sent messages of goodwill to Evan. He has received countless e-mails, visits, military gear, a soldier's bronze star, a bronze star with valor, a purple heart and other combat medals. He was also told that he will receive an American flag that flew on the Fourth of July in Iraq.

With a boost in appetite and morale, Evan recently began his second round of chemotherapy and is looking at a good prognosis, according to Gajjar. The Pertiles have seen the smile return to Evan's face now in photographs, and they credit St. Jude with helping make that possible.



PETER BARTA

"My wife and I are both in the medicine business, right in the middle of it. Even with that, it is very hard to navigate the system," Alex says. "The fact that St. Jude has everything there and just takes the child and the family and guides them through all of this is just amazing. All of a sudden, you feel like you are in absolutely the best place in the world." ●

Sole Mates

BY JOYCE M. WEBB

Thanks to the research and treatment at St. Jude, this 16-year-old is living her dream as an award-winning clogger.

They met for the first time when Hillary Husband was a toddler. She watched with rapt attention the heels that pounded the stage and was wooed by the sweet sound of jingle taps. Hillary didn't know the teens who were jigging in those clogging shoes. But by the end of the rousing performance, she was certain she had met her sole mate.

Now an intrepid 16-year-old with feet like lightning, Hillary is living her dream as a member of a national championship clogging troupe in Louisiana.

"Dance is my life," Hillary says.

Her repertoire includes tap, jazz, ballet, lyrical and dance line. But clogging, a hybrid of tap and Irish step dancing, is what gets her adrenaline pumping.

"I like it because I can do something not everybody can do, and I love the competition," she says. "I also like the teamwork and bonding with my friends on the team."



SETH DIXON

Slow tempo

In spring of 2008, after acing the first leg of school with a 4.0 grade point average and logging up to 14 hours a week at dance practice, Hillary spent spring break playing video games and engaging in girl talk during sleepovers.

The late nights were taxing, and she found herself nursing headaches and fatigue for most of her vacation. Afterward, she noticed a purple rash that stretched from her thigh to her toes. She dismissed it. The next day at school, she became dizzy. Climbing the stairs to class was like ascending Mount Everest. Somehow she made it halfway through dance line tryouts after school.

"I tried to practice, but my body wouldn't do what I told it to. The room started spinning, and I got really nauseated," Hillary says. Then she did something she had never done before.

"She sent me a text message to come pick her up. That raised a red flag," says her father. "For her to leave dance practice meant that she was really feeling bad."

Stiff competition

From dance tryouts to home and from home to the emergency room—everything happened quickly and unexpectedly. Michael and Katey Husband thought the flu or spinal meningitis was attacking their daughter's immune system, but lab work ruled out those diseases. Hillary was quickly transported to the St. Jude Children's Research Hospital affiliate clinic in Shreveport, Louisiana, for further testing.

The wait was interminable.

"The doctor called my parents out of the room. I know when that happens on TV at the doctor's office, that's not good," Hillary says.

Hillary was found to have

precursor B-cell acute lymphoblastic leukemia (ALL), a subtype of ALL involving blood-forming cells in the bone marrow.

"I was overwhelmed with pain—I hurt so much it was hard to stand," Katey recalls. "I remember being very angry—not so much as 'why me?' But I was waiting for somebody to come into the room and say, 'I'm sorry, Mr. and Mrs. Husband, we were mistaken.'"

It never happened.

"We knew we would get bad news; we just didn't know how bad. It was devastating," Michael says. "Cancer was always for somebody else. You felt for them; you prayed for them. But it's something that didn't happen to your family."

As for Hillary—sure, she cried for hours. All she could think about was whether she would dance again. She even wrestled with the thought of going bald from the chemotherapy. But everything made sense to her in retrospect. The headaches, the rash, the fatigue, the abdominal weight gain were the onset of leukemia.

"That's why my stomach was getting bigger; it wasn't weight gain. It was my spleen shaking hands with my belly button," she says.

Hillary's quick wit shines through in the most difficult of circumstances, which is why her friends were wary when she broke the news.

"It's really hard to tell your friends that you have cancer on April Fool's Day. They thought it was a joke. I argued

with them for a week," she says.

Hillary quickly prepared for a heel-toe battle with cancer. The affiliate arranged a flight to St. Jude Children's Research Hospital in Memphis, Tennessee, so that she could begin treatment right way.

A footprint in research

St. Jude has a storied success rate in leukemia research and treatment. When the hospital opened in 1962, the survival rate for children with leukemia was a grim 4 percent; today it's 94 percent.

"Our goal is 100 percent," says Deepa Bhojwani, MD, of St. Jude Oncology. Bhojwani is involved



SETH DIXON

Clogging, as well as the support and prayers of family and friends, imbued Hillary with strength during her heel-toe battle with cancer.



Hillary Husband (kneeling, second from left) maintains a 4.0 grade point average in school while competing on regional and national stages. In July, her clogging troupe won a national dance competition that featured more than 100 teams.

Katey Husband (at left), Nurse Practitioner Renee Rencher and Deepa Bhojwani, MD, applaud as Hillary demonstrates a few clogging steps in a St. Jude hallway. "Hillary doesn't let anything get in her way," Bhojwani says. "It's tough at times when her counts are low, but she finds the will to keep going."

in the Total XVI clinical study to improve the cure rate in children with precursor B-cell and T-cell ALL. A critical piece is minimal residual disease (MRD) monitoring.

"MRD is a very sensitive and sophisticated way of making sure leukemic cells are not hiding in the bone marrow," Bhojwani says. "We're able to identify one leukemic cell out of 10,000 normal cells using a technique called flow cytometry."

Hillary and other St. Jude patients with leukemia get their MRD results within a couple of days without delays in their treatments because of the hospital's onsite, state-of-the-art flow cytometry lab and pioneering research in MRD testing techniques. This convenience allows clinicians to closely monitor the response to treatment with greater frequency than most institutions.

"If we find that the MRD is not going down as fast as we'd like it to, then we can adjust their chemotherapy sooner to prevent them from relapsing," Bhojwani says.

Tapping inner strength

The first six weeks of Hillary's treatment were intense in order to decrease the number of leukemic cells in her bone marrow. Then she underwent two re-induction phases that lasted several weeks.

Hillary chronicled her experience in an online journal. Some entries were serious. Others offered a glimpse into her incisive sense of humor. For instance, one entry described the drug dexamethasone, which causes fatigue and mood swings.

"It's a combination of steroids and teenage hormones. I always joke that dex is like PMS in pill form," she wrote.

Today, Hillary receives maintenance chemotherapy at the St. Jude affiliate and returns to Memphis each month for follow-up procedures. Looking back, she says her experience with cancer has brought her family closer. Her ability to continue clogging and the prayers of family, friends and well-wishers

motivated her to face treatment with great expectations. Losing her hair wasn't all that bad, either.

"It's kind of cool because now it's curlier and thicker, and it came back a different color than my old hair. It's like I got free hair dye and highlights," Hillary says.

Her parents continue to be inspired by their daughter's resilience and her ability to find a silver lining in any situation.

"She always has a good attitude. She's an inspiration to us as her parents and to everyone she encounters," Michael says.

"Hillary is the most driven person I know. A lot of cancers and tumors are bigger than attitude, but even when your quality of life is low it's made better by a positive attitude," Katey says.

"I don't think our attitude would be as hopeful without St. Jude. I thank God that Danny Thomas was placed on this earth and was given the gifts and the talents to create such a wonderful place."●

Perspective

BY STEPHEN CARTER

It's in You to Give

"Lots of people ask me why I make the drive from Missouri to Tennessee every other week to donate platelets. It's simple. Knowing that I'm helping a child is the greatest pleasure I can get."

Many years ago, a boy from my hometown in Missouri went to St. Jude Children's Research Hospital for treatment. As a result of his experiences, I learned about the great research and clinical care that occurs at the hospital. After he passed away, I wanted to find a way to give back to St. Jude. I began donating money and, since I had just moved to Memphis, I also began donating platelets at the hospital's Blood Donor Center.

Even though I later relocated to Mississippi and then to Missouri, I knew I needed to continue helping the children. So, for the past seven years, I have returned to Memphis every two weeks to donate platelets.

Lots of people ask me why I make that drive from Missouri to Tennessee so often. It's simple. Knowing that I'm helping a child is the greatest pleasure I can get.

Ever since I began donating, I've been encouraging my friends and relatives to tour St. Jude and donate platelets. Some have taken me up on the offer; some haven't, but I spread the word as much as I can.

The donation process is actually enjoyable. I walk in with a big, old smile, and everybody in the Blood Donor Center greets me. Then I go through the interview process. They check my iron and take my temperature. Then I climb into an easy chair, put on my headphones and watch TV while I donate.



It's not hard. You could sit at home for an hour or so watching a movie on TV. Why not spend that time at St. Jude donating platelets—knowing that you're helping a child in need?

The drive home is always great. I go home with a smile, knowing that I've helped somebody. I never have a bad day when I come to St. Jude.

Since I've spent so many hours in the St. Jude Blood Donor Center, I've had the chance to meet a few of the children who come in there to receive platelets. Those kids are far stronger than I am. They always have a smile on their faces.

No matter where I am in the country, I'll continue to come back every other week. My message to you is this: Please help! The children of

St. Jude need as much help as they can get. ●

EVERY DAY St. Jude performs about 15 to 25 platelet transfusions for children undergoing treatment at the hospital. If the St. Jude Blood Donor Center does not have enough donated platelets, it must purchase them at a cost of \$500 to \$700 per unit. By donating platelets at St. Jude, you can help a child while helping the hospital save money. If you plan to be in the Memphis area, why not consider making an appointment to donate? Simply call (901) 595-2024 or dial toll-free 1-866-2STJUDE (278-5833), ext. 2024.



Laney Jo, age 2, acute myeloid leukemia

Your legacy can be her future.

You can play a vital role in helping secure a healthy future for children battling cancer with a gift to St. Jude Children's Research Hospital® through your will. Join others who share the desire to leave a legacy of hope to catastrophically ill children by considering a bequest gift to St. Jude. To learn more about these special gifts and the Danny Thomas – St. Jude Society that recognizes these contributions, please call us at 800-395-1087, visit www.stjudelegacy.org or complete the enclosed postage paid envelope today.

*Ensure that our research continues until the day we have conquered childhood cancer.
The promise of your charitable legacy helps make it possible.*

Finding cures. Saving children.

CHANGE SERVICE REQUESTED

A hero among heroes

Capt. Chesley "Sully" Sullenberger III pauses with St. Jude patients during a recent visit to the hospital. Sullenberger is the pilot who saved the lives of 155 people when he landed US Airways Flight 1549 on the Hudson River in January of this year. During his visit to St. Jude, he toured the hospital and filmed a TV commercial for ALSAC. Pictured with Sullenberger are (from left): Roberto Blanco, Lance Fletcher, Jakayla and Javon Bass, Aubrey Williams and Abby Geiser.

ANN-MARGARET HEDGES



Finding cures. Saving children.