



A Place of Their Own

Jayla and Felicia Lee love “their” hospital Pg. 12

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On the cover:
St. Jude patients Jayla (at left)
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Research Highlights

Scientists advance new approach to curing blood disorder

In the laboratory, a St. Jude team has successfully introduced two new genes into blood-producing bone marrow stem cells in an effort to ease beta-thalassemia and reduce treatment side effects.

Beta-thalassemia is a blood disorder that reduces the production of hemoglobin, the protein that carries oxygen to cells. Gene therapy offers hope of someday freeing thousands worldwide from the discomfort, risk and cost of lifelong transfusion therapy. Untreated, the disease leads to widespread organ damage and premature death.

The research, published in the journal *Blood*, raises the possibility of using an individual's own bone marrow cells with gene therapy to cure beta-thalassemia and other inherited blood disorders, including sickle cell anemia.

Derek Persons, MD, PhD, of Hematology and his colleagues found that the amount of the target protein, fetal-hemoglobin, in red blood cells jumped dramatically and eased disease symptoms when scientists transplanted hematopoietic stem cells (HSCs) carrying one gene to correct beta-thalassemia and another to give those newly corrected cells a survival advantage. HSCs are the parent cells in bone marrow that give rise to blood cells.

The approach relies on a gene-therapy system developed at St. Jude. The goal is to develop a strategy for increasing the number of corrected HSCs a patient receives without the need for additional chemotherapy. Persons said this paper demonstrates that the strategy works in the lab.



ANN-MARGARET HEDGES

Farewell to paper records

Sheri Spunt, MD, medical director of the Solid Tumor Clinic, and Don Baker, PharmD, of Information Sciences, work with the computerized provider order entry system that was recently installed in the Solid Tumor Clinic. Federal health officials have set a deadline of 2014 for health care providers to switch to an electronic system. St. Jude has made more progress toward this goal than most other U.S. hospitals. By late 2010 all new St. Jude patients are expected to have completely electronic health records, said Jerry Shenep, MD, St. Jude chief medical information officer.

New HIV transmission route discovered

Researchers have identified the first cases in which HIV almost certainly was transmitted from mothers or other caregivers to children through pre-chewed food. This feeding practice is common in many parts of the world.

Giving infants pre-chewed food has been reported to transmit infections such as Group A streptococcus and the hepatitis B virus, said Aditya Gaur, MD, of Infectious Diseases. However, he and his colleagues found the first evidence that the blood-borne HIV could be similarly transmitted. In the cases the researchers studied, HIV transmission was likely enabled by bleeding gums or open mouth sores.

The researchers conclude that this route of transmission has important global implications, including offering a possible explanation for some of the reported cases of "late" HIV transmission in infants, which had previously been attributed to breastfeeding. Results of this study appeared in the journal *Pediatrics*.



Inherited factors increase odds of developing ALL

St. Jude scientists have identified inherited variations in two genes that account for 37 percent of childhood acute lymphoblastic leukemia (ALL), including a gene that may help predict drug response. The work offers the first proof that inheritance plays a role in childhood ALL.

Mary Relling, PharmD, Pharmaceutical Sciences chair and the paper's senior author, estimated that individuals who inherit variations in the *ARID5B* or *IKZF1* genes are almost twice as likely to develop ALL as those without the variations. Even then, she said, the risk remains low.

"The genetic variations alone are not enough to cause the cancer. Like all cancers, pediatric ALL is a multi-factor disease," Relling said. "But these findings may give us a handle on the mechanism of the disease and drug responsiveness to it."

Inherited variations in *ARID5B* might also influence patient response to chemotherapy, particularly to the drug methotrexate. A report on this study appeared in the journal *Nature Genetics*.

"The work offers the first proof that inheritance plays a role in childhood ALL."

St. Jude named tops in academia

For the fourth consecutive year, St. Jude has been listed among the top 10 "Best Places to Work in Academia" by *The Scientist* magazine.

Survey participants ranked research resources at St. Jude as a top factor in determining workplace satisfaction.

"We are pleased that we continue to be seen as an outstanding place to do research, as this helps to ensure that we continue to recruit and retain the best and brightest researchers," said Dr. William E. Evans, St. Jude director and CEO. "The serious nature of the diseases we treat requires nothing but the best if we are to continue to make discoveries that advance cure rates."



GREG HARRISON, ST. JUDE'S MEDIA PRODUCTION

St. Jude announces sixth domestic affiliate

St. Jude has established its sixth U.S. pediatric hematology-oncology clinic at St. John's Children's Hospital in Springfield, Missouri. The affiliate partnership will offer greater access to St. Jude treatment protocols for children in the Missouri and northern Arkansas region. Joseph Laver, MD (at left), St. Jude clinical director and executive vice president, pauses in front of a clinic room with Kim Day, senior vice president of regional markets, Sisters of Mercy Health System.

Research Highlights

Researchers investigate origins of type I diabetes

St. Jude investigators have discovered how destructive immune cells gain access to insulin-producing beta cells and help cause diabetes.

The finding points to possible new strategies to halt or prevent type I diabetes.

In the lab, researchers demonstrated that to enter key areas of the pancreas known as the islets of Langerhans, immune cells known as T cells must “see” components of these insulin-producing beta cells before they are allowed to enter the islets. Once inside the islets, T cells trigger the inflammation that can lead to destruction of the insulin-producing beta cells. The result is type I diabetes.

The study answers a fundamental question about the role of T cell entry and accumulation in the islets in development of type I diabetes. A report on this research appeared in the journal *Immunity*. Dario Vignali, PhD, vice chair of St. Jude Immunology, is the paper’s senior author.

The results contradict a widely held theory that only a small percentage of T cells that infiltrate the islets were actively involved in causing type I diabetes.

“The new research argues that every T cell in the islet is important. What these T cells recognize that allowed them to gain access to the islets may provide us with clues as to what might be needed to prevent diabetes,” Vignali said. “This paper also presents a new clinical intervention strategy—blocking T cells from even getting into the islet cells in the first place.”



PETER BARTA

Everything's coming up silver

Nearly 140 St. Jude childhood cancer survivors attended the hospital's annual Survivors Day conference in October. This year's event celebrated the 25th anniversary of the After Completion of Therapy Clinic, which cares for long-term survivors of childhood cancer who have been treated at St. Jude. Survivors Day allows current and former patients to reunite with staff and attend educational workshops. Margie Zacher of St. Jude Epidemiology and Cancer Control, (center, left) and Melissa Hudson, MD, Cancer Survivorship Division director, (center, right) welcome St. Jude survivor Sandy Owen (right) and her husband, Tony.

Genes linked to H5N1 illness severity

Patients with the genetic foundation to marshal an efficient, rapid response to the H5N1 influenza virus are more likely than others to survive the bird flu, according to a team led by St. Jude investigators.

The study, published in the *Journal of Virology*, provides the first evidence of a genetic predisposition to serious illness following H5N1 infection. Researchers focused on H5N1, rather than the current H1N1 pandemic flu strain. Although H1N1 has sickened more individuals worldwide, H5N1 has proven more virulent.

In this study, researchers tracked differences in the H5N1 immune response to regions of five chromosomes. Within one of these regions was a candidate gene, hemolytic complement (HC), which investigators went on to show plays a critical role in modulating response to H5N1 infection.

The results may ultimately yield new anti-viral therapies or new genetic screening tests to identify previously unrecognized high-risk patients, said the paper's senior author, Richard Webby, PhD, of Infectious Diseases. Webby is also director of the World Health Organization Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds, which is based at St. Jude.

St. Jude faculty elected to Institute of Medicine

Michael Kastan, MD, PhD, and Mary Relling, PharmD, of St. Jude have been elected to the Institute of Medicine (IOM), a prestigious branch of the National Academy of Sciences.

Kastan, the hospital's Comprehensive Cancer Center director, and Relling, chair of St. Jude Pharmaceutical Sciences, are among 65 new members of the IOM. The election of Kastan and Relling brings the number of St. Jude IOM members to six. St. Jude has one of the highest numbers of IOM members among U.S. children's hospitals.

"To have two additional members of our faculty elected to the Institute of Medicine is a great honor for them and also for St. Jude," said Dr. William E. Evans, St. Jude director and CEO. "As we continue to focus on finding cures for catastrophic diseases, it is accomplished and recognized faculty like Dr. Kastan and Dr. Relling who are leading the way."

Kastan's research focuses on DNA damage and repair, tumor suppressor genes and causes of cancer related to genetic disposition and environmental contributions. Relling's research focuses on pharmacokinetics and pharmacodynamics in children and how genome variability influences a child's response to cancer chemotherapy.



Michael Kastan, MD, PhD



Mary Relling, PharmD

St. Jude has one of the highest numbers of IOM members among U.S. children's hospitals.

Exploring DNA damage

St. Jude researchers have discovered that switching off a key DNA repair system in the developing nervous system is linked to smaller brain size as well as problems in brain structures vital to movement, memory and emotion.

The work, published in the journal *Nature Neuroscience*, also provides the first evidence that cells known as cerebellar interneurons are targeted for DNA damage and are a likely source of neurological problems in humans. The study marks the first time researchers in the laboratory have switched off a pathway for repairing damaged single-DNA strands in an organ system.

The paper's senior author, Peter McKinnon, PhD, of Genetics and Tumor Cell Biology said the work provides a new model for understanding how single-strand DNA damage affects the nervous system and offers a new focus for tracking the origins of neurological disease. The research also reflects growing scientific interest in the responses to DNA single-strand damage and how this prevents a variety of human diseases.

The study marks the first time researchers in the laboratory have switched off a pathway for repairing damaged single-DNA strands in an organ system.

Research Highlights

Gene alteration identified in kids with ALL and Down

Researchers have identified a new chromosomal abnormality in acute lymphoblastic leukemia (ALL) that appears to work in concert with another mutation to give rise to cancer. This latest anomaly is particularly common in children with Down syndrome.

The new gene alteration was identified by St. Jude scientists following up on an earlier observation. They had previously found a recurring deletion in a region of DNA duplicated on the X and Y chromosomes. The region is known as pseudoautosomal region 1, or PAR1. The deletion causes overexpression of the *CRLF2* gene and is frequently found with mutations in JAK kinase genes. Together, these

mutations may drive the abnormal growth of lymphocytes in ALL.

The findings have already resulted in new diagnostic tests and potential tools for tracking a patient's response to treatment. The research, led by scientists from St. Jude, also highlights a new potential ALL treatment. Clinicians are planning trials of an experimental medication targeting JAK kinases.

This study appeared in a recent issue of *Nature Genetics*. Charles Mullighan, MD, PhD, of Pathology is senior author of the study, which involved scientists from 10 institutions in the United States and Italy.

St. Jude starts proton therapy clinical trial

St. Jude and the University of Florida Proton Therapy Institute have formed a research collaboration to provide proton therapy for St. Jude patients enrolled in a specific study.

The announcement follows the approval of the first clinical study to evaluate the use of proton therapy for rare brain cancers in children younger than 3 years old.

Under the clinical protocol, St. Jude will refer patients to receive proton therapy at the UF Proton Therapy Institute in Jacksonville, Florida. The purpose of this study is to assess the potential benefits of proton beam radiation on the developing brain as compared to photon therapy.

Proton therapy is being studied as a way to reduce potential damage to healthy tissue that may result from conventional radiation therapy.

"Proton beam therapy is potentially of great importance to St. Jude and our patients," said Joseph Laver, MD, St. Jude executive vice president and clinical director. "Although most proton facilities operating in the U.S. recognize pediatrics as a major area of focus, there is very little meaningful data using this modality in children. Working with the UF Proton Therapy Institute, we are well-positioned to answer key questions regarding this therapy for children with cancer."

Mina pivotal for immune system balance

A team led by St. Jude researchers has identified a gene pivotal for immune system balance. Ultimately, the discovery may aid efforts to tame allergic diseases such as bronchial asthma and infectious diseases caused by parasitic worms.

Named *Mina*, the gene is part of a signaling pathway that may provide targets for new treatments and provide insights into the disease-fighting immune system, said Mark Bix, PhD, of Immunology.

Bix studies two immune system cells, T-helper type 1 (Th1) and T-helper type 2 (Th2). Certain diseases are characterized by an imbalance between those cells. Researchers found that *Mina* regulates production of interleukin-4, a chemical messenger that plays a central role in balancing Th1 and Th2 cells.

Bix is senior author of a paper on this topic published in *Nature Immunology*.

HIV screening strategy created

Clinicians at St. Jude and Le Bonheur Children's Medical Center in Memphis have implemented the first routine, voluntary, opt-out HIV screening for adolescents.

In the journal *Pediatrics*, they outline a strategy for implementing the routine HIV screenings of adolescents that are recommended by the Centers for Disease Control and Prevention (CDC). Implementation of the CDC recommendation has been slow nationwide.

Investigators developed a protocol for 13- to-18-year-olds, in which screening is provided in an opt-out manner, with reminders incorporated into the computerized patient registration. Of the patients approached for screening, 86.7 percent of patients agreed to get tested and only 13.3 percent opted out.

"Routine, opt-out HIV screening for adolescents serves as a reminder for the busy clinician to address issues of sexual activity, risk and safer sex practices," said lead author Timothy Minnietar, MD, of St. Jude Infectious Diseases. Implementing routine HIV screening for adolescents makes pediatric health care facilities more "HIV-testing friendly," added senior author Aditya Gaur, MD, also of Infectious Diseases.



ANN-MARGARET HEDGES

Taking education to the community

Andrea Williams (at left) and Melanie Copeland, both of Infectious Diseases, prepare materials for the hospital's Connect to Protect program. The award-winning program seeks to educate children, teens and parents about HIV and AIDS prevention by mobilizing community-based and faith-based organizations.

Sickle cell study targets stroke prevention

St. Jude investigators are launching a national study of the drug hydroxyurea to prevent first strokes in children and adolescents with sickle cell anemia (SCA).

The effort will be the fifth at St. Jude involving hydroxyurea to treat children with SCA. The focus will be on SCA patients who have not suffered strokes but who have been identified as being at high risk for the complication by transcranial Doppler ultrasound (TCD) screening. The five-year project is expected to include a total of 26 medical centers and about 140 patients. The study has been named TWITCH, short for "TCD with Transfusions Changing to Hydroxyurea."

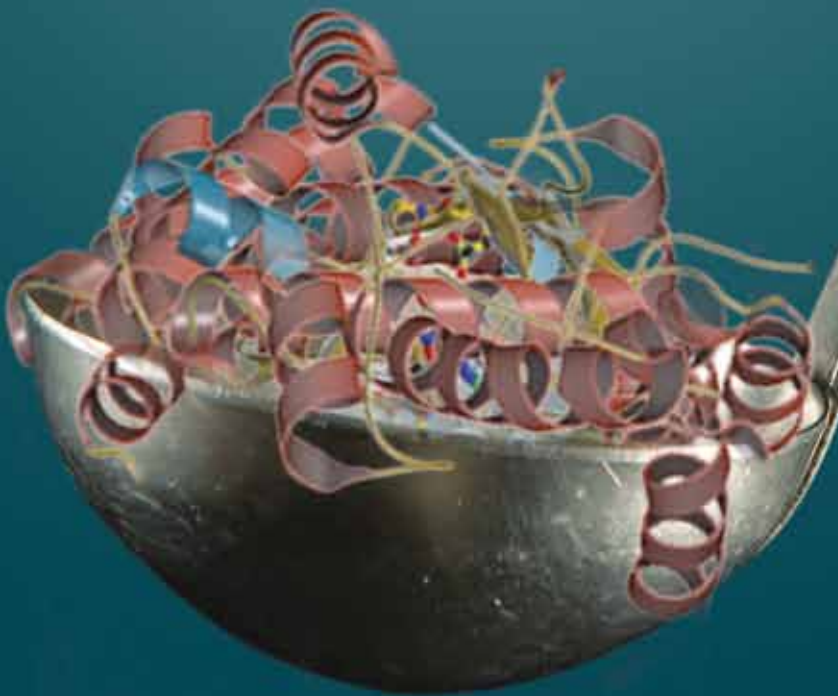
"Our goal with this study is to prevent brain complications in children with sickle cell disease," explained Russell Ware, MD, PhD, who chairs St. Jude Hematology and holds the Lemuel Diggs Endowed Chair in Sickle Cell Disease. Ware is the national principal investigator for this study funded by the National Institutes of Health.

Patients in the study will be randomly assigned to either continue a standard therapy of monthly blood transfusions and chelation to remove the resulting iron buildup or to receive a daily dose of hydroxyurea and monthly phlebotomy to remove excess iron. The goal is to compare the two treatments, including their ability to reduce the risk of a first stroke.

"Our goal with this study is to prevent brain complications in children with sickle cell disease."

Serving Up SCIENCE

At St. Jude, even the most casual lunchtime conversations may produce ideas and discoveries about childhood illnesses—and some may have applications for adult disorders such as Parkinson's disease.



BY ELIZABETH JANE WALKER

What are you having for lunch today? For employees of St. Jude Children's Research Hospital, an entrée in the hospital cafeteria may very well be accompanied by a side order of science. One recent gastronomic gathering at St. Jude ultimately yielded important research findings in two distinct disciplines.

When Katharine Sturm-Ramirez, PhD, joined Kennie Shephard, PhD, for lunch in the hospital's Kay Kafe, a scientific discovery was the last thing on their minds. Sturm-Ramirez had spent the morning involved in influenza surveillance in the lab of internationally renowned flu researcher Robert Webster, PhD. In another part of the hospital, Shephard had been working on Parkinson's disease research under the direction of developmental neurobiologist Richard Smeyne, PhD.

During lunch, the diners began to discuss the 1990 film *Awakenings*. Based on actual events, the movie chronicles the story of patients who survived a form of encephalitis that may have originated with the 1918 influenza pandemic. The patients suffer neurological symptoms similar to those of Parkinson's disease. In the film, the individuals temporarily "awaken" from their catatonic state when a physician administers the drug L-dopa, which has long been used in Parkinson's disease treatment.

"Later, Kennie came into my office and said, 'You know, we could look to see whether influenza can affect Parkinson's disease,'" Smeyne recalls.

Intrigued by the prospect, Smeyne and his lab teamed with Webster and his staff to determine whether survivors of H5N1 avian influenza might suffer from long-term neurological problems.

The results were as tantalizing to scientists as Beluga caviar is to an epicurean.

"We found that one strain of H5N1 absolutely does impact the nervous system," Smeyne says. "It causes all kinds of pathology in the brain that you only see in Parkinson's and Alzheimer's diseases."

The threat posed by other viruses, including the current H1N1 pandemic flu virus, is still being studied. Early indications are that the H1N1 pandemic strain carries a low neurologic risk.

At a recent meeting of the Michael J. Fox Foundation for Parkinson's Research, Smeyne was encouraged by the response from the scientific community.

"People were saying that our work has shifted the entire paradigm of Parkinson's disease and that now there is a major interest in whether viruses could cause neurological disease," he says.

Bill of fare

The influenza study is the latest in an impressive progression of courses served up in an environment where scientists with seemingly divergent interests collaborate on projects that have applications for pediatric catastrophic diseases.

Smeyne is accustomed to explaining why Parkinson's—an incurable brain disorder that affects approximately 4.1 million American adults—is studied at St. Jude.

"While the hospital's mission is to treat children, our research goals encompass basic developmental mechanisms that aren't necessarily limited to childhood cancer," he says. "The mechanisms that cause Parkinson's offer us insight into a variety of diseases, as well as into pediatric and adult brain tumors."

Parkinson's disease occurs when nerve cells in a part of the brain called the substantia nigra are damaged or destroyed. These neurons normally produce a chemical called dopamine, which helps muscles function normally. Individuals with Parkinson's disease experience tremors, muscular stiffness and other movement problems.

"The brain is a miraculous thing," Smeyne says. "It has so much redundancy built in that you have to lose 70 percent of the neurons before you see your first, tiny symptom of Parkinson's. That's the great news. The bad news is there are not many neurons left to work with by the time you discover the disease."

Smeyne and his colleagues are determined to find a way to stop the process before symptoms appear. "We are trying to develop a blood test to do that now," he says.

A slice of pi

During the past decade, Smeyne has emerged as a leading Parkinson's expert. As a result of his investigations, Smeyne is convinced that both genetic and environmental factors play a role in the disease's development.

In 2004, his lab demonstrated that sustained aerobic exercise prevented cell death in the substantia nigra of adult mice whose brains had undergone damage from molecules called free radicals.

Smeyne also found that a protein involved in the antioxidant response, called glutathione S-transferase pi (GST pi), also plays a key role in protecting these same dopamine neurons from environmental toxins or by other stressful conditions that can lead to the formation of free radicals. When GST pi is reduced or missing, the nerve cells can die or stop producing dopamine, resulting in the development of Parkinson's disease.

Pièce de résistance

Smeyne says his investigations into the effects of oxidative stress caused by free radicals are an integral part of the hospital's mission.

"By studying Parkinson disease, we are learning more about free radical damage in the brain," he explains.

"The concept and understanding of free radical damage is a basic biological process," he continues. "For example, one mechanism in which chemotherapy works is by generating free radicals that then kill cancer cells. So, anything we learn studying the mechanism of free radical damage and detoxification in the brain could potentially be applied to the protocols we use to treat our patients."

For decades, most school children have learned about the food pyramid, which helped them remember the basics of healthy eating. Smeyne uses a similar pyramid analogy to explain the importance of his work.

"Basic research is the base of everything we do," he explains. "The patient is at the top of the pyramid. All the basic research leads up to translational research, which leads up to the patient. My research on Parkinson's disease is sitting at the base. We are not working on childhood cancer, but we are learning about free radical biology; we are learning about neuroprotection; we are learning about all of these things that are basic biology."

Then Smeyne offers the pièce de résistance: "Everything we learn about these molecular processes will eventually translate into therapy for patients." ●



"My group studies basic developmental mechanisms that extend far beyond childhood cancer," says Richard Smeyne, PhD (center), who takes a break with (from left) Developmental Neurobiology colleagues Shankar Sadasivan, PhD; graduate student Haeman Jang; Amar Pani, PhD; and Ané Korff, PhD.



BY AMANDA MCGEE ROBBINS

Teenagers show adults how to put the “fun” in fundraising.

When Sheri Shramek heard about the St. Jude Rally Against Childhood Cancer program, she knew she had to get involved.

The advanced art teacher at Clinton High School in Mississippi recognized the potential to involve students in an important cause. But she also had a personal stake in encouraging her school to join the St. Jude Rally program: Thirteen years before, she had lost a daughter to a brain tumor.

“She was 11 when she was diagnosed. She never went to St. Jude, but St. Jude created the protocol and told our doctors how to treat her,” Shramek says. “That’s the reason I jumped on this quickly.”

Now in its third year, St. Jude Rally encourages high school students to support St. Jude. The program, built around a letter-writing campaign and school spirit, was tested in 45 schools, raising \$300,000 its first year. In its second year, St. Jude Rally grew to 123 schools and raised \$550,000. This year the number of participating schools is estimated to exceed 150.

The core of St. Jude Rally involves high school students sending letters to family and friends and asking them to support St. Jude. But most schools incorporate additional events to build excitement and raise more funds. At Clinton, students rallied a couple of months before their annual powder puff football game. They held “penny wars” among the classrooms, raffled Adirondack chairs decorated by art club students and sold St. Jude

Rally T-shirts. At the school’s powder puff game, organizers announced that Clinton students had raised more than \$32,000 in their first St. Jude Rally.

“It was amazing how involved and excited everyone got,” Shramek recalls.

Students at Edwardsville High School (EHS) in Illinois know just how motivated kids can be to help other kids fight catastrophic illnesses. EHS was the program’s top fundraising school last year and received the Jerry Nicholson Award from the ALSAC/St. Jude Boards of Directors and Governors.

At Edwardsville, the letter-writing event is held during the last hour of the school day, and last year 800 students crowded into the school’s common area to participate. “I thought kids would just want to get out of sixth period, but they take this seriously and are really sending out letters and raising money,” says Ellen Marty, president of the school’s Medical Careers Club, which plans St. Jude Rally activities.

For EHS Principal Norm Bohnenstiehl, the program not only underscores the school’s commitment to community service but also reflects his personal dedication to St. Jude. As a high school student in the 1960s, he participated in the Teen Marches that raised money for the hospital. “What better thing can you do,” he asks, “than help children with childhood cancer?”

To learn more about St. Jude Rally Against Childhood Cancer, visit www.stjude.org/rally. ●



A Place of Their Own

BY ELIZABETH JANE WALKER

Jayla and Felicia Lee may share their toys and dress-up clothes. But when it comes to the “pink hospital,” each sister stakes her claim.

On a brilliant autumn afternoon, two little girls lie puddled in a patch of lawn, eyes sparkling, laughter buoyed aloft like a colorful balloon. Leaping to their feet, the sisters bound across the turf like happy puppies, running for no other reason than to feel the swirl of air across their skin, the warmth of sun on their faces.

Dashing along a sidewalk, Felicia Lee glances up at the maroon silhouette of a child emblazoned on a nearby sign. “That’s me!” she shouts, pointing at the logo for St. Jude



Children's Research Hospital.

The parents of Felicia and Jayla Lee respond with wry smiles. If the 5-year-old sees a resemblance to herself in the hospital's logo, that's perfectly understandable. After all, Felicia and her 6-year-old sister, Jayla, believe the hospital was created especially for them. And, of course, they're exactly right.

Double trouble

Jayla and Felicia were both born with a genetic disorder called neurofibromatosis type 1, or NF1. Not only does the disorder cause

tumors to grow on the nerves, but it also may cause heart problems, high blood pressure and developmental delays. A progressive disorder that occurs in about one in 3,000 to 4,000 Americans, NF1 is accompanied by a risk of optic pathway glioma, a tumor that occurs along the nerve that sends messages from the eye to the brain.

To monitor possible NF1 side effects, Frederick and his wife, Elnora, took their daughters for frequent checkups. During a routine appointment in June of 2008, an ophthalmologist jumped in surprise when she looked into Felicia's eye.

"She pulled the machine away and just looked at me," Elnora recalls. "She didn't say anything at first. She just kind of breathed deeply." Then the doctor uttered five ominous words: "I think I see something."

The family immediately visited a neurosurgeon, who noticed a thickening on the optic nerve of Felicia's sister, as well. The physician advised Frederick and Elnora to take both girls to St. Jude.

"My whole life changed in a split second," Elnora recalls. "I thought, 'Not one, but *two*? Are my children going to die? How much is this going to cost?' In my mind, I was trying to figure out how much money we had in our bank accounts, because I knew that they would do MRIs and other expensive tests. We had insurance, but everyone knows that some things are not covered."

Concerned about finances and reeling with shock, the couple took their daughters to St. Jude. As soon as possible, the Lees inquired about the cost. They were astounded when they learned that they would not have to empty their bank accounts to pay for treatment.

"They told us to relax—that we would have no out-of-pocket

medical expenses. It was really overwhelming," Elnora says. "It took a heavy weight off so that we could concentrate on our children."

Treating the whole child

At first, the tempo was frenetic as Frederick and Elnora juggled numerous appointments and tests for the two girls. "We were running back and forth," Elnora laughs. "My husband would be on one side of the hospital; I'd be on the other. Maybe we'd be able to meet for lunch; maybe not. But eventually it did smooth out."

St. Jude oncologist Ibrahim Qaddoumi, MD, explained to the couple that an optic pathway glioma is not located in the eye itself. The optic pathway begins at the point where the optic nerve extends from the eye; the nerve passes through the eye canal, crossing to the other side of the brain, extending around the temporal lobe and ventricle all the way to the cortex.

"Kids with NF1 are at risk for malignancies—mostly brain tumors—and the vast majority of those are optic pathway gliomas," he explains. "These children are even at high risk for some leukemia types. It's a really complicated disease."

Qaddoumi said that Felicia would receive about 18 months of chemotherapy for her brain tumors. Because Jayla's condition was not as severe—she had a suspicious lesion on her optic nerve—she would undergo frequent testing.

Christine Odom, a genetic counselor at St. Jude, helped the Lees better understand the genetic aspects of neurofibromatosis. Because Frederick also has the disorder, the couple had a 50 percent chance of each of their children developing NF1. That is exactly what happened. Although Jayla and Felicia inherited the disorder, their oldest daughter,



Jayla (at left) and Felicia Lee practice their culinary skills in a St. Jude waiting room.

Daubre, and Felicia's twin brother, Frederick Jr., were unaffected. "About 15 to 20 percent of children with NF1 will develop an optic pathway glioma," Odom says. "Kids with NF1 are also at lifelong risk of developing other cancers, so they must receive regular checkups throughout their lives."

Felicia has almost completed her chemotherapy regimen. Jayla undergoes testing every other month; thankfully her lesion has not developed into a tumor. At St. Jude the girls also receive physical therapy, speech therapy, occupational therapy and medications to offset the attention deficit disorder that is a hallmark of NF1.

"I worked with Jayla twice, but have worked with Felicia once a week," says Allison James, a speech-language therapist in Rehabilitation Services. "Felicia and I worked on articulation, her language skills, and her ability to correctly formulate sentences and answer questions."

As a former educator, Elnora

appreciates the fact that St. Jude clinicians also educate the parents about their children's condition. "It makes a difference that they take the time to talk to you and help you understand everything," she observes.

Because an optic pathway glioma grows slowly, it is sometimes classified as a benign tumor, says Pediatric Nurse Practitioner Liz Burghen. Although the tumor does not spread to other areas of the body, it tends to affect the patient's vision.

"Felicia does have some decreased vision, but it is minimal," Burghen says. For that reason, Felicia receives regular checkups in the St. Jude Eye Clinic. Because the body's hormones can also be affected by an optic pathway glioma, Felicia's condition is also monitored by the hospital's endocrinologists.

Parents helping parents

The Lees arrived at St. Jude three days after Elnora's ordination as a minister. "I was ordained, and then: Boom. Here I am. I realized I

couldn't ask, 'Why me?' Instead, I said, 'Why *not* me? Maybe I can help someone while I'm here.'"

Because she remembers the terror and uncertainty that she felt upon arrival at the hospital, Elnora is especially attuned to the stress that new families experience.

"She will actually notice new families and go talk to them on her own," Burghen says. "The child may not have the same condition that her children have, but she will mentor the parents and give them advice on navigating the hospital."

Elnora has noticed that when parents are overwhelmed, the child becomes anxious. "You can't freak out, because it makes it worse for the child," she says. "I try to help new parents understand that they need to be as positive as they can. That's when your faith really steps in. That's when you have to press through, say a little prayer and just get over it. The kids are watching you; they're listening to everything you say. So by being positive,

“My whole life changed in a split second. I thought, ‘Not one, but two? Are my children going to die? How much is this going to cost?’”

you help them to be positive, too.”

Elnora’s children seem to have inherited her optimism. Felicia and Jayla are known throughout St. Jude for their musical laughter, their energy, their enthusiastic embraces. “Felicia in particular is hilarious,” says Heather Bradley, RN. “And she travels at a run all the time.”

Like bees spreading pollen, the

Lee girls distribute hugs throughout the hospital. Hugs for the security guards, the nurses and the cafeteria workers; for the photographers and the doctors and the therapists. If the girls can’t reach high enough, they are apt to hug staff members’ knees. “Felicia and Jayla are sweet, lovable and have the cutest smiles,” says Jackie Gilliam, who works in

Assessment Triage. “It’s a pleasure to be a part of taking care of such wonderful girls.”

“They have more energy than the law allows,” Elnora responds with a grin.

Like typical sisters, Jayla and Felicia have a mercurial relationship—best friends one moment; competing for attention the next. “This is *my* hospital, not yours,” Felicia tells Jayla. “You just come here, but this is *my* hospital.” But Jayla knows the hospital was created especially for her.

And, of course, they’re both exactly right. ●



For Felicia, laughter, hugs and “high-fives” are requisite components of any checkup with Ibrahim Qaddoumi, MD, of Oncology and Pediatric Nurse Practitioner Liz Burghen.

By JANICE HILL

SETH DIXON



Pharmaceutical Sciences Chair Mary Relling, PharmD (center), and her colleagues study how genome variability influences a child's response to cancer chemotherapy. Much of Relling's work occurs in a pharmacogenomics laboratory dedicated to the memory of Joan Gignac.

For a quarter of a century, Roy and Joan Gignac gave generously to St. Jude Children's Research Hospital in thankfulness for the health of their children and the success of their business.

Joan died in 2008, and last year Roy honored her life in a way that reflected her values and selfless spirit—with a generous gift to support the pioneering research conducted by Pharmaceutical Sciences Chair Mary Relling, PharmD.

Last summer, seven of the Gignacs' nine children, 21 grandchildren and five other family members accompanied Roy to Memphis to dedicate the Joan F. Gignac Pharmacogenomics Research Laboratory and to see firsthand what a lifetime of generosity can accomplish.

"We really had no idea what our parents had done for St. Jude over the years until our visit," said his son Mark.

The Gignacs' gifts to St. Jude began when they responded to a telethon shortly after their family business, EDS, became a successful manufacturer of power supplies and battery chargers for the medical and industrial field.

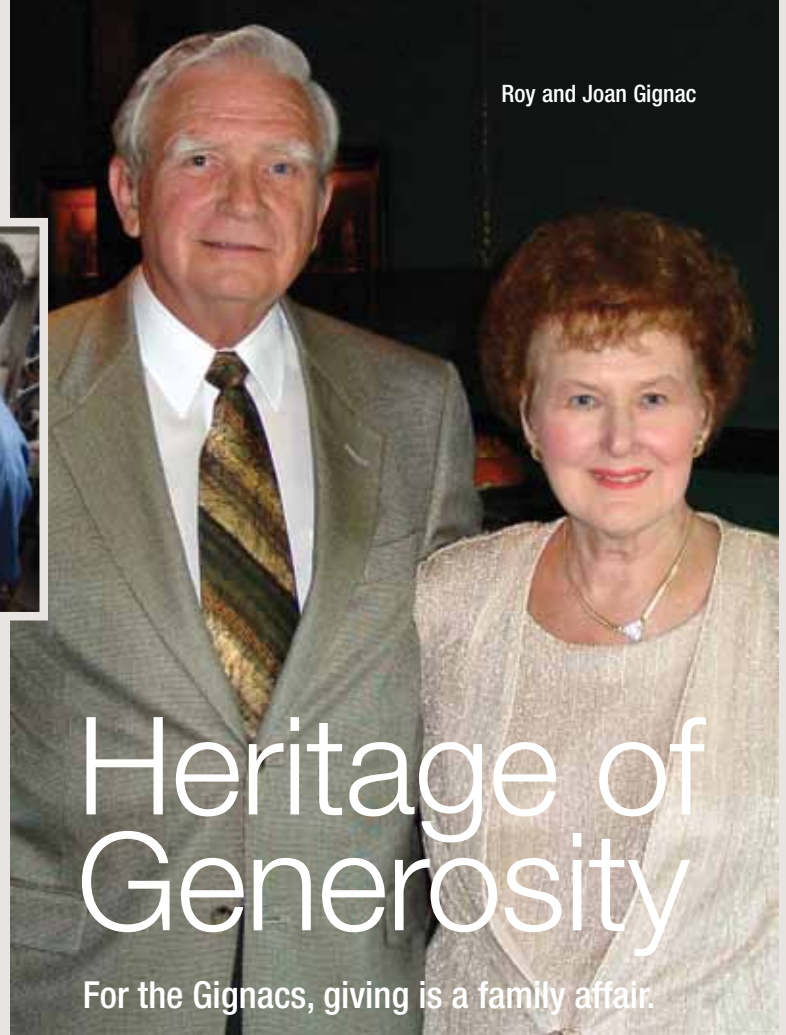
"Sometime after our first gift, a lady from St. Jude called and asked for donations to purchase a prosthetic arm for a patient who was a young draftsman," recalls Roy, who was an engineer.

"How much is the cost of the arm?" he asked the caller. When he learned it was approximately \$25,000, Roy said, "How about we give you the whole amount?"

The woman told Roy he was the first person she had called who had agreed to give. "That was when we truly became involved," Roy says.

As their business grew, the Gignacs contributed

Roy and Joan Gignac



Heritage of Generosity

For the Gignacs, giving is a family affair.

to many causes, including St. Jude. Then, about 15 years ago, they decided to make larger gifts to fewer organizations where they would have the greatest impact.

St. Jude was one of their choices, Roy said, because "like me and my business, St. Jude is goal oriented, careful with expenditures and totally dedicated to serving people."

Among their major gifts was an endowment created 10 years ago for the Joan and Roy Gignac Endowed Chair of Pathology and Laboratory Medicine, held by James Downing, MD, the hospital's scientific director.

Roy brought his family to the dedication of Relling's lab to encourage them to support the hospital. The idea worked. Two daughters and a granddaughter subsequently hosted St. Jude fundraising events.

Now remarried, Roy and his wife, Sophia, have a combined family of 16 children, 38 grandchildren and 10 great-grandchildren. Some of Sophia's children also have caught Roy's enthusiasm for St. Jude.

He is proud that the family tradition of philanthropy continues.

"My children all make their own living," he says. "They know they will receive something from me, but they also know it is important to give to true needs, like those of the children of St. Jude." ●



Ride to Recovery

BY MIKE O'KELLY

With the help of St. Jude, teenage equestrian Elizabeth Walters returns to competition.

Riding high atop her horse, Montini, Elizabeth Walters was accustomed to galloping over grassy terrain and vaulting over fences, fallen logs and watery pits. From her position in the saddle, she had a commanding view of the obstacles strewn before her.

“Arriving at St. Jude had a very calming effect. I felt like we were not alone from the moment we entered the front gate.”

At age 15, Elizabeth had qualified twice for the national competition in the equine sport of three-day eventing, but her biggest hurdle occurred when she discovered that she had non-Hodgkin lymphoma.

Elizabeth's teenage world had been populated by school, friends and horseback riding, but she was quickly introduced to a new environment where unfamiliar words such as chemotherapy and biopsy were part of her vocabulary. As an uncertain future loomed, and frightened at the possibility that she might never ride again, Elizabeth and her family turned to the staff at St. Jude Children's Research Hospital.

Ominous hoofbeats

Elizabeth was introduced to horses and riding through her mother, Jeannie Rogers, who has always had a love for the sport. Elizabeth started competing in minor events at the age of 7, and she began participating in more serious competitions a few years later. Her primary competition is eventing, the same equestrian sport that is in the Olympics. It is a grueling sport that consists of three phases: dressage, show jumping and cross country. The three-day competition requires riders to be physically strong, technically adept and closely bonded with their horses.

In dressage, also known as “horse ballet,” riders are given a test they must memorize and then perform for a judge. Show jumping consists of about a dozen jumps in an enclosed arena. Riders are timed and penalized for knocking down poles. Elizabeth's favorite event—cross country—is performed in an open field and incorporates large jumps over natural obstacles.

While practicing cross country in September of 2007, Elizabeth fell from her horse and compressed three vertebrae. She felt severe back pain for several months, which eventually subsided, but the pain returned the next summer. The back pain was worse than before. She now felt invisible bruises on her body and began having trouble breathing at night.

Elizabeth and her family first attributed the back pain and bruises to the riding accident and dismissed the breathing difficulties to her longtime asthmatic condition. Three physicians believed the pain was caused by the jarring Elizabeth's body took while riding.

Not satisfied with the physicians' diagnoses, Jeannie called the doctor who had cared for Elizabeth a year earlier to see if he could perform an X-ray. The X-ray revealed a shadow; a CT scan the next day revealed a mass was pressing against Elizabeth's heart and lungs. The physician suspected the mass was cancerous and performed a biopsy the next day. The mass was found to be non-Hodgkin lymphoma.

“My first thought was that everything had been going so well for me. I had been competing on my horse, having a great time in school, and it was like my world completely stopped,” Elizabeth says. “I was so worried about not getting better ever or taking years to get better.”

Jeannie shared in Elizabeth's disbelief. She had a limited family history of cancer and was intently focused on watching her daughter compete at the next big event.

“I was scared to death because I didn't know anything about it. We didn't know what to do or

where to go,” Jeannie says.

For guidance, Elizabeth's father, Mims, turned to a family friend who was familiar with St. Jude. Elizabeth's doctor quickly referred her to St. Jude and she was accepted for treatment.

Entering the arena

“Arriving at St. Jude had a very calming effect,” Jeannie says. “I felt like we were not alone from the moment we entered the front gate.”

At St. Jude, Elizabeth was enrolled in a protocol for her type of non-Hodgkin lymphoma that consisted of five rounds of aggressive chemotherapy designed to shrink the mass. Non-Hodgkin lymphomas are a diverse group of cancers that are derived from white blood cells known as lymphocytes, which are divided into two groups—B cells and T cells. Elizabeth had a lymphoma that was a subcategory of mature B-cell lymphoma. Her type, termed primary mediastinal diffuse large B-cell lymphoma, accounts for about 2 percent of all lymphomas and is named because it originates in the mediastinum, the area around the heart and near the chest bone. People with this type of cancer often have trouble breathing because the mass may press against the trachea, limiting the amount of air that passes through.

Most people who develop this type of lymphoma are younger women, says Elizabeth's attending physician, Monika Metzger, MD, of Oncology. Metzger recalls a vast contrast between her first meeting with Elizabeth and Jeannie and the second time they met.

“Initially, she and her mom were very frightened. They were both in

tears,” Metzger says. “Then we discussed the treatment, and it was just amazing. She was a different person.”

A wild ride

The aggressive chemotherapy had its side effects as Elizabeth lost most of her hair and felt weak or sick much of the time. Because of the intensity of the seven-day treatments, Elizabeth stayed in the hospital, with Jeannie alongside her during their inpatient stays. The time between treatments varied from one to two weeks. Elizabeth returned home to Alabama between each round.

“At first I was terrified about my hair,” Elizabeth says. “Then I realized that it was just going to happen, and it never affected me much.”

What did affect Elizabeth was her inability to spend time with her friends and horse while she was at home. She desperately wanted to visit Montini but was often too weak to get out of the car at the barn. Elizabeth would settle for stroking his head through the open car window.

Mother and daughter used the time spent together during inpatient stays to watch TV shows, play video games and talk. One inspirational routine they shared was peering out the window from the Linda R. Hajar Family Resource Center on the second floor of the hospital’s Patient Care Center. As they watched patients and families walk to and from the hospital entrance, they crafted stories



Elizabeth Walters meets with Monika Metzger, MD, of St. Jude Oncology during a regular checkup.

of healing and hope about the people who passed below the window.

Before Elizabeth's fifth and final round of chemotherapy, a scan showed what appeared to be a residual mass in her mediastinum.

"At that point, we like to see our patients in complete remission, so we needed to do a biopsy again to make sure that this was not active disease," Metzger says. "Fortunately, it revealed that it was

just inflammatory tissue—and not active disease—which meant that we could continue with her last course of chemotherapy."

Horse power

Elizabeth finished her chemotherapy in early February of 2009, just two months after arriving at St. Jude. She looked forward to regaining her strength and returning to the activity she loved the most.

"It was very slow at first. I was really weak," says Elizabeth of her return to riding. "I lost every bit of muscle that I had, but it was so great to get on my horse for the first time. After a week of riding, it was just like nothing had ever happened."

In June of 2009, Elizabeth competed in her first event after her treatment, finishing fourth out of 21 riders in her division. A few weeks after the event, Elizabeth began experiencing chest pain. A scan done by her local oncologist revealed a slightly enlarged mediastinal mass. The mass was removed through a procedure called a thoracotomy at St. Jude, which involved an incision in the chest. The mass was found to once again be inflammatory tissue.

Elizabeth has again returned to competition with a fresh outlook on the world thanks to the treatment and care she received at St. Jude.

"Once I was at St. Jude for a little while, I knew it was the right place," Elizabeth says. "Everyone was so nice. Being there, it really made it all better." ●

Non-Hodgkin Lymphoma

Non-Hodgkin lymphomas (NHLs) are tumors of the peripheral lymph nodes, thymus or abdominal organs, such as the bowel, but can appear in other sites. These tumors differ substantially from lymphomas seen in adults. In children, NHL may involve bone marrow, blood, skin and the central nervous system.

Approximately nine in 1 million children under age 15 will develop non-Hodgkin lymphoma each year.

About 80 percent of children with NHL can be cured; the cure rate for children with localized

stages of the disease is approximately 90 percent.

St. Jude researchers are looking for better ways to refine treatment for lymphoma according to the extent of the disease and the tissue subtype. Specific therapies are being developed to target against cell surface antigens expressed by lymphoma cells or their molecular lesions. Scientists are also conducting molecular studies to search for the mechanisms of the development of lymphoma.



Form Reveals Function

A focus on protein structure offers insight into the roots of disease and new treatments.

BY MARY POWERS

In a windowless room the size of a large walk-in closet, the hunt is on. A half dozen St. Jude Children's Research Hospital scientists and graduate students stare at four computer monitors arranged in a semicircle. The researchers' voices are barely audible above the hum of electronic equipment as Daniel Scott, PhD, uses a computer mouse to manipulate a robotic arm two time zones away.

Scott steers the arm to load individual crystals of purified protein into a machine called a synchrotron. The crystals were grown in the St. Jude Structural Biology laboratory of Brenda Schulman, PhD, where Scott works as a research specialist. Just days earlier, the crystals were frozen in liquid nitrogen and shipped to the U.S. Department of Energy's Lawrence Berkeley National Laboratory in California.

Structural biologists use this mammoth, donut-shaped synchrotron to generate high-energy X-rays ideal for measuring the distance among atoms in crystals of biological molecules. Sitting in Memphis, Scott directs the X-rays through one crystal after another in a process known as X-ray crystallography.



The mission and resources at St. Jude are a perfect fit for Brenda Schulman, PhD, (at right), who discusses a project with David Miller of Structural Biology. A Howard Hughes Medical Institute (HHMI) Investigator, Schulman was also the hospital's first Pew Scholar in the Biomedical Sciences.

Those gathered around him are looking for a sign on the computer screen—in this case dots known as a diffraction pattern—that a crystal will stand up to the X-rays well enough to reveal a structure. Each diffraction pattern is as unique as its protein template. Scientists like Schulman use the patterns to determine a protein's structure on an atom-by-atom basis. From this information come new medicines or a new understanding of how a misstep in a single protein deep inside a cell gives rise to cancer or other diseases.

A closer look

With luck, the crystals will yield enough data to keep investigators working all night. Determining a protein's structure sometimes requires collecting thousands of diffraction patterns. "The biggest problems take the most work," Schulman says. "Those are the problems I like the most."

Structural biology is a field that draws researchers from across the scientific spectrum. They share an interest in how form—a molecule's 3-D shape—determines function.

"We take apart proteins to understand how they work. Only once you know the three-dimensional structure of a molecule can you understand what is going wrong with it," says Stephen White, DPhil, Structural Biology chair. White and his Structural Biology colleague Eric Enemark, PhD, also rely heavily on X-ray crystallography in their research.

In their quest, structural biologists collaborate with scientists from other disciplines and wield tools such

as X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy and computer graphics. X-ray crystallography relies on frozen crystals but NMR spectroscopy allows scientists to study proteins as they move and interact. The technique combines radio waves with powerful magnets and computers to yield structures.

St. Jude has X-ray crystallography diffraction equipment as well as NMR spectroscopy. Investigators also have regular access to a synchrotron called the Advanced Photon Source at the Argonne National Laboratory near Chicago, Illinois. St. Jude belongs to a consortium of institutions that built and now fund the device.

Attracting widespread attention

Schulman's research focus is a small protein known as ubiquitin. A key regulator of a variety of cell functions, ubiquitin is part of a pathway that cells use to get rid of damaged, improperly assembled or unneeded proteins.

Schulman is particularly interested in a handful of enzymes that attach ubiquitin to a molecule slated for elimination. "Defects in these pathways have been widely associated with diseases such as cancer, neurodegenerative disorders and viral infections," she says. The list includes such childhood cancers as brain, eye and kidney tumors.



Grace Royappa of Structural Biology uses the nuclear magnetic resonance (NMR) spectrometer at St. Jude. The structural and dynamics information gleaned from NMR studies helps scientists understand the function of different proteins in cells.



“Finding the conditions that form a crystal is like looking for a needle in a haystack,” says David Duda, PhD, of Structural Biology. Duda prepares to examine a tray of proteins to check whether crystallization is occurring. Scientists need the crystals to help determine a protein’s structure.

Co-director of the St. Jude Cancer Center’s Molecular Oncology Program, Schulman also holds joint appointments in the Structural Biology and Genetics and Tumor Cell Biology departments. But her work has attracted attention far beyond St. Jude. In 2002, she was the first faculty member to be named a Pew Scholar in the Biomedical Sciences by the Pew Charitable Trusts. Since then, three more St. Jude scientists have received the honor.

A few years later, she was named a Howard Hughes Medical Institute (HHMI) Investigator. Founded by the late industrialist Howard Hughes, HHMI promotes scientific creativity by providing select investigators

with long-term, flexible funding.

Schulman is one of three St. Jude faculty with links to Hughes. HHMI Investigator Charles Sherr, MD, PhD, also holds the hospital’s Herrick Foundation Chair in Genetics and Tumor Cell Biology. Michael Dyer, PhD, of Developmental Neurobiology is an HHMI Early Career Scientist.

Dr. William E. Evans, St. Jude director and CEO, says the hospital benefits enormously from having HHMI investigators on the faculty.

“Hughes provides outstanding people with resources needed to do their best work, and this fits perfectly with the overall strategy of St. Jude,” he says. “Science is a collaborative enterprise. Our Hughes investigators are well-connected internally to enhance our collaborative culture and are well-connected within the HHMI, linking us to a broad array of outstanding scientists.”

Expect the unexpected

Schulman says the HHMI support gives her freedom to pursue unexpected results. One example is research into the regulation of a family of enzymes called cullin-RING ligases, or CRLs, which transfer ubiquitin. Originally, David Duda, PhD, a research specialist in Schulman’s lab, conducted an experiment on a CRL for a different reason. An unanticipated result led to a 2008 paper in the journal *Cell* showing how CRLs change their shape in order to promote ubiquitin transfer to targets. Duda was a lead author of that report. CRLs’ tasks include controlling the cell’s entrance into cell division. Since uncontrolled cell division is a hallmark of cancer, researchers hope a better understanding of the complex

will lead to new cancer-control strategies.

Schulman credits the hospital’s Human Resources department and Academic Programs office with helping her recruit outstanding postdoctoral fellows and laboratory staff. “A lab is only as good as the people in it,” she explains.

Back in the computer room, it is a good night for Schulman and her staff. By the time she leaves shortly before noon the next morning, she has the first hints of two new protein structures. They need additional work to provide the necessary fine detail, but it is progress. “We will solve them,” she says. ●

Perspective

BY MARTIN YAN

Food for Thought

A world-renowned chef ponders the children and mission of St. Jude.

In May of 2009, I had the opportunity to visit St. Jude Children's Research Hospital. Chefs in the hospital's Kay Kafe routinely use my recipes to prepare a variety of Asian dishes for St. Jude patients, families and staff.

During a cooking demonstration, I invited a couple of young patients to cook alongside me on stage. What impressed me was the energy and enthusiasm in that place. I counted at least half a dozen future cooking show hosts and hostesses in that room!

We are accustomed to learning from our elders. This is especially true in Asian culture, where the elders are respected and revered. After I visited St. Jude, I came away with a totally new impression on age and learning. I believe that we can all learn a great deal from many of these children who never give up and challenge themselves.

At St. Jude, I learned much about courage and hope. These are things that I have not learned from teachers who are older and more experienced. It was truly a humbling experience.

During my visit to the hospital, I was struck by the wholesome and visitor-friendly atmosphere. It was so homelike; St. Jude did not look or feel like a hospital at all. The employees really go out of their way to create an environment that, for

patients and visitors alike, feels like a home away from home, instead of a cold and impersonal medical facility.

Before I went to St. Jude, I was not aware that all children at the hospital are treated without regard for their ability to pay. When I found that out, I was both impressed and moved. There is nothing more important in life than taking care of our most valuable asset—our children.

Speaking as a parent, I know that most of what I do each day I do for my children. I am sure most parents feel the same way. While we support and care for our own children privately, we don't seem to do enough on a societal level. The truth is, there are still many children out there who are in need of

help, and we can do a better job to make sure that they receive it.

St. Jude is a pioneer in the study and treatment of pediatric catastrophic diseases. It deserves to be supported by us. We are so used to saying that our children are our top priority. Let's put our money where our mouth is.

The celebrated host of more than 3,000 cooking shows broadcast worldwide, certified Chinese Master Chef Martin Yan has hosted the PBS cooking show Yan Can Cook since 1982. His diverse talents have found expression in 30 cookbooks, including his latest, Martin Yan's China. He is also a popular public speaker and a restaurateur. ●



Chef Martin Yan and St. Jude patient Danielle LaCompte demonstrate proper chopstick use in the hospital's Kay Kafe.

ANN-MARGARET HEDGES



Anna – acute lymphoblastic leukemia

Your legacy can be her future.

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Target House turns 10

In September 2009, Target House celebrated its 10th year of providing St. Jude patients and families with a home-away-from-home during treatment. Celebrity friends such as Olympic gold-medalists Shaun White and Scott Hamilton, actress Kimberly Williams-Paisley, singer Amy Grant and designer Sean Conway celebrated the event with patients, families and members of the Thomas family. Olympic snowboarder Shaun White (at right) takes a break from the festivities to play foosball with St. Jude patient Kevin Freeman.

PETER BARTA



Finding cures. Saving children.