St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder

Promise

Autumn 2005

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

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

Promise.

St. Jude Children's Research Hospital, Memphis, Tennessee

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St. Jude Children's Research Hospital's mission is to find cures for children with catastrophic diseases through research and treatment.

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Promise

Features

Highlights

Perspective

On the cover: St. Jude patient Bekah Lloyd. Photo by Laura Hajar. Thanks to Sanga School of Horsemanship for their assistance with this photo.

Highlights

Responding to Katrina

St. Jude staff members quickly mobilized to assist families in the Gulf Coast area after Hurricane Katrina ravaged that part of the country in August. The hospital assisted with family care for non-St. Jude pediatric cancer patients in the hurricane-damaged areas of New Orleans.

Those patients were referred to St. Jude affiliate clinics at Our Lady of the Lake Regional Medical Center, in Baton Rouge, and the Louisiana State University, Department of Pediatrics, in Shreveport. A team of St. Jude physicians, nurses, pharmacists and social workers took medical supplies to the Baton Rouge affiliate, where the health care workers also helped evaluate patient and family needs.

Some patients from Baton Rouge were transported to Memphis in private planes provided by individuals for that purpose.

JERE PARDEK

Patients from the Gulf Coast region arrive in Memphis as part of the hospital's Hurricane Katrina relief effort.

Block that gene

Drugs that block the enzyme Odc prevent the onset of cancers that would otherwise be triggered by a family of cancer-causing genes called *Myc*, according to St. Jude investigators. Scientists showed that disabling Odc disrupts the ability of *Myc* genes to speed up cell division. Investigators showed that disrupting just this one target delays the onset of cancer in a laboratory model of human Burkitt lymphoma.

The discovery of the link between Odc and *Myc* in tumor development is important because *Myc* genes are activated in up to 70 percent of human cancers. A drug that disrupts their activity might therefore prevent or slow the development of a wide variety of cancers. John Cleveland, PhD, of Biochemistry was senior author of a report on this work that appeared in the May 2005 issue of *Cancer Cell*.

Royal Society fellow

Tom Curran, PhD, chair of Developmental Neurobiology, has been elected to the Fellowship of the Royal Society—the United Kingdom's national academy of science. Two other faculty members, Nobel Laureate Peter Doherty, PhD, and influenza expert Robert Webster, PhD, were previously elected to the society. Membership in the Royal Society is said to be among the highest accolades a scientist can attain, short of a Nobel Prize.

Oh, baby—what a discovery

Treating babies who have sickle cell anemia (SCA) with oral liquid hydroxyurea may prevent the onset of long-term complications triggered by this disease, according to results of a preliminary study by St. Jude investigators.

The onset of damage caused by SCA can occur as early as three months after birth. Starting treatment before those complications begin could significantly reduce the chance of organ damage and premature death. Winfred Wang, MD, St. Jude Comprehensive Sickle Cell Center director, was senior author of the paper, which appeared in the online edition of *Blood* in June 2005.

A switch in time

Cells control mitosis (cell division) by assembling a biochemical switch to block it or by disassembling the switch to trigger it, according to investigators at St. Jude and the Technical University of Munich.

Researchers found that when the switch called SCF-NIPA is intact, levels of an enzyme called cyclin B1 drop, preventing the enzyme from activating a third protein called Cdk1. SCF-NIPA thus prevents the cell from dividing by interfering with the activity of the Cdk1 and cyclin B1 proteins.

If a cell divides prematurely, the result could be two abnormal cells. This discovery helps explain how cells delay mitosis until the appropriate time. Stephan W. Morris, MD, and Hiroyuki Kawaguchi, MD, PhD, of Pathology and Hematology-Oncology departments, co-authored a report on this work, which appeared in the July 2005 *Cell*.

Arf and eye development

A gene known for its role in preventing cancer also prevents excessive growth of blood vessels in the developing eye, according to St. Jude investigators.

The *Arf* gene prevents buildup of cells called pericytes, which nurture the growth of certain blood vessels in the eye during embryonic development, the researchers said. *Arf* also works with a gene called *p53* to trigger suicide in cancerous cells. But in the eye, *Arf* works through a second mechanism, independent of *p53*. The discovery that *Arf* also restricts blood vessel growth in the eye of the embryo was surprising, says Stephen Skapek, MD, of St. Jude Hematology-Oncology. Skapek was senior author of a report on this discovery that appeared in the August 3, 2005, issue of *The EMBO Journal* of the European Molecular Biology Organization.

It Takes a TEAM to Make a Touchdown

Thanks to the St. Jude Neurobiology and Brain Tumor Program, victory is within reach for kids with medulloblastoma.

Quarterback Tyler Rewis relies on a team of researchers and clinicians in the St. Jude Neurobiology and Brain Tumor Program to vanquish a brain tumor called medulloblastoma.

Tyler Rewis is no different than any other quarterback. He relies on his teammates to thwart the burly opponents who are intent on tackling him. But one thing sets this 11-year-old apart from other quarterbacks. Much of Tyler's success is due to another team—a group of researchers and clinicians at St. Jude Children's Research Hospital.

When Tyler began complaining of headaches in the fall of 2003, his mom assumed he had sinus problems. But Diane Rewis soon learned that Tyler had a tumor in the part of the brain that gives him the coordination he needs to run plays and intercept passes. A surgeon offered Tyler's family some sage advice. "He told us that if it were his child, he would take Tyler to St. Jude," recalls Diane. "I said, 'Well, then that's where we'll go.'"

When they arrived in Memphis from Georgia, the Rewis family learned that a group of scientists and clinicians working in an area called the Neurobiology and Brain Tumor Program (NBTP) would run interference for the

By Marc Kusinitz, PhD
and Elizabeth Jane Walker

young quarterback in his attempt to beat medulloblastoma.

Planning the plays

The success of the NBTP depends on exquisite teamwork by scientists and clinicians across the institution. Led by Tom Curran, PhD, of Developmental Neurobiology and Larry Kun, MD, of Radiological Sciences, the NBTP is one of the largest pediatric brain tumor programs in the country. NBTP can rally a highly experienced, multidisciplinary team of health care specialists on behalf of children like Tyler.

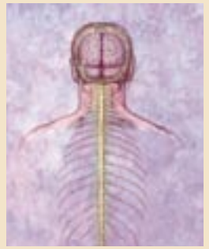
Researchers in the program are trying to discover changes in the genes and proteins that are responsible for initiating and guiding normal development of the nervous system. These scientists are also trying to find out what happens when things go awry. Meanwhile, clinicians are developing and testing new therapies based on drug treatments and irradiation to improve treatment of central nervous system tumors. A third group is investigating ways to improve intellectual and learning abilities among long-term survivors of pediatric brain tumors.

Bench to bedside

As leader of the NBTP's Fundamental Neuroscience group, Curran has made significant contributions to understanding the molecular (protein) signals that drive the development of medulloblastoma, the most common malignant brain tumor in children. Curran recently showed that a drug called HhAntag could block a key signal driving medulloblastoma, and reverse this cancer in a laboratory model of the tumor. The finding could lead to development of a relatively non-toxic, oral medication that increases the likelihood of curing medulloblastoma, while reducing long-term side effects.

Led by Amar Gajjar, MD, of Hematology-Oncology and Richard Gilbertson, MD, PhD, of Developmental Neurobiology, the NBTP's Translational Research Group adapts discoveries made in the laboratory into life-saving and less-toxic treatments for children.

Gilbertson and his colleagues discovered an overabundance of a protein called ERBB2 in children who have advanced metastatic (spreading) medulloblastoma and a relatively poor outcome. Gilbertson's team also showed that a test for ERBB2 in the tumor cells might help doctors identify children who need a novel approach to treat their tumors; children without this ominous protein might benefit from a milder course of treatment that minimizes radiation's long-term effects. In addition, these scientists have opened a unique clinical trial in which patients with recurrent brain tumors that express ERBB2 will be treated with a new drug that inhibits the protein's activity.



NBTP: Looking beyond medulloblastoma

The Neurobiology and Brain Tumor Program (NBTP) is a dynamic collaboration between basic scientists and clinicians battling many kinds of brain cancer.

In an effort to reduce side effects, the NBTP is also pioneering the use of 3-D radiation treatments in children with brain cancer, a program headed by **Thomas Merchant, DO, PhD,** of Radiation Oncology. Although irradiation is one of the most effective therapies for children with brain tumors, physicians have often hesitated to use this potentially life-saving therapy due to effects on children's cognitive development and academic performance. But St. Jude can now give many children technologically sophisticated radiation therapy that seems to reduce or eliminate the impact on cognitive development.

Merchant took a technique used to treat adult cancers and adapted it for children. The technique combines CAT scans and MRI to create pictures that a computer then turns into 3-D images of the tumor in the brain. By combining these images with computer-controlled radiation beams and meticulously positioning the treatment table on which the patient lies, radiation hits the tumor from numerous precisely calculated angles. This process obliterates the cancer and relatively spares healthy tissue. The team's experience and advancing technology make local irradiation a safer, more effective intervention for many types of childhood brain tumors.

Breakthrough studies require an improved understanding of the defects in cancer and appropriate models for testing novel drugs. Here are a few other NBTP researchers who are doing just that:

- **Suzanne Baker, PhD,** of Developmental Neurobiology is developing new models to study the function of cancer-causing genes in normal nerve growth and cancer development in the brain.
- **Peter McKinnon, PhD**, of Genetics and Tumor Cell Biology and his colleagues study the ability of cells in the nervous system to repair DNA damage and how disruption of these responses leads to brain cancer.
- **James Morgan, PhD**, of Developmental Neurobiology studies genes that control the delicate balance between nerve cell death and survival in both the adult and developing brain. In Morgan's laboratory, researchers study genes that contribute to disorders in which there is excessive nerve cell death in adults, such as Parkinson's disease, as well as medulloblastoma where the life-death balance is tipped in favor of cell survival during childhood.
- **Gene Reddick, PhD**, of Radiological Sciences uses sophisticated magnetic resonance imaging to measure changes in white matter, the complex highways connecting all key parts of the brain. This process allows him to quantitate treatment-related effects in correlation with both radiation delivery and cognitive (learning) status.

SETH DIXON

Tyler Rewis returns to St. Jude for checkups every three months. While he's undergoing tests to monitor his eyesight, hearing or lung capacity, a multidisciplinary team of researchers and health care specialists are working together to discover ways to improve treatment for him and other children with brain tumors. The hospital's Neurobiology and Brain Tumor Program is one of the largest pediatric brain tumor programs in the nation.

Medulloblastoma therapy

Gajjar and Gilbertson also head the Medulloblastoma Research Group, which offers cutting-edge therapies based on the latest discoveries made at St. Jude. One ambitious clinical trial (SJMB03) seeks to develop genetic profiles of medulloblastomas that can predict how well an individual's tumor will respond to therapy. Projects are designed to find safer and more effective ways to help physicians tailor therapies for individual patients and increase the success rate of treatment.

NBTP also benefits from a program that turns laboratory discoveries into new investigational drugs. This drug discovery program, in place at St. Jude for the past two decades, served as the model for a national initiative funded by the National Cancer Institute. Designed to expand the number of drugs screened against childhood cancers, the program is being led by Peter Houghton, PhD, of Molecular Pharmacology.

And St. Jude treatment doesn't end with the last day of anti-cancer therapy. A team of researchers and clinicians in Behavioral Medicine study new psychological, pharmacological, and educational therapies aimed at minimizing learning problems among long-term survivors of brain cancer who are treated with wide field irradiation. In collaboration with Shawna Palmer, PhD, of Behavioral Medicine, SJMB03 is the nation's first clinical protocol to adapt a randomized study design to a program evaluating long-term reading skills.

From test tube to the end of treatment, NBTP is creating new knowledge and saving the lives of children with brain tumors. Tyler Rewis is a shining example of that effort. An academic honor student, the sixth grader spends his free time playing baseball, swimming, fishing and playing video games with his buddies. And—thanks to the efforts of the NBTP—Tyler knows that when he grows up he may just have a chance to play football for his favorite team, the University of Georgia Bulldogs. Now, that's teamwork at its best.●

JOHN ZACHER

A Conversation with Marlo Thomas about

Thanks and Giving

Marlo Thomas, national outreach director for St. Jude, discusses the program that encourages consumers to show their thanks for the children in their lives who are healthy while giving to those children who are not.

Last year, the *Thanks and Giving* campaign launched with appearances on the *Today* show and other network broadcasts, a book and CD from you, and many retailers joining in the dream of your father. What can we expect from this year's campaign?

This year's *Thanks and Giving* campaign builds on the tremendous response and momentum created by our success in launching the program last year. Once again, people will see us everywhere this holiday season—on television and in their favorite magazines and newspapers, in movie theaters, on American Airlines flights, on the Internet, and when they're in their favorite stores and malls. Our book and CD, *Thanks & Giving All Year Long*, are being reissued. They feature joyous—and sometimes hilarious—stories and songs about giving, sharing and family holidays from such contributors as Jennifer Aniston, Tiger Woods, Sheryl Crow and Kermit the Frog. All proceeds go to St. Jude, of course.

An important key to our campaign is that we are creating a *national* annual tradition the day after Thanksgiving. We remind shoppers to give thanks for the children in their lives who are healthy and to give to those who are not…so that one day all children will be healthy. The great support and enthusiasm of our corporate, retail and media partners is dramatically raising public awareness that cutting-edge research at St. Jude benefits children and families in every community in this country and around the world.

Which partners have returned this year?

We're thrilled to report that our original partners are returning enthusiastically—and as others have seen the heartfelt response of shoppers to *Thanks and Giving*, they've been eager to join us. The list includes CVS/pharmacy, Domino's Pizza, Kay Jewelers, Sears, 7-Eleven, Target, The Walt Disney Co., Williams-Sonoma Inc. and many others—some of the country's most respected brands. (To see a complete list, visit *www.stjude.org*.)

How will retailers ask customers to support St. Jude?

As people do their regular holiday shopping, they can give to help save children's lives by adding donations at the cash register or by purchasing special merchandise that benefits St. Jude. Even as they prepare for their own holiday celebrations, they'll be participating in our vital work of finding cures and saving children.

Celebrities were heavily involved in last year's *Thanks and Giving* effort. What about this year?

Celebrities bring excitement, star power and attention to what we do. It's a way for them to use their talents to give thanks and to help advance our life-saving work. When my father started St. Jude, the stars of his time—Frank Sinatra, Bob Hope, Sammy Davis Jr. and Ella Fitzgerald—helped him raise the funds that built the hospital. Now the stars of our generation have become part of the St. Jude family. Antonio Banderas, Faith Hill, Queen Latifah, Sarah Jessica Parker, Ray Romano and Robin Williams will all be with us this year as part of our TV spots and movie trailer. Their involvement plays a huge role in the visibility and impact of *Thanks and Giving*.

***Thanks and Giving* seems to combine the best of corporate and grass roots giving. How has this helped increase support and awareness for the hospital?**

Thanks and Giving has two vital roles crucial to the future of St. Jude. One is financial support for our groundbreaking research and treatment. We've become the third-largest health care charity in the United States, and our success is built on public support. *Thanks and Giving* creates a broad national public outreach at a key time of the year.

SETH DIXON

St. Jude patient Lauren Lewis and her mom, Benita, shop at Pottery Barn, one of the hospital's Thanks and Giving partners.

Thanks and Giving also raises national awareness of St. Jude as the place where parents can turn when there is no help anywhere else. For example, last year the mother of a boy with medulloblastoma faced the situation every parent dreads. Doctors at his local hospital had operated on his tumor but couldn't remove all of it, and he was at high risk for relapse. The mother read a *Thanks and Giving*-related article in *Redbook* magazine about a St. Jude patient with medulloblastoma. She and her husband immediately consulted with our Dr. Amar Gajjar and realized St. Jude was the best place for their son. That's why raising awareness is so important—it really does save children's lives!

This year's campaign features a magnifying glass over the St. Jude logo. What's its significance?

It catches your eye, doesn't it? The magnifying glass icon, encircling our St. Jude logo, conveys our constant examination of any and all options to save a child today, and our relentless search to find the breakthroughs and discoveries that will find cures and save children in the future. We never stop looking for cures for any child. Ever.

How do you think your father would feel about the way St. Jude has grown and built such strong corporate relationships to support fund raising?

My father would be as excited as I am that we have found another way to reach out with our message of hope. His dream and his promise was that no child should die in the dawn of life. By raising more funds and letting more moms and dads know of our work, we are fulfilling that promise. I wish I could call him each day and tell him of each new partner who joins us. I can almost hear the joy in his voice. He would be very proud of all of us.●

A New Twist to an old GAME

SETH DIXON

During the countless hours Brenda Schulman, PhD, spends in her lab, she often marvels at how everyone at St. Jude works together toward the same mission—from staff who sterilize glassware for the labs to engineers, electricians and others who make sure everything is working. "Moving my lab recently gave me insight into the inner workings of this place, and it's amazing," she says. "Collaboration extends far beyond the boundaries of the labs."

By Victoria Tilney McDonough

Each cell in the body is a playing field for a game much like "Capture the Flag." One researcher is on her way to a victory.

Many of us, in childhood, enjoyed a game called Capture the Flag. With much strategizing, hiding and running, two teams of many players attempt to capture the other team's flag and bring it back victoriously to their side without being tagged. During this showdown, players try to tag as many players from the other team as possible and bring them to "prison," thus decreasing the number of adversaries.

In a busy lab at St. Jude Children's Research Hospital, Brenda Schulman, PhD, and a group of her Structural Biology colleagues are studying their own version of Capture the Flag, learning how "adversaries" in cells are tagged and brought to a prison where they are then disposed of.

Tag, you're out

Even as a kid smitten with blocks, shapes and math puzzles, Schulman was fascinated by how things fit and work together—specifically, how cells in the body could respond to changing environmental demands and cues.

A cell in a person's body is like, let's say, the field on which a game of Capture the Flag is being played. On that cell, players can sneak around wreaking havoc for the other team. Like a playing field, a cell can contain unneeded or abnormal material that can cause illness or even death. Some materials in the cell have important jobs that must be done at specific times and then must be eliminated once the tasks are completed. Fortunately, cells have an ingenious process to get rid of this unwanted material. Each cell contains a protein called ubiquitin, which consists of 76 amino acids. These 76 players roam the cell, tagging unwanted or waste material. Like captured players escorted to the other team's prison, the tagged material is brought to a waste area, called the proteasome, where it is chopped up into bits or degraded. This waste-disposal system is called the ubiquitin-proteasome system because ubiquitin recognizes damaged, incorrectly assembled or otherwise unwanted proteins and tags them for destruction.

This research is no game; further discoveries about the process may help lead to treatments for cancer, Parkinson's, Alzheimer's and other diseases.

Capture the ubiquitin

"Most of the processes we study are controlled by proteins that are built up and broken down at a frenetic rate," Schulman says. The cell must turn on and off a variety of biochemical pathways that serve thousands of critical functions, ranging from cell division and brain development in a baby to immune responses. The cell regulates these pathways to maintain conditions conducive to its own health and ability to perform its assigned function.

"We're still trying to figure out what these proteins do normally in the first place so that when there's a defect in the patient's cellular make-up, we will know what has gone wrong on that level," Schulman says. "The pathway we're studying is fundamental to human cellular regulation."

By studying the 3-D structure of proteins participating in the "Capture the Ubiquitin" game, Schulman and her team can better understand how cells keep their biochemical pathways operating in an orderly way, and how their disruption can lead to disease. The investigators are especially interested in how this process controls the levels of molecules that drive cell division, because cancer can develop if these molecules are not tagged and disposed of at the appropriate time. With further research, investigators could provide drug makers with crucial information on how to target molecules that fail to get tagged.

Schulman and her team use X-ray crystallography to study the protein structures and how they bind to one another. After purifying proteins, the researchers grow microscopic crystals that look like the sugar crystals on a stick you might get with a cappuccino at a fancy café. Once grown, the crystals are shipped to one of a handful of national laboratories, such as the Advanced Photon Source at Argonne National Laboratory in Illinois; there, the crystals are bombarded by huge X-ray beams. These X-rays show diffraction patterns from which computer-generated, 3-D images are created. From those images, Schulman and her team can figure out how specific proteins in the ubiquitination pathway bind to each other and in what combinations, thus revealing the nature and sequence of biological pathways.

"Research like mine is not for the impatient," Schulman explains. "You just have to jump and hope there is water in the pool at the bottom. I mean, I can see the water in the pool; it's there, I just don't know how long the jump will be."

And the game goes on

Working at St. Jude has already helped Schulman take giant steps in her work. "This is a very collaborative environment," she says." We work with many other labs and researchers; we share what we are doing—our ideas, our questions. I'm excited about being able to pursue these adventurous projects."

Since arriving at St. Jude more than four years ago, Schulman has been selected as a Pew Scholar, a Howard Hughes Medical Institute investigator and a Presidential Early Career Award for Scientists and Engineers recipient. Schulman admits that her work is her passion, consuming most of her time and thought.

"Many mornings, I have one or two or several messages on my St. Jude voice mail from myself calling in the middle of the night," she says. Instead of writing down an idea or thought, she dials her work number. In the morning, the red light on her phone blinks impatiently with her nighttime brainstorms.●

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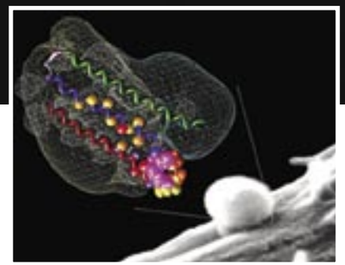

The magenta-colored features of CbpA specifically attack pIgR.

Getting the jump on pneumonia

By Carrie L. Strehlau

Respiratory infections are the No. 1 killer of children around the world. St. Jude researchers are determined to change that statistic.

A tiny, green tree frog spots lunch on a branch above its head. Its four legs suction their way to the top leaves—one leg at a time. It's a methodical climb—each toe grasping a different part of the branch. Little does the frog know of its similarity to one of the largest bacterial molecules to attack the human body.

In 1997, researchers at St. Jude Children's Research Hospital discovered a protein on the surface of pneumonia bacteria that allows the bacteria to attach to human cells. It's called choline binding protein A or CbpA. Recently, St. Jude investigators discovered that the protein's shape—large and paddle-like—helps pneumonia germs attach to cells that line the throat and lungs and ultimately invade the bloodstream.

"It's big, it's complicated, and it has many arms," says Elaine Tuomanen, MD, Infectious Diseases. "It can attach to different cells using one or the other of those arms in a sequential manner. CbpA is critical to first getting a bacterium into a person and then moving that bacterium from the nose into the lungs, from the lungs to the blood, and then to the brain. Think of a tree frog jumping from one kind of cell to another to another and sticking to it with its suction cups."

Suction-cup fingers

CbpA binds to a molecule on the cell called pIgR, which transports antibodies made inside the body across cells, releasing them on the surfaces of the nose and lungs. If a pneumococcus bacterium is hovering on the respiratory tract's lining, this germ binds to pIgR and pushes it back through the cell to the bloodstream. Once on the other side of the cell, the pneumococcus breaks free of pIgR and enters the blood, where it can multiply and infect the body. *Streptococcus pneumoniae* is the only bacterium known to use CbpA to invade human cells by binding to pIgR.

The fact that CbpA targets a number of different cell types makes it useful to St. Jude researchers. "If we know how to get rid of the function of the protein, then we could very reasonably imagine how to make a highly immunogenic vaccine that would be broadly protective," Tuomanen says. "That is our aim."

Tuomanen worked closely with Richard Kriwacki, PhD, Structural Biology, to try to understand how each of the "suction cup fingers" on CbpA works.

"We got a bird's-eye view of the molecule showing where all of its corners and crannies were," Tuomanen says. "Knowing the structure of it helps us point to areas that could function as bridges linking the bacteria to the human cell. Imagine the number of different possibilities."

LAURA HAJAR

Richard Kriwacki, PhD, of Structural Biology worked closely with Elaine Tuomanen, MD, of Infectious Diseases to understand how a protein on the surface of pneumonia bacteria helps those germs attack the body.

Creeping toward a vaccine

The discovery of CbpA's shape will guide researchers in their efforts to use part or all of this protein as the basis of a vaccine against *Streptococcus pneumoniae*.

"The fact that we know the structure of this important protein means we can begin to develop a vaccine that is more effective in children than those currently out there," Kriwacki says. "In addition, by understanding the structure of these domains of CbpA, we now understand the molecular basis for the attachment of pneumococci to human cells. It is an important first step in discovering drugs that would specifically disrupt this attachment process."

The broadest pneumonia vaccine, designed to protect against 23 of the 90 kinds of *Streptococcus pneumoniae,* does not work in younger children because their immune systems do not naturally respond to the bacterial sugars that make up the vaccine. Pneumococcal vaccines for children must instead be modified by binding those sugars to special proteins that stimulate the children's immune systems.

"Such vaccines are so complex that they target only a few specific strains of pneumonia bacteria," Tuomanen says. "So children are always under-protected. Our discovery of CbpA's shape has the possibility to make another generation of vaccine where the protein needed to alert the immune system of children is broadly represented in almost all pneumonia strains."

Pouncing on a killer

Respiratory infections are the No. 1 killer of kids in the world. These kinds of infections are also often fatal in children whose immune systems have been suppressed by cancer treatment or other therapies. Each year in the United States, pneumococcal disease causes 3,000 cases of meningitis; 5,000 cases of pneumonia and 7 million cases of ear infection. "The number of children who die of pneumococcal infection worldwide is astronomical," Kriwacki says.

With the opening of the GMP at St. Jude—of which Tuomanen was instrumental—the hospital now has an effort to modify the vaccine development process further and faster.

"I'm particularly proud of the fact that several groups in the Children's Infection Defense Center at St. Jude are working on vaccines and they have used the GMP to accelerate development of new therapeutics for orphan infections in kids. It expands the St. Jude mission from the bench to the bedside to the context of infectious diseases," Tuomanen says. "When you think about the enormity of preventing just ear infections—the most common reason a child goes to the doctor—then you see that this type of a vaccine could have a really big impact."●

Freedom from **Fear**

She rides horses, hangs out with friends and dreams of that perfect "flower-power" car. Thanks to St. Jude, Bekah Lloyd is not wasting one, glorious minute of freedom.

By Elizabeth Jane Walker

It wasn't quite the wilderness experience Bekah Lloyd had expected. When the 14-year-old recently agreed to camp in a friend's backyard, she imagined the evening would be idyllic: they'd pitch a tent under starry, Idaho skies, giggle and whisper confidences, and finally drift to sleep. But the evening involved much more than tent stakes and sleeping bags; it included things that go "splash" in the night.

First, the girls struggled to set up the tent. Then Bekah's friend tumbled off the deck while carrying blankets and hurt her foot. At 2:30 a.m., the intrepid campers awoke to a strange, hissing sound.

"The sprinkler heads in the yard are going off," laughs Bekah as she recalls the scene. "The one underneath us pops a hole in the floor, and the sprinkler's going off inside the tent! It was fun; disturbing, but fun!"

The fact that Bekah can have zany backyard-camping adventures like other teens is a joy to her mother, Whitney Lloyd. After all, it wasn't too long ago that Whitney was frightened about letting her daughter participate in "normal" activities. Bekah has severe chronic neutropenia, a rare blood disorder that leaves her unprotected against infection. The bacteria that healthy people overcome easily can threaten the lives of children like Bekah.

Her symptoms initially befuddled Bekah's hometown pediatrician. "The doctor ordered a blood test, and then we sat in the lobby and watched him walk back and forth from his office to the lab for about two hours," Whitney recalls. "Finally, he called us into his office, and said, 'Well, the good news is we got out our textbooks and found something she fits.' I was just sitting there thinking, 'They don't know enough about this to fix it.' Then we went to a hematologist, who said, 'I'll show you what there is in my book about it.' There was an article about two inches long; that's all there was."

At first, Russell and Whitney Lloyd lived like prisoners in their home, terrified of exposing their daughter to the microscopic killers lurking in public places.

"Right after her diagnosis, the doctors would call us and say, 'Her counts are really low. Don't take her to the mall; don't take her to the grocery store; don't take her to church,' Whitney says. "So for about six months we lived like hermits. And then one day we went, 'You know what? We can't live like this anymore. We have to be as normal as we can be.'"

After a harrowing year when Bekah fought 11 infections, doctors referred her to St. Jude Children's Research Hospital. And the Lloyds' lifestyle began to change.

Finding an ally

Neutropenia occurs when white blood cells called neutrophils do not perform their job of surrounding and destroying bacteria that invade the body. Individuals develop the disease if their bone marrow does not produce enough neutrophils or if these white blood cells are destroyed prematurely. Cancer, chemotherapy and other drugs sometimes cause neutropenia. But some people, like Bekah, are either born with the disorder or develop it during their lifetime.

Bekah vividly remembers her arrival at St. Jude as an apprehensive 10-year-old. "I was in the fifth grade," she says. "I had

LAURA HAJAR

Although Bekah Lloyd has severe chronic neutropenia, a rare blood disorder that leaves her unprotected against infection, she now enjoys the life of a normal teenager. During a trip to St. Jude for checkups, she visits Sanga School of Horsemanship, where she learned to ride several years ago while undergoing treatment.

Whether she's snowboarding, performing in the theatre or just hanging out with her friends in Idaho, Bekah Lloyd still relies on St. Jude for support. "I know I can call any time and talk to someone and know that they understand," Whitney says. "That's comforting, because for so long, no one did understand."

been sick for a really long time when the doctor sent me to St. Jude, and they told me they were going to do a bone marrow test. The test was pretty scary, but everybody was so loving and so caring. They really supported me and helped me through it."

Bekah quickly forged bonds with staff members in other areas of the hospital, including Martha Rieman, a nurse practitioner in Hematology-Oncology. "Bekah is a beautiful, intelligent and poised young woman," says Rieman, who keeps Bekah's picture in her office and has even attended one of Bekah's theatrical performances.

Whitney says the support the family received at St. Jude provided as much balm as the treatment did. "I know I can call any time and talk to someone and know that they understand," Whitney says. "That's comforting, because for so long, no one did understand."

Liberation at last

Winfred Wang, MD, of St. Jude Hematology-Oncology currently follows about 10 St. Jude patients with chronic severe or moderately severe neutropenia. When he arrived at St. Jude in 1979, many patients with this disease died from infections. But in 1990, St. Jude joined several other centers in a study to see if a new drug could help these patients. A manmade form of a natural human hormone, granulocyte-colony stimulating factor (G-CSF) is designed to help the body make neutrophils.

"Before 1990, there was no effective treatment for increasing neutrophil production," Wang recalls. The study, which provided data for FDA approval, showed that G-CSF was at least 90 percent effective in correcting the neutropenias of these patients. "It's only since G-CSF became available that those types of patients are surviving—and actually doing pretty well in most cases," Wang says.

Three years ago, Bekah began taking G-CSF injections. "G-CSF has been life changing for Bekah because she can be a normal kid," Whitney says.

Once home schooled, Bekah now attends a local high school. An aspiring actress, she takes voice lessons, babysits, hangs out at the mall with her friends, plays soccer and dreams of her "dream car"—a lime green Volkswagen bug convertible. "I want one with fluffy seats and spinning wheels that are in the shape of flowers," says the teen.

Recently, Bekah accompanied her church youth group to a local park where they fed homeless people. "These people literally had nothing, and that was their one meal a week," Bekah says. "It was really neat to help out. I'm planning on going out there again soon."

The Lloyd family also gives back by helping raise money at St. Jude fundraising events in Idaho and Oregon. "We couldn't give Bekah health on our own without St. Jude," Whitney explains. "It's been overwhelming and humbling for us to be the recipient of that generosity. Our insurance won't pay for G-CSF unless you're a cancer patient, and the injections cost about $60,000 a year. We see the difference it makes in her and how many fewer visits we're making to the doctor."

Whitney is thankful that patients who came before Bekah participated in research that paved the way for her daughter's successful treatment. She says the hospital's research component sets St. Jude apart from other institutions.

"St. Jude has several goals in mind, but the care and comfort of a child never is a sacrifice," she says. "St. Jude is looking for a cure not just for the individual patient but for the disease itself. If someone's not looking for those cures, then treatments aren't going to be developed. It's important to be saying, 'Why are we doing this? Why are the kids going through this?' And I think that's what makes St. Jude different; it makes them stand out."●

PHOTOS BY LAURA HAJAR

"We do whatever it takes to make our patients well, and sometimes that means just being a friend and telling them that they will get through this," says La-Kenya Kellum, RN.

A Compassionate Calling

St. Jude nurses apply their skills and their hearts to make patients well.

BY TANUJA COLETTA

In November of 2000, Sarah Johnson found out she had cancer. Her best chance for survival was to come to St. Jude Children's Research Hospital. Despite being told about the hospital's excellent care, all Johnson—then 14 years old—could think about was leaving her friends in Illinois.

"At first I was shocked, and then I bawled," she says. "All I knew was that I had to uproot my normal life and get used to a new 'normal' filled with doctors' appointments and medicine."

Little did Johnson know that a new friend was waiting for her at the hospital.

A new employee at the time, La-Kenya Kellum, RN, accompanied the teenager and her mother to many of Johnson's appointments. "We have the same personality—bubbly and optimistic—so we got along just great," Johnson remembers. "La-Kenya has always been there for me and made me feel like I had a family at St. Jude."

Now a nursing coordinator, Kellum says that forming friendships is the best part of being a St. Jude nurse. "We do whatever it takes to make our patients well, and sometimes that means just being a friend and telling them that they will get through this," she explains.

Kellum is one of nearly 250 nurses in Patient Care Services who work in various roles, from the outpatient clinics and inpatient floors to administration and research. Each is well-trained, knowing precisely when to apply their highly specialized skills and when to follow their hearts.

Special hug

The nursing shortage in the United States is entering its eighth year, making it one of the longest-lasting droughts in half a century. However, St. Jude leaders saw the warning signs early and took measures to attract the best nurses in the country.

"Knowing that our needs are greater because of how sick our children are, we were very aggressive in making sure that we had the caliber of people that we need at St. Jude," says Gen Foley, RN, vice president of Patient Care Services. "It's a multifaceted process. One of the pieces is creating a professional environment so we can say to a nurse, 'You can be the nurse that you went to school to be.' The whole atmosphere of being involved in a process that's helping the next generation of patients reach even better survival rates is a huge motivator."

Foley credits three factors with easing her recruiting efforts: the hospital's low nurse-to-patient ratio, the high level of training each nurse receives and a shared decision-making process that gives nurses a voice in decisions that affect their jobs.

While a typical children's hospital could pair one nurse with five to 10 patients, St. Jude nurses are usually assigned to just two or three kids. In the Intensive Care Unit, a single child could even have two nurses. "Because of the complexities of our patients, that's what we feel it has to be," Foley says.

Routinely St. Jude nursing care extends to patients' family members.

One day, Kellum was walking through the hospital and saw a woman quietly crying in the lobby. The woman's granddaughter was struggling to hang onto life. "She wasn't one of my patients, and I didn't have much to offer, so I just sat with her and gave her a hug," Kellum says. Sadly, the granddaughter passed away. A short time later Kellum received a note from the girl's grandmother. "She thanked me for sitting with her that day," Kellum says. "She said I gave her a 'special hug' that helped comfort her. I had no idea that such a small act could mean so much."

Kellum keeps that note tucked inside a notebook that she carries to remind herself that simple acts of kindness can be just the medicine some people need.

The St. Jude way

"I've wanted to be a nurse my whole life," says Kathleen Anno, RN, a clinical nurse specialist. "It's a never-ending learning experience."

Anno worked as a bedside nurse in pediatrics for 10 years before getting into teaching. She says the skill level of nurses at St. Jude is second to none. "It can't be stressed enough how specialized we are," she says. St. Jude was one of the nation's first hospitals to have nurses specialized in pediatric oncology. "We have the St. Jude way of doing things," Anno says. "It's the best way we know how."

St. Jude can offer superlative care thanks to dedicated donors. "We don't have to worry about cost when it comes to patient care," Anno says. "We do the best by our patients."

Nurses go through an extensive orientation program and are encouraged to attend training and continue their education while they work. Nurses also sit on leadership committees and have the opportunity to do research, a luxury at many institutions.

Michael Lochbihler, RN, says it's the patients, as well as the approach to nursing, that has kept him at St. Jude. "I love coming to work each day," he says. "I'm able to give great nursing care because of all the training that we get."

Anno says the collaborative relationship between nurses and physicians is another unique feature at St. Jude. "Doctors listen to nurses here," she says. "If nurses have concerns, they know that they will be taken seriously."

Gregory Hale, MD, clinical director of St. Jude Stem Cell Transplantation, says nurses are integral to the patient care team.

"Nurses at St. Jude are dedicated not only to providing the absolute best care for our patients, but also to carrying out the prescribed clinical research treatments and tests that have made St. Jude famous," he says. "They're at the patient bedside 24 hours a day filling many roles, including administering treatment, assessing patients to determine if a change in care is required, providing emotional support to patients and families, and carrying out much of the research for the hospital's clinical trials."

Anno says "team" is a great way to describe the approach to nursing at St. Jude. "The staff truly works for one common goal—the patients," she says. "We're a family."

When people ask me, 'How can you work at St. Jude? Isn't it sad?' all I can say is, 'How can I not work at St. Jude? It's incredible.'

Kathleen Anno, RN, says the skill level of nurses at St. Jude is second to none. "It can't be stressed enough how specialized we are," she says. St. Jude was one of the nation's first hospitals to have nurses specialized in pediatric oncology.

Decision makers

Three years ago when Michael Lochbihler, RN, came to St. Jude to apply for a position, a little, balding girl sat beside him before his interview. "She said, 'You gotta work here; it's the greatest place on earth,'" he says. "I was sold."

Now a nursing coordinator, Lochbihler says it's the patients, as well as the approach to nursing, that have kept him at St. Jude. "I love coming to work each day," he says. "I'm able to give great nursing care because of all the training that we get."

Last year, St. Jude celebrated the first year of its Shared Decision Making process, which gives nurses and other caregivers a way to give input and have decision-making authority in policies that directly affect patient care. At the heart of the process are several multidisciplinary councils that provide forums for employees to share news about projects and events, as well as new medical products and services. "Although common in academic circles, we believe it is the only multidisciplinary shared decision making model in the country in health care," says Foley.

The process empowers nurses and allows them to be the best they can be. "It enables us to have the resources we need, which ultimately means we can concentrate on our patients. That's how we can really make a difference," Lochbihler says.

Making a difference often means finding time to interact with kids at their level. "You have to remember that our patients are kids," Lochbihler says. If they want to play video games, then I play video games. If they need to sit and talk, then I do that, too. So when people ask me, 'How can you work at St. Jude? Isn't it sad?' all I can say is, 'How can I not work at St. Jude? It's incredible.'"

That kind of dedication is invaluable to patients like Sarah Johnson. Now 19 years old, Johnson was able to beat her cancer after months of chemotherapy and a bone marrow transplant. She's now back in Illinois attending college.

Each time Johnson comes back to St. Jude for a check-up, she makes plans to see Kellum, once her nurse and now her friend. "She's the best," Johnson says. "She says she'd be happy to be out of a job if they could just find the cure to cancer tomorrow. I think that's how all the nurses feel. St. Jude is like no place I've ever known."●

JERE PARDEBEK

"Isaiah has been battling his disease as if it were a match. He has shown what a competitor he is," says Kelly Smith, wrestling coach for Charles Page High School. "It has been wonderful to watch his teammates, people from church and our town stand behind him."

The Most Challenging MATCH

Wrestler and guitarist **Isaiah Banks** learns to find his center.

By Victoria Tilney McDonough

For Isaiah Banks, those few seconds careening through the air is life at its finest. All his worries evaporate, and he is part of the sky, the trees, the earth. Then he bounces back onto the trail, hands gripping the handlebars, the fat tires of his dirt bike spitting gravel in his wake. He catches his breath, and again, heads back for another moment of freedom off the ground.

Also a guitar player, Raymond Barfield, PhD, MD, of St. Jude Hematology-Oncology would sit in Isaiah's room after the boy's transplant and play for him. Barfield would fill the room with classical guitar music; there was little need for words.

Isaiah Banks is not your average 18-year-old. Whether he is flying over bumpy trails on a dirt bike, dancing his fingers across the strings of his acoustic guitar or concentrating on pinning down an opponent on the wrestling mat, Isaiah knows that staying centered and focused is the only way to live. This attitude has proved essential for him, especially since October 2004 when he was found to have a particularly risky form of acute lymphoblastic leukemia (ALL).

Pinned to the mat

It all started with a sore rib during wrestling practice. Like a dark water stain, the pain spread; within a week it extended to his collar bone and shoulder joints, culminating in a headache that felt like his head was being squeezed in a vise. The severe headache prompted a rushed trip to the emergency room. Within 30 minutes, Isaiah and his mother, Susan, were told his white blood cell count, at 124,000, was "higher than that of many terminal patients." The doctors suspected leukemia.

For Susan and Isaiah, the experience was a whirlwind; no time to think, to breathe. Within two weeks, Isaiah started a 54-day regimen of chemotherapy at his local hospital in Oklahoma. A month later, his doctor discovered that he had an especially dangerous form of leukemia—Philadelphia chromosome-positive ALL. Because of his older age at diagnosis and because the chromosome's presence indicates a high relapse risk, Isaiah needed a stem cell transplant at St. Jude Children's Research Hospital. This was not good news for a young man who was throwing all his energies into a future of wrestling and college.

The worst match

If the day Isaiah met with St. Jude doctors to discuss a stem cell transplant were a color, it would be black. On second look, however, it would warm around the edges, light fingering its way around a window shade. "That was a rough day. There were a lot of tears," says Susan.

By then, Isaiah's disease was in remission, and he felt that God had cured his cancer. However, Raymond Barfield, PhD, MD, of St. Jude Hematology-Oncology showed him data and explained that temporary remission after chemotherapy was common with this kind of cancer; the best way to battle his disease was to attack before the elusive Philadelphia chromosome made another appearance. "You shouldn't have to discuss death and hardship like fighting cancer with your 17-year-old child," Susan says. "It was really difficult for him—and for me—to hear."

Between this consultation and the transplant, Isaiah spent some time alone, coming to terms with the news. "He had to go off by himself and do some crying and just find the strength," explains his mother. "Once he did that, he was ready to go the distance. It was as if he had to go off and work on this kind of acceptance on his own and then come back with the wrestling spirit of 'this is my worst match and I've got to win it.'"

Determined to win

Although the side effects and experiences during stem cell transplants vary person to person, patients typically stay in

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"Isaiah is amazing. On one hand, he's this competitive wrestler. On the other, he's this beautiful guitar player," says Theresa Oliver, who works at Target House where Isaiah and his mother stayed for many months. "He seems tough, but he's really a teddy bear—and always a gentleman. He writes music, and he sang me a song about being saved and having faith. It really touched me."

You've got to live life to the fullest because you might not have tomorrow.

or near the hospital for 100 days and are monitored closely for negative reactions such as graft-versus-host disease or infections. Even before the transplant, Isaiah was determined to be home by day 100. He asked his doctors and nurses if they believed he could do it. Each told him that with his determined spirit, anything was possible.

When Beth Hensley, RN, entered his room, he asked her, too. "I had to tell him that if this did not happen he shouldn't feel like he had failed somehow," says his nurse. "He told me that he really believed his faith would get him through, and that he would give 200 percent to reach that goal. I was impressed with his determination and his faith. Both seemed exceptional for a boy his age."

After several donor options fell through, Susan surfaced as the best choice. Usually a parent isn't a close enough match, but in this case, she turned out to be as good a match as a sibling would be—the best match possible.

"It was a God moment," Isaiah says.

His mother nods and adds, "We are lucky; we've had a lot of God moments."

The days Isaiah spent on the transplant floor tested his mettle; he tapped into a depth of spirit even he didn't realize he possessed. "The radiation you have with the transplant made me so sick I just wanted to die," says Isaiah. But despite that, he gave everything he had to recovery—taking his medications, doing physical therapy faithfully and even riding a stationary bicycle to prevent his "wrestling muscles" from disappearing.

"More than most kids his age, Isaiah has a deep sense of faith. He also seems to be aware of death in his world view and to understand the seemingly endless physical and emotional layers that come with an illness like cancer. But Isaiah is very headstrong; I love the kid," says Barfield.

Also a guitar player, Barfield would sit in Isaiah's room after the boy's transplant and play for him. The walls were covered with photos, Bible scripture and cards of encouragement from friends and family. Barfield would fill the room with classical guitar music; there was little need for words.

Isaiah was out of the hospital on the eighty-sixth day.

SETH DIXON

Besides being Isaiah's mom, Susan is also his stem cell donor. She says she has treasured spending the last year with her son. "We have come to rely on each other and on our faith in ways we hadn't known possible," Susan says. "Not too many people get the chance to get close to and share so much with their teenager."

Encourager, warrior, enthusiast

Since his diagnosis, Isaiah has come to think of himself as an old soul; he says he sees life for what it is. "You've got to live life to the fullest because you might not have tomorrow," he says. "Say what you want to say now because it might be the only chance you get." Isaiah has had graft-versus-host disease and other complications since his transplant, but he continues, in his wrestling spirit, to battle his cancer—an opponent that seems to weaken as he gets stronger.

Although she says people might think she's crazy, Susan insists she wouldn't trade a moment of the last year for anything. "We have come to rely on each other and on our faith in ways we hadn't known possible," she says. "Not too many people get the chance to get close to and share so much with their teenager." Hearing her say this, Isaiah reaches out and touches his mother's hair. He strokes it for a moment then returns his hand to his lap.

When asked what he'd want people to remember about him, he pauses and then says, "Encourager, warrior, enthusiast. I'd want to be remembered as a person others could come to if they needed advice during a difficult experience. To be able to give some godly wisdom because of what I've been through. Not that I'm like God, but rather that I'd be able to offer a godly direction on what to do. I feel like I'm on my way to being that person. I won't totally be that person 'til I get to heaven, but I can strive to further myself every day instead of being stagnant."●

SETH DIXON

All the Right Questions

By Elizabeth Jane Walker

To find answers for children with "orphan diseases," one St. Jude researcher digs into the mysteries of the human cell.

Alessandra d'Azzo, PhD, of Genetics (above, right) discusses her work with St. Jude Research Technologist Fameeka Jenkins. d'Azzo and her colleagues study three rare genetic diseases caused by defective or missing enzymes. One of the world's top researchers in the field of lysosomal storage disorders, d'Azzo is trying to find ways to replace those enzymes in children who suffer from these diseases.

Answer: Enzyme-replacement therapy.
Question: What is Lauren Ryan's best hope for a cure?

If you're a *JEOPARDY!* fan like 13-year-old Lauren Ryan is, you know that sometimes the question is really the answer. One investigator at St. Jude Children's Research Hospital has dedicated her career to posing the crucial research questions that offer hope to children like Lauren.

Alessandra d'Azzo, PhD, studies three rare genetic diseases with names that would challenge even the most astute game show contestant: G_{M1}-gangliosidosis, sialidosis and galactosialidosis. These

I feel so blessed. It's truly a miracle that God has put somebody on this earth who is specifically working on my daughter's disease.

diseases are part of a group of diseases called lysosomal storage disorders.

Lysosomes are the cell's recycling centers. These tiny bags of enzymes break down biological materials into their basic building blocks; the recycled materials are either used to make new molecules or are discarded. If an enzyme in a lysosome is defective or missing, the lysosome can't do its job, and the product that should be broken down accumulates. Because the cells no longer function properly, the body's organs don't work correctly, bones don't form normally and muscles don't develop as they should. Most children with these disorders also experience brain damage that leads to cognitive and motor delays.

"If you lack even one of these enzymes, you have a devastating disease," says d'Azzo, who holds the St. Jude chair in Genetics and Gene Therapy, a position endowed by Jewelers for Children.

What is teamwork?

During the past couple of decades, d'Azzo has emerged as one of the world's top researchers in the field of lysosomal storage disorders. She is one of the reasons Kristin Weader and Vincent Ryan decided to bring their daughter to St. Jude for treatment. At St. Jude, Lauren is followed by John Cunningham, MD, of Hematology-Oncology. But the teenager has also grown to know and love the researcher who toils in the lab to find a cure. It's the kind of teamwork that makes St. Jude unique.

Every summer, Lauren and her parents travel from Pennsylvania to Tennessee for her annual checkup. "Dr. d'Azzo usually comes in with Dr. Cunningham after all the tests are done," Kristin explains. "He goes over the test results with us, and she updates us about her research and the progress that she's made during the year."

Lauren has galactosialidosis (pronounced gal-ACT-o-sy-al-i-DO-sis), a disease so rare that her parents have never even met another child with the same condition. When Lauren was born, doctors in Pennsylvania told her parents that she would not live to be 1 year old, and if she did live past that age, she would have severe mental retardation. Lauren has respiratory and digestive problems, as well as issues with her heart, eyesight, hearing and joints. But she is a bright and compassionate young lady who plays the piano, sings in her school's chorus, enjoys Harry Potter books and dreams of auditioning for the *JEOPARDY!* game show. Currently, her disease is progressive and incurable, with Lauren's physicians limited to managing her symptoms. But d'Azzo is working feverishly on research that offers hope to Lauren and her parents

What is progress?

While pursuing doctoral degrees in Italy and the Netherlands, d'Azzo never dreamed that so much of her career would be dedicated to finding cures for three related diseases. "I chose the three out of totally serendipitous findings," she says. "I've found that in science the best possible discoveries are those kinds—it's not what you actually plan or expect to find, but the unexpected finding that is important."

She began by studying an enzyme called beta-galactosidase. d'Azzo discovered that children with the disease G_{M1}-gangliosidosis inherit a defect in that enzyme. Other children have a deficiency in an enzyme called sialidase; those patients have a disease called sialidosis. "Out of a sheer coincidence, I discovered the primary defect in a third group of patients," d'Azzo says. She discovered that in one group of patients, a beta-galactosidase deficiency was accompanied by another, even more important defect: a problem with the sialidase or neuraminidase enzyme that was defective because of the loss of an additional enzyme, protective protein/cathepsin A, or PPCA. Those patients—including Lauren Ryan—have galactosialidosis. "I developed my whole program around these three enzymes," d'Azzo says. "It has been incredibly rewarding because we have learned a great deal about the diseases themselves."

She also developed laboratory models for all three diseases. Then her task was to find a way to replace the missing enzyme. In theory, if the enzyme is introduced into a patient's bone marrow, then the bone marrow would begin producing normal amounts of that enzyme. "We are now getting to the point that we can translate what we have found back into the clinic," d'Azzo says. "If you have a way to provide these children with a continuous source of the missing enzyme, you could cure a lot of the characteristics of the disease." But the enzymes are big molecules, much too large to cross the protective barrier that shields the brain from harmful substances in the blood stream. Since the diseases d'Azzo studies affect the central nervous system, overcoming this blood-brain barrier is important.

d'Azzo looked for a way to produce sufficient quantities of the enzyme so that it could be administered as a drug to affected children. Eventually, she and her colleagues turned to an unlikely source: the butterfly. That's right, cells from these insects can be infected with a baculovirus that contains a desired gene. The infected insect cells then produce the necessary enzyme. d'Azzo then figured out how to crystallize large amounts of that enzyme. "It turned out to be perfect," she says. Laboratory mice with galactosialidosis responded well to the enzyme. "Their systemic organs were all corrected," d'Azzo says.

In the next couple of years, d'Azzo hopes to work even more closely with St. Jude clinicians to move toward providing enzyme replacement therapy to children like Lauren. It is a long and involved process that demands teamwork, time, patience and resources. Eventually, the enzyme might be produced in the hospital's Good Manufacturing Practices facility, a production center for drugs, vaccines, proteins, gene-based molecules and other biological products.

d'Azzo says St. Jude is the perfect place to pursue that dream. "It's very rare to find an array of absolutely fantastic scientists, clinicians and core facilities in one place," she says. "I think we can absolutely make a difference. We have made gigantic steps, but we still have a lot to learn. I am sure that eventually this knowledge we are gaining will be translated into helping children."

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Thirteen-year-old Lauren Ryan suffers from a rare, debilitating and progressive disease called galactosialidosis. Lauren's best hope for a cure lies in enzyme replacement therapy, which Alessandra d'Azzo, PhD, is perfecting in the lab. "Dr. d'Azzo is really dedicated to finding a way to help Lauren," says Lauren's mom.

What is hope?

Meanwhile, Lauren is not waiting around for that elusive cure; she's far too busy planning her future. Lauren is excited about the possibility of playing soccer in a new league that accommodates kids with special needs. She plans to make the honor roll in the seventh grade, as she missed it by only .13 of a point last year. And she's debating what to be when she grows up…Should she be a nurse? A school teacher? A librarian? "I'm still trying to think of what I want to do," she admits.

Kristin says her daughter is already a teacher—a person who provides daily lessons about how life should be lived. "Lauren is someone who willingly gives up her whole allowance (and then some) to put in the offering at Bible school because "the hungry people in the world need it more than me,'" Kristin says. "She's someone who has taught me more about love and courage than anyone else....Someone who has a strong faith and believes with all her heart that God has a plan for her life. And so do I!"

When discussing d'Azzo's research, Kristin's voice breaks with emotion. "Dr. d'Azzo is really dedicated to finding a way to help Lauren," she says. "I feel so blessed. It's truly a miracle that God has put somebody on this earth who is specifically working on my daughter's disease."●

Perspective

The Right Place

By Jeff Probst

"Bright colors! Smiling faces! Kids laughing and playing! Wait a second…this is a hospital and research center for kids with cancer?"

As host of *Survivor*, I've traveled all over the world and been dropped in the middle of some fascinating cultures, but nothing prepared me for the "world" I would enter as I walked through the front doors for my first visit to St. Jude Children's Research Hospital.

Bright colors! Smiling faces! Kids laughing and playing! Wait a second—am I in the right place? This is a hospital and research center for kids with cancer? Well, if you've been to St. Jude, you already know the answer. I was in the right place, and those first few moments are still the best way for me to describe my feelings about St. Jude.

Two of the first kids I met at St. Jude were 11-year-old Ali Mills and 3-year-old Emma Grace Hampton. Ali and I became fast friends as we spent the day together and did a media tour of interviews promoting a campaign with Chili's Grill & Bar. Ali was a delight—so smart, so fun, so well-spoken about her cancer and the work being done at St. Jude. During a break, we raced through the hospital, and Ali won. Her prize was "a cute outfit," and I think she had it picked out before we even began the race. Her mom, Nancy, is one of the most amazing women I've ever met, and it was easy to see where Ali's spark for life came from.

Ali was also a bit of a big sister to Emma Grace, but Emma Grace held her own through our own series of interviews. A perpetual smile and easy giggles from Emma Grace made the afternoon one of the most loving I've ever had. Her mom, Trish, was as dedicated a mom as any child could ask for. The connection they shared was clear to everyone.

I kept up with Emma Grace's progress through updates from St. Jude, and I stayed in touch with Ali through our phone calls. We talked about school, Ali's hair growing back and which boys she liked.

Emma Grace passed away June 6, 2005, at the age of 4. I am smiling as I write this, remembering our last day together as we shared sushi. Yeah, that's right, a 4-year old who eats sushi. That was Emma Grace.

Ali passed away April 12, 2005, just two days before I was to arrive at St. Jude to see her. Ali's impact on me is hard to share in the limited space of this column. She reminded me that every single day on this planet is a gift and that if you are not living your life every single day you are a fool. Her picture sits on my mantle. We were friends. I miss our phone calls. She inspired me then, and she inspires me now.

As I think back on my first few moments at St. Jude, I am reminded of why this facility is so vital. It is a cocoon of love that encourages all of these kids to live every single day, in spite of the cancer they are living with, while the doctors and researchers only a few doors away search tirelessly for the cures that will one day make St. Jude obsolete.

I am fully committed to St. Jude, and I ask you to make a commitment as well. Don't toss this magazine, or set it under a 'to do" pile. Sit down, right now, reach out and help St. Jude continue their work.

Jeff Probst, host of the Emmy-Award winning television show Survivor*, has helped Chili's Grill & Bar raise $2.5 million for St. Jude through the Create a Pepper to Fight Childhood Cancer campaign.*●

LAURA HAJAR

Ali Mills teaches Jeff Probst a lesson or two—about life and peppers—at Chili's Grill & Bar.

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