

Promise

AUTUMN 2014



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Promise

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On the cover:

Music therapist Amy Love and Farrah Courville Photo by Peter Barta



St. Jude President and Chief Executive Officer James R. Downing, MD, with St. Jude patients (from left) Gayatri Linga, Jacob Frommer, Sofia Campoverde and Pierre Riley

"If not St. Jude, then who?

There is nobody else who is going to step up and become the leader in research and treatment for pediatric cancer across the globe. This is what we need to do. This is our future."

The Innovator

By Elizabeth Jane Walker

Nearly 30 years ago, an

up-and-coming pathologist arrived at St. Jude Children's Research Hospital for a job interview. Switching off his car's ignition, James R. Downing, MD, considered the hospital's two modest buildings and turned to his wife, Mariea.

"I don't think I can work here. It's too small," he told her.

The Michigan native had completed his medical and laboratory training at prominent medical centers with expansive facilities. In comparison, St. Jude had fewer than 1,000 employees and a tiny inpatient department. But that evening, Downing returned to his hotel in a quiet and reflective mood.

"How did it go?" his wife asked.

"You know, this place is like no other place I've ever been before," Downing replied. "I think I have to come here."

Defining discovery

At St. Jude, Downing found a remarkable place of discovery and interaction—a hospital where scientists and clinicians worked in tandem, moving advances from the lab directly into the

clinic, and taking observations from the clinic back to the lab. It was the perfect place for an energetic young clinician to hone his research skills.

Quickly finding his niche, Downing began helping St. Jude become a world leader in the treatment of children with cancer and other life-threatening diseases. Melding clinical and research interests, Downing amassed an impressive body of research, attaining international prominence as a leader in the field of cancer genomics.

After serving the hospital in several

capacities—including as Pathology chair, scientific director, executive vice president and deputy director—Downing was named the hospital's sixth president and chief executive officer in July of 2014.

Unprecedented project

In 2012, TIME magazine heralded the Pediatric Cancer Genome Project, spearheaded by Downing, as one of its top medical breakthroughs. That project, conducted in collaboration with Washington University in St. Louis, sequenced the complete normal and cancer genomes of 700 children with cancer. Results of the project are helping scientists make new discoveries about some of the most aggressive and least understood childhood cancers.

"This information will change the field across the world, and not just for pediatric cancer, but also for adult cancer and other genetic diseases," Downing says. He is now leading the St. Jude clinical genomics program, an effort to move genomics into the clinic to better diagnose and treat children with cancer. The ultimate goal is to sequence the genome of every cancer patient who comes through the doors of St. Jude.

"We'll use that information to determine who is responding to treatment and who is not," Downing explains. "If they're not responding, how can we use that information to better treat them?"

A focused vision

Downing's vision for St. Jude is ambitious and audacious—just like the institution itself.

"Our future must be based on St. Jude being the innovator. This is our history; this is our future," Downing asserts.

Assuming leadership during a particularly vibrant era, Downing enthusiastically lists some of the hospital's attributes, including its world-renowned

programs in leukemia, brain tumor, translational science, survivorship and solid tumor research. "And of course we provide outstanding multidisciplinary care to our patients," he says.

"We are a place of innovation," he continues. "And what is the engine for that innovation? It is our focused vision. We have an unrelenting commitment to finding cures. That is what we are about."

Moving forward

When Downing arrived at St. Jude nearly 30 years ago, he assumed he could predict the trajectory of his future.

"I figured I might be here five years. I'd get my training, I'd become a more sophisticated scientist, and I'd move on," Downing recalls. "But then I started to learn what St. Jude was about."

From time to time, other medical and research centers attempted to woo him away, prompting him to weigh options and evaluate the opportunities offered by other world-class institutions.

"It was always at St. Jude that I would be able to accomplish more," Downing says, "to push the envelope and try to accomplish things that other people couldn't even dream about."

St. Jude retains those characteristics today, Downing says.

"I'm energized to move forward," he says. "We have phenomenal faculty and staff, and we have a support structure that's unparalleled. Millions of donors across the United States donate funds so that we can do things that impact every child in the United States and every child around the globe. That support allows us to do things that others can't do and to provide services that other hospitals can't provide.

"It's been a great journey," he says, "but the most exciting time is ahead of us." ■

A Place of Innovation



Downing's vision for the hospital:

- Keep the patient and family at the center of everything St. Jude
- Significantly increase the number of patients who come to St. Jude for treatment
- Develop a program to follow patients who have genetic variations that increase their lifetime risk of developing cancers
- Set the global gold standard for using genomics to help diagnose and treat children with cancer
- Enhance the hospital's program in immunotherapy, a treatment that harnesses the immune system to fight cancer
- Expand St. Jude LIFE, the long-term follow-up study of childhood cancer survivors
- Expand select non-cancer programs, such as bone marrow transplantation and gene therapy for sickle cell anemia
- Create a long-term follow-up program for patients with sickle cell disease
- Enhance the hospital's clinical facilities with new inpatient rooms, redesigned outpatient areas and the world's only proton therapy center dedicated solely to the treatment of children
- Set the global agenda on pediatric cancer by doubling the size and scope of the International **Outreach Program**



An innovative clinical trial for high-risk Hodgkin lymphoma enables one energetic 11-year-old to sail through therapy.

By Elizabeth Jane Walker

uring the past few months, Mary Browder
Howell has ridden horses, paddled a canoe,
climbed rock formations, played golf and tennis,
captained a sailboat, maintained a 100 average in
schoolwork and competed in the world finals of a
problem-solving competition. She has also undergone
treatment for high-risk Hodgkin lymphoma.

"I'm too busy to have cancer," explains the 11-year-old, with a dazzling smile.

Fortunately, an innovative clinical trial at St. Jude Children's Research Hospital has enabled this energetic preteen to sail through therapy—all without missing a single ballet rehearsal with her dance troupe back in Kentucky.

Busy for Cancer

Concern to consternation

Last winter, Renee and Jason Howell were concerned when their high-spirited daughter fought off two bouts of pneumonia within six weeks, losing several pounds, running a low-grade fever and feeling lethargic. But concern turned to shock when an X-ray and CT scan revealed tumors in Mary Browder's neck and chest.

"I knew something was wrong, but you never think your child is going to have cancer," Renee says.

Their pediatrician encouraged the couple to take their daughter to St. Jude.

"It's ironic," muses Mary Browder. "About 30 minutes before we got the call saying we were coming to St. Jude, Mom had signed my sister's Math-A-Thon permission slip."

During the next few weeks, kids in Mary Browder's school district would show their support by raising \$35,000 for the hospital through St. Jude Math-A-Thon, an education-based fundraising program.

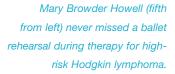
Devious disease

The Howells learned that Mary Browder had Hodgkin lymphoma, a cancer of the lymph system. St. Jude pathologists classified her disease as advanced, or high risk, because the tumors were accompanied by fevers, fatigue and weight loss.

Monika Metzger, MD, of St. Jude Oncology, says the gradual, nearly imperceptible onset of symptoms is typical.

"Hodgkin lymphoma is a sneaky, slow-growing cancer that almost resembles a chronic disease," Metzger explains. "Many times, patients don't even realize how sick they feel, because they may have had it for a year or more before they're diagnosed. When they start chemotherapy, they actually feel energized. It's like putting on a new pair of glasses and realizing how bad your eyesight was before."

The standard treatment for Hodgkin lymphoma includes treatment with vincristine, a drug that kills cancer cells but also causes nerve pain. Children may also receive radiation therapy, which can cause long-term problems such







Monika Metzger, MD (at right), of St. Jude Oncology enrolled Mary Browder Howell in a new clinical trial for children with high-risk Hodgkin lymphoma. The regimen enabled Mary Browder to avoid the nausea, vomiting, pain, fatigue and radiation therapy usually associated with Hodgkin treatment.

as secondary cancers and heart problems. And the risk of infertility is high in many Hodgkin treatment regimens.

A new clinical trial at St. Jude aims to change that scenario.

Just before Mary Browder arrived in Memphis, Metzger opened a clinical trial for children with high-risk Hodgkin lymphoma. Not only does the study eliminate the paincausing vincristine, but it also eliminates or drastically reduces radiation therapy and offers a low risk of infertility.

"When Dr. Metzger discussed this study with us, we literally jumped at the opportunity," Jason says. "We had been so concerned about the radiation issues. Since we had the luxury of being at St. Jude, we virtually took for granted the baseline quality of care. We viewed Dr. Metzger's study as an opportunity to enhance this quality of care even more. I cannot imagine a reason to deny our daughter that type of gift."

One-two punch

The new clinical trial replaces vincristine with brentuximab vedotin, a drug that delivers a one-two punch to cancer cells. First, a monoclonal antibody seeks out a Hodgkin lymphoma cell and attaches itself to the cell's surface. Then a second drug moves in for the kill. The St. Jude clinical trial is the first pediatric study to incorporate this antibody into frontline treatment.

"For a long, long time," Metzger says, "I've been trying to do something novel with Hodgkin lymphoma treatment. This drug was specifically approved for Hodgkin lymphoma, and it has had amazing results in adults with relapsed and refractory disease."

Children who respond to the antibody treatment may

avoid radiation therapy altogether. If radiation is required to kill remaining cancer cells, the children receive a highly targeted treatment.

"We irradiate only the affected lymph nodes," Metzger says. "So the selected patients who do need radiation get only a minimal fraction of what they would have gotten even five years ago."

Bald, busy, beautiful

From the moment of diagnosis, Mary Browder and her family made a conscious decision to embrace a positive attitude.

"We told Mary Browder that she could define her experience with cancer and its treatment, or she could let it define her," Jason recalls. "She seized this concept immediately and put it to work in dealing with things

What is Hodgkin lymphoma?

- Hodgkin lymphoma is a cancer that starts in the lymph system (part of the immune system) and causes affected lymph nodes to
- Hodgkin lymphoma accounts for about 6 percent of all pediatric cancers.
- 6,000 to 7,000 new cases of Hodgkin lymphoma are diagnosed annually in the U.S.
- Children younger than age 5 rarely develop Hodgkin lymphoma.
- Hodgkin lymphoma is more common in boys than in girls.

internally, but also in dealing with the focus and attention from friends, family members and even strangers. She has owned this experience through this approach."

The Howells' efforts to increase their daughter's comfort level set the tone for navigating the challenges ahead.

Throughout treatment, Mary Browder blogged with her classmates back home, excelled at her schoolwork, devoured mystery and mythology books, worked hundreds of crossword puzzles and returned home for dance rehearsals. She learned to give herself injections. She even rocked her bald head.

"I am now officially BALD," she wrote in early February.

"This morning we went to have my head shaved, but first
we got to see what I would look like with a whole bunch of
different types of hairstyles. It was really fun to see myself
with bangs, pixie, bob, and my personal favorite, a Mohawk."

Her beautiful, bald head became a palette. Mary Browder encouraged her friends and family to paint shamrocks, polka dots, flowers, purple ribbons and a Charlie Brown caricature on her head.

Between medical treatments, Mary Browder and her family visited Graceland, the Stax Museum of American Soul Music, the Memphis Zoo, the Pink Palace and the Rendezvous restaurant.

"We adjusted her chemotherapy schedule so that treatment didn't interfere with her life and her activities," Metzger says.

Limitless possibilities

In spite of that frenetic schedule—perhaps because of it—Mary Browder remained upbeat throughout her treatment. It helped that the clinical trial enabled her to avoid nausea, vomiting, pain, fatigue or radiation therapy.

In late May, she celebrated her last chemotherapy treatment—and then hopped in the car to travel to Iowa for the world finals of an academic problem-solving competition.

"We were told that the drug combination could potentially decrease the risk of nausea and vomiting as well as decrease pain. This held true in Mary Browder's case," Renee observes. "Another great 'side effect' was the reduced need for radiation following chemo. Mary Browder had scans after the second round, and it was found that she would not need any radiation. This was wonderful news, as radiation can have the risk of secondary cancers later in life.

"Overall, her quality of life was maintained during

treatment, while at the same time, hopefully, curing her of this disease," Renee says.

Now, the girl who is "too busy to have cancer" is looking for other exciting activities to pursue. There's no doubt she will find them. ■

Why choose St. Jude for Hodgkin lymphoma treatment?

- St. Jude is the only National Cancer Institute-designated Comprehensive Cancer Center devoted solely to children.
- St. Jude has created more clinical trials for cancer than any other children's hospital in the U.S.
- The nurse-to-patient ratio
 at St. Jude is unmatched—averaging
 1:3 in hematology and oncology,
 and 1:1 in the Intensive Care Unit.
- Patients have access to a multidisciplinary team sub-specialized in Hodgkin lymphoma and non-Hodgkin lymphoma.
- New risk-adapted therapies
 (such as the one Mary Browder Howell
 received) are designed to reduce the
 long-term side effects
 of treatment.
- St. Jude is headquarters to the Pediatric Hodgkin Lymphoma Consortium, a multi-center effort to develop novel treatment strategies for children with Hodgkin lymphoma.
- St. Jude provides long-term follow-up care to monitor and manage late effects of Hodgkin lymphoma.



ary Daniel, DDS, doesn't like to get stern with his young dental patients, but some situations call for desperate measures.

For instance, when a 3-year-old refuses to obey his mother and grandmother as they coax him to sit still in the dentist's chair, Daniel takes charge.

"What's your name, little boy?" Daniel asks in his best Donald Duck voice. The boy, who loves Mickey Mouse

Clubhouse, is startled for a second. Then he sits still.

"Will you open your mouth for me?"

It's a voice Daniel learned when he was about the same age as his patient, a talent passed down from his father.

"Sometimes it backfires and they go running to their mom's knee," Daniel says, with a grin.

It may seem odd to find a dental clinic tucked into the corner of a cancer hospital with a worldwide reputation for



saving children's lives. But the St. Jude Children's Research Hospital Dental Clinic provides services that are far from routine. This dental care may help save the lives of children who may be hundreds or thousands of miles away from their family dentists.

The clinic's two dentists look for potential problems, such as cavities, that could lead to serious issues down the road. Staff members also educate parents and children

about the critical role dental hygiene plays in the treatment of cancer, HIV infections, sickle cell disease and other disorders. Scrupulous oral hygiene is critical for St. Jude patients, because any infection can be lethal to a child with a compromised immune system. Children undergoing treatment also are at risk for a number of dental-related issues that demand the expertise of staff specially trained to deal with such rare complications (see sidebar on page 10).

Hands-on learning

Decked out head to toe in pink and sporting fake butterfly and rose tattoos, 5-year-old Brooklyn Chudy wiggles around in the dental chair, fascinated with an oversized set of choppers lying on the table beside her. Dental Clinic coordinator Diana Hill hands Brooklyn a toothbrush and invites her to demonstrate how she brushes her teeth. The pony-tailed girl from Missouri scrubs a little on the front of the teeth. Using humor and encouragement, Hill shows Brooklyn how to brush her teeth, gums and tongue.

The dental care at St. Jude is far from routine: This care may help save children's lives.

Next, Daniel talks with Brooklyn-no Donald Duck voice necessary this time. He rubs numbing jelly on her gums and gives "sleepy medicine" for the tooth before filling a cavity. Soon the procedure is over, and Brooklyn is on her way to her next appointment.

Twelve years ago, when Chris Rowland, DDS, began practicing dentistry at St. Jude, most of his patients were either preparing to undergo bone marrow transplants or had encountered dental problems during therapy. Today, the service has expanded to many other St. Jude patients as part of their routine care. The Dental Clinic staff sees about 1,100 patients and performs approximately 5,160 procedures each year-a number that has increased dramatically since Rowland's arrival in 2002. That means more opportunities to catch infections in early stages or teach proper dental hygiene. While Rowland and Daniel handle the dentistry, Hill and dental assistant Kim Willis educate patients about dental care.

Why is dental care crucial for St. Jude patients?

To minimize infection risks A simple cavity could quickly become a serious infection in a child undergoing therapy. Cancer and its treatment can suppress a child's infection-fighting ability. If an infection takes hold and is not treated, it could spread and become

life threatening.

- To combat salivary issues Chemotherapy and radiation therapy may shut down the salivary glands, giving a child a perpetually dry mouth. Because saliva helps wash away bacteria, its absence can also make a child vulnerable to infection. St. Jude Dental Clinic staff members educate patients and provide them with the special toothpastes, mouthwashes and artificial saliva necessary to prevent or treat such issues.
- To monitor tooth development Chemotherapy, radiation and bone marrow transplants can affect tooth growth and development. Teeth

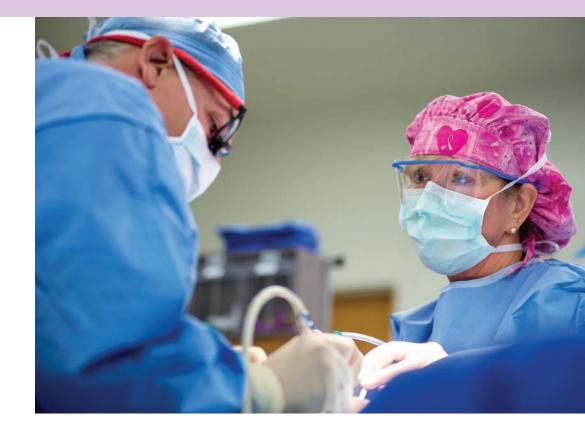
- may be smaller than normal, have shorter roots or fail to develop at all. The younger the children, the more likely they are to have these kinds of problems.
- To prevent or treat mucositis Poor dental health may increase the likelihood of developing mucositis, an inflammation and ulceration of the mucous membranes lining the mouth

and digestive tract. A common side effect of chemotherapy and radiation, mucositis causes pain that can inhibit a child's willingness or ability to eat. Staff members in the Dental Clinic help patients avoid or deal with mucositis. St. Jude dentists are also researching the use of laser therapy to alleviate and treat inflammation in patients with this condition.

St. Jude Dental Clinic staff members are specially trained to deal with issues children may encounter as they undergo treatment for cancer, HIV infections, sickle cell disease and other disorders.



In the hospital's surgical suite, Cary Daniel, DDS (at left), and Diana Hill attend to a patient whose dental needs are too extensive to be treated in the clinic.





Some patients, particularly from impoverished countries, may not have had regular access to dental care before coming to St. Jude. To educate families and reduce stress on patients, parents are encouraged to accompany their children to the examination area.

"We want parents to understand the importance of oral hygiene and dental care," Rowland says. "If we don't have the parents engaged, then the child might not keep it up."

Rowland and Daniel also provide educational opportunities for medical professionals, including nursing staff, students, dental residents and fellows from around the world.

"This helps increase the standards of care for kids, no matter where they are being treated," Rowland explains.

Gaining trust

During their time at St. Jude, patients may contend with fatigue, rounds of chemotherapy, radiation or bone marrow transplants. But just like healthy children, they frequently ask one simple question all kids want to know when they visit the dentist: "Will it hurt?"

Rowland has a reassuring answer to that inquiry. "Will it hurt? You tell me! I'm going to take my water sprayer, and my assistant is going to take Mr. Thirsty, and we're going to wash your teeth. If anything bothers you, just raise your hand, and we'll make it comfortable."

About half the children who visit the clinic receive fillings, extractions and other procedures, Rowland says. But inevitably, both children and parents leave the clinic with smiles on their faces.

"That's a great thing about my job. I get the privilege of simply proving to them that it's not painful," Rowland says. "It's gratifying to take a nervous kid and make them a compliant patient with minimized fear. One of the best parts of my job is walking them through it and gaining their trust in the end."

Sometimes patients do more than just trust their St. Jude dentist-they admire him.

"One of my patients had a teddy bear named 'Dr. Rowland,' and she brought the bear with her during visits," Rowland recalls.

"I'm thankful to report that he never had any cavities." ■

ith an elfin grin, Kyle Watson approaches the piano, eager to tickle the ivories in preparation for his first recital.

Nervous?

"Oh, no!" he declares, dismissing the question with a quick shake of the head and flip of the hand.

"Him?" his mother, Chasity Watson, teases. "He loves the attention."

Weeks before the musical event in a St. Jude auditorium—invitation only, and everybody who knows and loves Kyle is invited—he is rehearsing his selections and preparing his wardrobe.

"He has a new blue shirt and tie," announces his mom, eyes twinkling.

"And...tell what kind," he prompts her.

"A big-boy tie; no clip-on."

"Yep, that's right!" he affirms, delighted.

At 7, Kyle possesses the confidence and tolerance he needs to take on not only the keyboard, but also the cancer treatment he's undergoing at St. Jude Children's Research Hospital.

He arrived in February from Louisiana and, to him, it was important to continue his music. Kyle had begun piano lessons in October 2013 and had started memorizing recital pieces.

But cancer interrupted the plan.
"He was upset," Watson says,
"because he would miss his spring
recital."

When Kyle arrived at St. Jude, he met music therapist Amy Love. Kyle told her of his appreciation for piano; she immediately added an electronic keyboard to her collection of instruments. The more Kyle listened and learned and practiced, the more he hoped for a recital.

Love set out to make that happen.

Hitting the right note

"Music is therapeutic," Love explains.

"Research shows that music is the only thing that lights up all of our brain at once. For kids like Kyle, music helps build fine motor skills, improves concentration and task orientation, and assists with reading and learning a language.

And music gives Kyle something to celebrate," Love adds.

Kyle is being treated for a rare combination of germ cell tumors: germinoma and embryonal carcinoma. As part of his treatment, Kyle has undergone brain surgery, spinal surgery, chemotherapy and radiation therapy.

"He's had minimal sickness. Chemo hasn't slowed him down one little bit," his mom reports, "but he did get upset thinking he was going to have to miss a year's worth of piano."

"I had already picked my song, 'Swans on the Lake,' for my recital," Kyle adds.

"So they came up with the idea of a recital here," Watson says. "While we're in Memphis, Kyle particularly looks forward to seeing Miss Amy (Love) every week."

Rhyme, rhythm and song

Kyle is not the only patient who has fallen for Love. She makes her rounds, guitar strapped to her back, pushcart in tow, piled with drums and ukuleles; little xylophones and jingly bells on bracelets;



"Research shows that music is the only thing that lights up all of our brain at once. For kids like Kyle, music helps build fine motor skills, helps with concentration and task orientation, with reading and learning a language."



even a cylinder that, when shaken, sounds like a thunderstorm. Love's ever-present electronic tablet contains song lists.

As she passes through the corridors, children grin, parents nod and, by the dozens, she calls them by name.

Entering a patient's room, she greets a dour little face and gently announces, "I'm glad to be with you today, and I'm really glad for all the music we will play."

A silent boy reaches out a slim arm

for the drum she holds, the mallets and noisemakers she offers.

"Which song would you like today?"

Voices and choices

Love says she enjoys offering choices to children who may not feel that they have control over other aspects of their life.

"Music is a way of releasing a lot of tension in your body. People sing at weddings, funerals, graduations, on the radio, so why not in the hospital? You should have access to ways to express yourself—a music voice," Love says.

The boy in the bed chooses the drum, the song, and, as it turns out, the meter.

"Kids aren't always feeling well, but sometimes they have a lot of energy they have to get out of their bodies," Love says.

As she sings, the boy beats out the rhythm-moderate, then slow; fast, then ridiculously fast; ridiculously slow, and

back and forth. The patient grins at his own mischief with music. And the two musicians laugh together.

Heart, mind, spirit

"Sometimes we use music therapy to promote physical goals," Love explains. "You can use a steady pulse of music as a rhythmic cue for walking a specific pace or for learning a certain phrase with intonation, because the neuro-pathway for music is different than the one for speech.

"I may go into a patient's room and the child is anxious," Love continues. "I match the tempo of my guitar picking to the child's heart rate. As I slow the tempo, the child's oxygen saturation may increase and the blood pressure may decrease."

Music, she says, also has a place in legacy building.

"We're rolling out heartbeat therapy," Love says. "We can put a microphone in a stethoscope, record the child's heartbeat and create and perform a song over it, making that heartbeat into a beautiful memory."

At regular sing- and play-a-longs in the Kay Kafe lobby for kids and adults who happen by, Love is prepared when a little girl begins to cry: Another child has the instrument she wants. Love pulls out jingly bell bracelets, and harmony is restored.

Harmony of spirit. Harmony of sound. Budding pianist Kyle Watson understands.

"I love all the harmonies," Kyle says. "When I watch a movie or listen to music, I notice the harmonies. I notice when the singing starts. I can pick out the instruments, especially the piano.

"You know, I'm having a recital in the auditorium. Would you like to come? I'm playing three songs: 'Swans on the Lake,' 'Jesus Loves Me' and 'Let It Go.' I can't wait."





Amy Love's duties range from planning performance events such as Kyle Watson's piano recital (top photo) to encouraging Daniel Rowe (lower photo) and other children to dance away excess energy.

What is music therapy?

A clinical and evidence-based practice, music therapy can be used to achieve both musical and non-musical goals. One musical goal for a patient such as Kyle Watson might be learning to play piano. A non-musical goal might be using drums to improve motor skills. Music therapist Amy Love also helps patients attain emotional goals, such as learning to express themselves by writing and performing songs and discussing song lyrics. Creativity also helps patients cope with disease and its treatment.

Thwarting the Threat



By Anita Houk

St. Jude scientists uncover secrets of bacteria that can be deadly to children with sickle cell disease.

Heartbreaking.

That's how Temaiko Odum remembers the moment she learned that the medical screening for her newborn daughter, Leah, confirmed sickle cell disease, an inherited blood disorder.

"Leah was about a week old," Odum says. "I found out she had an illness that was not curable. What were we going to do?" Odum immediately obtained a referral to St. Jude Children's

Research Hospital.

Symptoms of sickle cell disease include anemia, severe pain, swelling of the hands and feet, and high fevers due to weakened defenses against infections. A prime cause of those fevers is the bacteria pneumococcus.

For children like Leah, pneumococcal infections can be fatal. The bacteria can cause pneumonia, meningitis, bloodstream infections, sinusitis, middle ear infections and other illnesses. To thwart infection, antibiotics and vaccines are used regularly, but they are not always effective.

Now, a new St. Jude study helps to clarify why available vaccines for pneumococcus don't work on some patients. The study also may guide development of more effective approaches to combat pneumococcal infections.

Targeting vulnerable kids

The first time Leah was hospitalized, she was a preschooler.

"She was very sick, in the hospital about five days," recalls her mom. "She had a pneumococcus bacteria infection. It was scary."

A host of bacteria live in and on the human body, for the most part causing no significant trouble. But pneumococcus finds a soft target in children with sickle cell disease.

"All of us are colonized in lots of places by bacteria," explains Joshua Wolf, MD, of St. Jude Infectious Diseases.

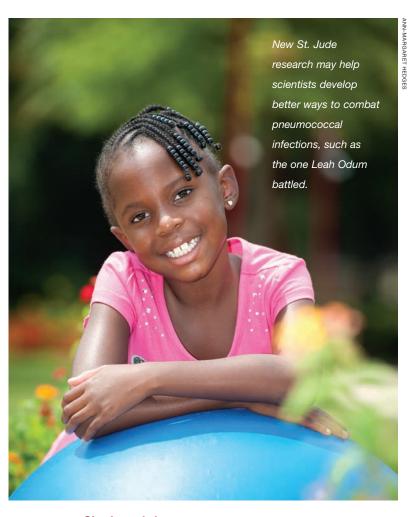
Wolf works directly with patients, focusing on how pneumococcus spreads and adapts.

"Bacteria live in our skin, nose, throat, gut, mouth, eyes," he says. "Bugs that normally live in the nose and throat almost never cause disease in normal, healthy people, but they're able to cause serious and life-threatening infection in sickle cell patients. What the medical community has done over the past 15 years is develop lots of ways to try to prevent that by using vaccine strategies and antibiotics. But these are imperfect, and some kids die of these infections."

Leah takes penicillin daily to prevent infection from taking hold. In spite of that precaution, she can still suffer setbacks. Infections are a constant threat.

"At St. Jude, they're always concerned about sickle cell patients running fevers," Odum says. "If Leah has a fever of 101 degrees or more, they want me to bring her in. Most of the time, for fever, they do blood work, see if there's any type of infection and give her preventive antibiotics.

"Leah is now 7, and she hasn't had any hospitalizations in almost two years."



Cloak and daggers

Scientists have identified at least 90 types of pneumococcal bacteria, but current vaccines are effective against only 10 percent of those.

"Pneumococcus is thought to have been with mankind for thousands of years," explains Jason Rosch, PhD, of St. Jude Infectious Diseases. "It has learned how to be transmitted and how to fight back against our immune system."

The bacteria rapidly swap and alter DNA as a strategy to elude defenses erected by vaccines.

"Scientists have understood that this DNA exchange is occurring," Rosch says. "We just didn't realize how rapidly it may be occurring in some of these patients. The issue we've seen in recent years is that, as soon as you roll out vaccines, the bacteria swap their genetics back and forth."

One bacterium can swap DNA with its neighbor, weakening a vaccine, or making it ineffective.

The DNA swap generally occurs when pneumococcus changes its capsule, or coat—literally, a sugar coatingmaking the bacteria invisible or immune to the vaccine.

Rosch and Wolf teamed with St. Jude computational biologist Robert Carter, PhD, and other colleagues to produce the first large-scale sequencing of pneumococci from children with sickle cell disease. The researchers sequenced 322 pneumococcal samples collected from sickle cell patients and 327 samples from the general public.

As they uncovered differences in the genetic code, the team discovered why pneumococcal bacteria may pose such a threat to children with sickle cell disease.

"We thought we'd see changes in the pneumococcus capsule, or coating; that's what we were looking for," Wolf says. "But we also found that the bacteria we obtained from children with sickle cell disease showed genetic changes in other areas of the bacterial genome." A genome is an organism's DNA, containing all of its genes and the instructions needed to build and sustain life.

The researchers found that in children with sickle cell disease, pneumococci had acquired mutations in genes that regulate how bacteria acquire metals, especially iron, and the way they acquire amino acids – the body's building blocks.

"Those particular gene changes occurred in areas in which children with sickle cell disease are constitutionally different from normal kids," Wolf says. "We think the bacteria have adapted to the special nature of children with sickle cell disease. We're now trying to understand how

this evolution of the bacteria occurs and how the bacteria adapt."

The importance of vaccination

Even though current vaccines do not provide complete protection against pneumococcal threats, evidence shows that the inoculation benefits at-risk kids.

Vaccines force bacteria to change, and the energy needed to mutate can sap a bacteria's ability to cause disease, explains Wolf.

"So, even though the vaccine is imperfect, it is helping to reduce the risk," Wolf says. "That underlines the importance of making sure patients get available vaccines, as appropriate."

Rosch says St. Jude scientists are working on vaccines designed to take better aim at specific bacterial infections affecting the general population as well as vulnerable St. Jude patients. The vaccine project takes a different approach to encouraging the immune system to protect children who are at high risk for infection.

Odum, for one, could not be more appreciative for the help St. Jude has offered her daughter. "Leah is doing well with her sickle cell disease," Odum says. "She's not sick a lot. She hasn't had the fever and pain in her joints, elbow and knees that she had in the past.

"I just love the treatment she receives at St. Jude," Odum adds. ■

Sickle cell disease

Sickle cell disease gets its name from the shape of its abnormal red blood cells.

In a healthy person, oxygen-carrying red blood cells are round and soft, smoothly flowing through small blood vessels.

In sickle cell disease, red blood cells become hardened and shaped like a sickle or banana.

These misshapen blood cells can block blood vessels, preventing oxygen from reaching some body tissues.



There are 3 types of sickle cell disease:

- sickle hemoglobin C disease
- sickle beta thalassemia disease
- sickle cell anemia (the most common form), also known as hemoglobin SS disease, or homozygous sickle cell disease

Sickle cell disease is the most common inherited blood disorder in the world:

- About 100,000 people are affected in the U.S.
- 300,000 babies are born each year worldwide with sickle cell disease.
- About 1 in 500 African Americans in the U.S. are born with sickle cell disease.

Supporting

Courageous Children

More brands than ever join St. Jude Thanks and Giving.

By Leigh Ann Roman and Lynda Nance

ittle Chloe Tuttle has lived on two continents and can speak three languages. But perhaps this 2-year-old twin's most amazing accomplishment is her courageous battle with the brain tumor ependymoma. That is a fight Chloe is winning so far—thanks to St. Jude Children's Research Hospital.

At 11 months old, Chloe moved with her family from Florida to China because of her parents' jobs. Not long afterward, her mother and father, Lynda and Alex, noticed Chloe tilting her head to the left. Several doctors' appointments in China yielded no answers. During a trip back to the U.S., tests revealed a brain tumor. Chloe underwent an operation at a Florida hospital to remove the tumor, but doctors there weren't sure what else could be done.

Then Lynda saw a St. Jude program on television.

"As soon as I saw St. Jude, I told Alex, 'That's where we're going," Lynda says.

After obtaining a referral to St. Jude, Chloe underwent two more brain surgeries to remove tumor growth and received chemotherapy and radiation therapy. Although

Chloe and her mom had to live away from her dad and twin sister, Hanna, during treatment, the assistance of St. Jude made the transition easier.

"At St. Jude, we had a place to stay, we had a meal card, a way to get around," Lynda says. "That meant so much for us. Here, we had support."



"Doctors often send their toughest cases to St. Jude because we have the world's best survival rates for some of the most aggressive cancers." That's one of the messages Marlo Thomas, national outreach director for St. Jude, will share this year, with a little help from patients (left to right)

Dharma Rodriguez, Kayla Snodgrass, Helen Forgey, Chloe Tuttle, Jaiden Perry and Ryan Auten.

Generous spirits

Now out of treatment and having regular checkups, Chloe is taking part in one of the hospital's largest fundraising and awareness programs: the St. Jude *Thanks and Giving*® campaign. This union of celebrities, media, retail and corporate partners asks consumers to donate during the holiday season and to join

St. Jude in finding cures and saving children.

Created by Marlo, Terre and Tony Thomas, the children of St. Jude founder Danny Thomas, the St. Jude Thanks and Giving campaign has raised more than \$488 million since its inception in 2004.

"We have been blessed to have the extraordinary support from our wonderful donors, our loving celebrity friends and our dedicated corporate partners," says Marlo, national outreach director for St. Jude. "I am so proud and happy that they are part of the St. Jude Thanks and Giving campaign. Their support means so much to children like Chloe and their moms and dads, and helps us stay true to my father's founding promise that families never receive a bill from St. Jude—for treatment, travel, housing or food—because all a family should worry about is helping their child live.

"I am grateful for their generous spirit and compassion to help St. Jude raise the funds that allow us to continue our mission of finding cures and saving children's lives."

Partners in the mission

Corporate partners for the St. Jude Thanks and Giving campaign include Kmart, CVS/Pharmacy, Ann Taylor, DICK'S Sporting Goods, Kay Jewelers, Domino's, Williams-Sonoma Inc., GNC, HomeGoods, AutoZone, New York & Company and Brooks Brothers, to name a few.

Beginning in November, shoppers will see the St. Jude logo identifying retailers who are raising funds for St. Jude to help children like Chloe.

Kmart was again the top fundraising partner for the St. Jude

Two-year-old Chloe Tuttle is doing her part to help raise funds through the St. Jude Thanks and Giving campaign. This unprecedented union of celebrities, media, retail and corporate partners asks consumers to donate during the holiday season and to join St. Jude in finding cures and saving children.

Thanks and Giving campaign in 2013, raising a record-breaking \$21.9 million. Since becoming a corporate partner in 2006, Kmart has raised more than \$59.2 million for the children of St. Jude—more than any corporate partner in history. This year, the building that houses the St. Jude LIFE study and the After Completion of Therapy Clinic Presented by Kmart was renamed The Kmart St. Jude Life Center.

New partners in the St. Jude Thanks and Giving campaign this year include The Limited and longtime St. Jude supporter Chili's® Grill & Bar, a partner that raised more than \$50 million over 10 years for the St. Jude mission.

Williams-Sonoma Inc., a 10-year veteran of the campaign, brings two new brands to the program this year: Rejuvenation, and Mark and Graham. Both will offer specialty merchandise during the campaign.

Spreading the word

The St. Jude Thanks and Giving campaign also enjoys the support of celebrity friends Jennifer Aniston, Sofia Vergara, Michael Strahan and Latin GRAMMY winner Luis Fonsi, who join Marlo and St. Jude patients in TV spots. These celebrities also are in a movie trailer that shares the St. Jude story nationwide in theaters including Regal Entertainment Group, AMC Theatres, Cinemark USA, Carmike Cinemas and many others.

The campaign is supported with a national media blitz that includes TV appearances by Marlo and St. Jude patients. In what has become a holiday tradition, Marlo will appear on NBC's TODAY show for five consecutive days during Thanksgiving week to share inspiring stories about patients and the hospital's lifesaving work.

The St. Jude Thanks and Giving campaign wouldn't be complete without the official kick-off event, the St. Jude Give thanks. WalkTM, scheduled for November 22 in 66 cities. The non-competitive 5K fundraiser has raised \$17 million since it began in 2009.

This outpouring of support enables St. Jude to provide exceptional care for children such as Chloe who-even after brain surgery and radiation therapy—can still chat with her

Taiwanese grandparents in Chinese and her Hispanic grandmother in Spanish.

> When she talks to her sister, Hanna, Chloe switches easily from Chinese to Spanish to English. "We are always amazed," Lynda says. "They're very bright little girls."■

A Tribute to **Robin Williams** By Leigh Ann Roman



n August 11, the world lost an iconic entertainer and an incredibly generous man who was a true friend to St. Jude Children's Research Hospital.

Robin Williams brought smiles and joy to St. Jude patients, just as he brought laughter to fans worldwide who watched him in his many comedic roles on television and in movies.

Williams was a celebrity supporter of St. Jude for a decade, freely offering his time and talent in TV commercials with St. Jude patients such as Darcy Cassidy (pictured top left), who was filmed with Williams in 2013.

"He was funny and nice," says Darcy, 10, who has been fighting a rare brain tumor at St. Jude since 2009.

Darcy's mother, who met Williams the day of the filming, described the actor

as humble. "He was compassionate. He really cared," she says. "He made us feel like we were the superstars."

Williams showed his support for St. Jude through his participation in many celebrity events, including the Shower of Stars, a star-studded event in 2003 that was hosted in Memphis by Marlo Thomas, Terre Thomas and Tony Thomas, the children of St. Jude founder Danny Thomas.

The actor was also connected to the St. Jude family through his work with Tom Shadyac, the brother of Richard Shadyac Jr., who is president and chief executive officer of ALSAC, the fundraising and awareness organization for St. Jude. Tom Shadyac, a movie director and producer, worked with Williams when he directed him in the title role of the 1998 movie *Patch Adams*.

Williams' commitment to St. Jude is shared by his daughter, actress Zelda Williams, a well-known gamer who this year helped launch a new videogame charity program for St. Jude called St. Jude PLAY LIVE.

The legendary humor and gentle nature that characterized Robin Williams was evident in his work with St. Jude, just as in some of his best-loved roles in movies and TV.

St. Jude National Outreach Director Marlo Thomas remembers Williams as an exceptional man and a comic genius whose generosity and dedication to the children of St. Jude were always apparent.

"He was the genuine article," she says. "The adoration he felt for the precious, brave children of St. Jude was only matched by the enchantment they felt for him in return."

Research Highlights



survival rates to unprecedented heights. The election also honors Pui for his work with doctors worldwide to further the study and treatment of childhood cancer.

Headquartered in Taipei, Academia Sinica supports research activities in disciplines such as mathematics and physical sciences, life sciences, humanities and social sciences. The Convocation of the Academia Sinica includes more than 200 distinguished scientists.

Pui elected to Academia Sinica

St. Jude Oncology Chair Ching-Hon Pui, MD, has been elected as an Academician of Academia Sinica. The honor is given in recognition of Pui's research, which has successfully eliminated the need for radiation in the treatment of leukemia and helped push childhood leukemia

"Dr. Pui's work has changed the way the world thinks about and treats childhood leukemia," said James R. Downing, MD, St. Jude president and chief executive officer. "This honor recognizes his leadership, pioneering research and contributions, made not only to children at St. Jude, but to pediatric cancer patients across the globe."

St. Jude celebrates siblings

Luca de Jong and other St. Jude siblings walk the red carpet as part of the annual Sibling Star Day event held this summer. The event recognizes brothers and sisters of St. Jude patients for their all-star efforts. The St. Jude Child Life Program hosted the sports-themed day of activities for siblings, ages 4 to 19.

Siblings decorated and personalized sports pennants, waving them proudly during a red-carpet walk from the front entrance of the hospital to the Danny Thomas/ALSAC Pavilion. Employees and volunteers lined the route, cheering and applauding the



honorees. The siblings also received medals to honor their contributions as part of the patient care team.

St. Jude receives top honor for supporting military personnel



St. Jude has received the highest honor given by the U.S. government to recognize employers who provide exceptional support of employees serving in the National Guard and Reserve. Of more than 2,800 U.S. corporations nominated, St. Jude was chosen as one of 15 to receive the Secretary of Defense Employer Support Freedom

Award from the Employer Support of the Guard and Reserve of the Department of Defense.

"We deeply appreciate our employees who serve in the military for their contributions to the St. Jude mission and to our country," said James R. Downing, MD, St. Jude president and chief executive officer. "We are honored to receive this recognition and gratified to know that our employees appreciate our support of them and their families during times of deployment."

Army National Guardsman Curtis Johnson, Facilities
Operations and Management, and veteran Racquel Collins,
PhD, Pathology (pictured at left), are two of approximately
100 hospital employees who are veterans or are on active
duty.

Lifestyle choices especially important for childhood cancer survivors

Adult survivors of childhood cancer who don't get enough exercise and eat an unhealthy diet more than double their chances of developing metabolic syndrome. This disorder includes symptoms like high blood pressure and a large waistline. Those factors increase the risk of heart disease, diabetes and other serious health problems.

St. Jude researchers found the link by studying 1,598 childhood cancer survivors. They ranged in age from 19 to 60 years old. All were enrolled in the unique St. Jude LIFE study, in which adults who were treated at St. Jude as children return to the hospital for tests. The tests help scientists learn more about the health challenges facing childhood cancer survivors.

Of the survivors in this study, almost a third had metabolic syndrome, and nearly three-quarters did not follow a heart-healthy lifestyle. Lifestyle contributed to survivors' odds of developing metabolic syndrome more strongly than did risk factors related to their cancer treatment.

"The findings suggest that if childhood cancer survivors maintain a healthy lifestyle by staying active and eating a diet low in fat, sugar and salt, and rich in fruit and vegetables, they should be able to influence whether or not they develop metabolic syndrome," said Kirsten Ness, PhD, of St. Jude Epidemiology and Cancer Control.

The study appeared recently in the journal Cancer.

New leads on hushing the "voices" of schizophrenia

A missing gene and the resulting defective connection between brain structures may leave individuals vulnerable to the "voices" that are a common symptom of schizophrenia.

The St. Jude study is the first to tie a specific brain circuit to the "voices," delusions and other psychotic symptoms of this chronic brain disorder. The circuit links parts of the brain that interpret sound.

Working in a laboratory model of schizophrenia, researchers reported that losing one copy of a gene named *Dgcr8* reduced the

flow of information between the brain structures. "We think this sets the stage for stress or another factor to come along and cause auditory hallucinations," said Stanislav Zakharenko, MD, PhD, of St. Jude Developmental Neurobiology.

The research also provides a new focus for efforts to develop drugs that quiet the "voices" of schizophrenia with fewer side effects than current medications. A report on this research appeared in the journal *Science*.

Attaching an "on" switch for protein regulation

Humans use accessories like boots and gloves to adapt to their environment. Inside cells, proteins accessorize too, and for similar reasons.

In this case, the "accessories" are small molecules that cells rely on to adapt to changing conditions. The small molecules attach to proteins to change their fate and function.

St. Jude scientists have discovered how an important "on" switch is attached to the cellular machinery that helps accessorize proteins. The study involved a specialized accessory called NEDD8—the "on" switch for the machinery that accessorizes 10 to 20 percent of the thousands of proteins that work in cells. The

researchers discovered the mechanism that ensures NEDD8 is properly positioned on that machinery.

"This discovery is a major advance in understanding the machinery cells use to regulate an astonishingly vast number of proteins they depend on—as well as the diseases that arise when the system malfunctions," said Brenda Schulman, PhD, of St. Jude Structural Biology, and a Howard Hughes Medical Institute investigator. Problems with NEDD8 have been associated with cancer and other diseases, including the infectiousness of HIV, the virus that causes AIDS.

The research appears in the journal Cell.

Discovery may lead to new antibiotics for staph infections

St. Jude scientists have discovered an enzyme that regulates production of the toxins that contribute to potentially lifethreatening Staphylococcus aureus infections.

Researchers also showed that the same enzyme allows Staphylococcus aureus to use fatty acids acquired from the infected individual to make the membrane that bacteria need to grow and flourish.

The results provide a promising focus for efforts to develop a much-needed new class of antibiotics to combat staph and other Gram-positive infections. Staphylococcus aureus is the most common cause of staph infections, including methicillin-resistant

Staphylococcus aureus (MRSA), the drug-resistant infection that is a growing problem in hospitals.

"Staphylococcus aureus is a clear and present danger to patients worldwide," said Charles Rock, PhD, of St. Jude Infectious Diseases. "We set out to answer a long-standing question about bacterial membrane biochemistry and discovered a master regulator of the virulence factors that make staph infections so destructive and dangerous. The pathway we identified offers an exciting new target for antibiotic drug development."

The study appeared in Proceedings of the National Academy of Sciences.

Shape-shifting protein discovery may aid drug development



St. Jude structural biologists Diana Mitrea, PhD (at left), Richard Kriwacki, PhD, and their colleagues recently discovered the mechanism underlying a shape-shifting regulatory protein that fulfills multiple roles in the life of cells and aids in tumor suppression. The results could aid cancer drug development.

The research focused on the protein nucleophosmin 1 (NPM1), which plays a critical part not only in tumor suppression but in cell division, protein production and other cell processes. Until now, however, how NPM1 fulfilled its varied responsibilities was unknown. The study was published recently in Proceedings of the National Academy of Sciences.



The mom of a St. Jude patient reflects on what she received as a result of her child's treatment journey.

Time

First and foremost, St. Jude has given me 11 more years with my daughter. Without their lifesaving treatment, I would not have been able to watch her grow into the graceful woman she has become.

Courage

My daughter's battle with cancer gave me the courage to face a mother's darkest fears. I believed I was a strong woman, as most mothers do, but I found out that my inner strength will support me when exhaustion and terror are battling to overcome me. St. Jude helped me find that strength as I watched my daughter battle for her life.

Compassion

St. Jude showed me that cancer doesn't discriminate. Whether they have lots of money, little money, from the big city or remote towns-St. Jude treats all children and their families with great respect despite family circumstances. I have found that I am more compassionate to those who seem different than me.

Tolerance

Not everyone handles life's hurdles gracefully, especially while undergoing treatment for cancer. Now, when I am faced with rude behavior or am cut off on the highway, my first thought is that something stressful must be happening in that person's life.

Grandchildren

Without St. Jude working to find a cure for osteosarcoma, I wouldn't have my daughter's two gorgeous children.





Appreciation for the outdoors

I always enjoyed being outside, but after being in a position of only seeing the seasons pass by through a window because of a sick child, the great outdoors is truly great.

Gray hair

I went from a few strands peppering my brown hair to someone who could pass for the bride of Frankenstein if my hair is parted just right. But, rather than cover my head with chemicals, I embrace that gray as a reminder of a journey I took with my child.

Nuances

My daughter can have an eyelash out of place or have a tiny inflection in her voice, and I will pick up on those small nuances. I am more tuned in to her than I could possibly imagine, even after 11 years. This has transferred to other people, too. More times than not, I am right when I think I hear something troubling in a friend's voice or actions.

Trust

When faced with a diagnosis of cancer, it is hard to trust that things will turn out for the best-whatever "best" might be. I learned to trust the doctors, the nurses, the drugs, my intuition, my daughter.

Desire to pay it forward

I know I can never repay friends and strangers for their kindness to our family when cancer hit our daughter. So, passing on kindness to others is a way of repaying those who gave of themselves in some way to help us. Pay for someone else's coffee, make a meal for a co-worker, send

> a greeting card just to say hello....As Marlo Thomas says, "Be thankful for the healthy children in your life." Give to St. Jude."■

Catherine Greenslade's daughter, Emily Land, is pictured during treatment (far left) and today, with her husband and children.



To help me live.

Martavion's treatment at St. Jude is putting a stop to his strokes caused by sickle cell disease. Because you give, his family won't ever receive a bill for treatment, travel, housing—for anything. So they can focus on what matters most—helping their child survive.

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Never Have I

Never have I been my diagnosis,
Strong and sure I have always been.
My doctors told me I am ferocious.
Never have I been my diagnosis.
Never have I felt hopeless.
Always, yes, always will I win.
Never have I been my diagnosis,
Strong and sure have I always been.

This poem is one of 30 written by St. Jude patient Deidra Abbott as part of her college's senior seminar. The collection of poetry chronicles Deidra's experiences as a survivor of mesenchymal chondrosarcoma, an extremely rare cancer of the cartilage. After graduation in December of 2014, Deidra intends to pursue a writing career. To read some of the other poems in the collection, visit stjude.org/promise-abbott-poetry.



Finding cures. Saving children.