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Photo above:
The black-and-white image on this page shows how bacteria accumulate on the inside wall of a central line. Find out how St. Jude is working to reduce such infections worldwide: page 15.

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She may have left her spade in North Carolina, but Hannah Allison has brought a sense of vibrant curiosity along with her to St. Jude, where doctors and researchers are doing their own digging—seeking a cure for Ewing sarcoma.
By Elizabeth Jane Walker

Hannah Allison is always on the lookout for a treasure—scouring her gravel driveway for interesting rocks, meticulously excavating a hill near her home for a cache of metal that she can sell to make some spending money.

But recently, the 12-year-old put these ventures on hold to travel to St. Jude Children’s Research Hospital. There, doctors and researchers are searching for the ultimate trove for kids like Hannah—a cure for Ewing sarcoma, a cancer that grows in the bones or in the soft tissues.

Hannah is no stranger to hospitals and medical procedures. Four years ago, a horrific fire sent the little girl and two of her siblings to a burn unit for 55 days. Nearly 20 percent of Hannah’s body was burned, requiring excruciating treatments and skin grafts to her arm and back.

Finally, life returned to normal. Then, Hannah discovered a knot in her upper left leg and groin area. Another challenge

“We thought it was a hernia,” Hannah says, crisply relating the events that brought her to St. Jude. “We went to another doctor, and he said it was a lymph node. I took some antibiotics, and then we went to a specialist. Then we went to another hospital, where I had an ultrasound and a CT scan. They found out it was cancer that day.”

When Hannah’s family learned she had cancer, they assumed it was confined to her pelvic area.

“But we found out there were more than 40 tumors in her lungs, as well,” recalls her mom, Melissa.

“As a mother, my heart seemed to leave my body. My mind went to mush; my world was upside down. Because of the fire, Hannah had already met tragedy head-on. My only

ST. JUDE has created more clinical trials for cancer than any other children’s hospital in the nation.
thought was, ‘Why is something else happening to her?’”

Although Ewing sarcoma is the second most common type of bone cancer in children, it is still extremely rare. Between 200 and 250 children and young adults are diagnosed with Ewing sarcoma each year in the U.S. Because Hannah’s cancer had already spread to her lungs, there was a high likelihood that standard therapy—chemotherapy, surgery and radiation therapy—might not completely eradicate the tumor, or the cancer might return after treatment.

At their North Carolina hospital, Hannah’s oncologist offered the family some advice.

“We think she would benefit from going to St. Jude,” the physician said. “She meets all the criteria to be treated on a new research protocol they have there.”

“When the doctor said, ‘St. Jude,’ warmth went throughout my body,” Melissa recalls. “I felt that’s where God wanted her to be.”

In good hands

For years, Hannah’s grandmother has hung photos of St. Jude patients on her refrigerator—to remind her of the children who benefit from her monthly donations to the hospital. Last December, Hannah suggested that her grandmother hang those photos on the Christmas tree, where the entire family could see them. Ironically, a few weeks later, Hannah became a St. Jude patient herself.

“When we arrived at the hospital, I was amazed at how many children are fighting cancer,” Melissa says. “It overwhelmed me.”

Almost all of those children are treated on clinical trials, which are studies designed to determine the best way to prevent, diagnose or treat diseases. St. Jude has created more clinical trials for cancer than any other children’s hospital in the nation.

Because cancer had already spread to Hannah’s lungs, she qualified to enroll in the ESFT13 clinical trial as a high-risk patient. Children in the high-risk arm of that study receive two cycles of experimental chemotherapy followed by standard Ewing sarcoma treatment. Afterward, patients receive additional chemotherapy to help prevent relapse.

“In this trial, we’re testing a novel set of drugs before standard treatment begins,” explains Fariba Navid, MD, of St. Jude Oncology, principal investigator for ESFT13. That drug combo incorporates three medications with cumbersome names: irinotecan, temozolomide and temsirolimus.

Several years ago, a St. Jude researcher found that adding temozolomide to irinotecan was highly effective against relapsed Ewing sarcoma. In ESFT13, Navid and her colleagues are testing to see how well newly diagnosed patients respond to that combination.

Another St. Jude faculty member conducted early studies with the drug temsirolimus.

“In the lab, research showed that if you add temsirolimus to chemotherapy it becomes more effective,” Navid says. “It seemed like a good fit to combine all three of those drugs.”

The final portion of the clinical trial also builds on a previous St. Jude study, which combines drugs that target the blood vessels to prevent them from feeding any tumor cells that may remain. The entire treatment lasts nearly a year.

“When I explained to Hannah that she would be going into the hospital to get her next treatment,” Navid says, “she wanted me to tell her exactly what the drugs were, how they were going to be given, how many days she was going to be there and exactly what was going to happen. It’s impressive
**SCIENTISTS** have sequenced and are analyzing the genetic features of more than 100 children with Ewing sarcoma to find possible new targets for treating the disease.

that she’s so involved and interested in her treatment. She also keeps us laughing. She recently used a whoopee cushion to play a joke on her nurse practitioner. I love the fact that she’s taking this in stride and not feeling sorry for herself.”

**Ewing expertise**

St. Jude has a team of experts who specialize in taking care of children with Ewing sarcoma. A skilled surgical team is available to perform limb-salvage operations or other surgeries, when necessary. Clinicians have access to the latest imaging techniques—such as contrast-enhanced ultrasound and diffuse weighted imaging MRI—as well as radiation treatments that include intensity-modulated radiation therapy and proton beam therapy.

Soon, patients with Ewing sarcoma tumors will be able to receive proton therapy on the St. Jude campus. This treatment can be focused precisely and intensely on the tumor, sparing healthy tissues from radiation exposure. The facility, slated to open next year, will be the world’s only proton therapy center dedicated solely to the treatment of children.

Working with European researchers, St. Jude scientists have also sequenced and are analyzing the genetic features of more than 100 children with Ewing sarcoma to find possible new targets for treating the disease.

**The best place**

In Hannah’s North Carolina hometown, the sixth-grader is known for her curiosity, high energy and sense of adventure. She loves to take things apart and dig things up—enticed by the mystery of what lies beneath the surface.

“Sometimes I take a hammer and break rocks apart to see what’s inside,” she says.

Years ago, someone buried a junk car in a hill near Hannah’s home. Intrigued, she began to dig for the vehicle. The hole became deeper and deeper and deeper. Hannah was convinced that treasure was within her reach.

“My husband and I discussed filling in that hole, but we knew that if we did, she’d just take the dirt back out again,” her mom says.

When Hannah uncovered metal items, she took them to a junkyard and sold them. Friends and family members began bringing her lawn mowers, weed eaters, metal chairs. She carefully disassembled each item and took those pieces of metal to the scrap yard—thrilled with her newfound income.

At St. Jude, the little girl who used to search for rocks and dig for scrap metal now turns her curiosity toward the medical environment, pushing buttons, checking out equipment, asking questions. “Just like the investigating and the digging she did at home, she’s got to see how everything works at the hospital,” her mom says.

During a recent hospitalization, Hannah entertained herself by checking out every piece of equipment in the vicinity.

“Dr. Navid, I’ve got to show you how high this bed will go!” she said, when her oncologist stopped by for a visit.

“The nurse is going to come in here, and we’re going to get in trouble,” Navid answered with a laugh, as Hannah manipulated the bed’s controls.

Whether she is exploring the hospital's nooks and crannies or pulling hijinks in the clinic, Hannah enlivens St. Jude with her humor, curiosity and honesty. Her mom is confident they chose the best place to bring Hannah for treatment.

“Everybody here has been wonderful, giving us all the information we need, answering all the questions we have,” she says. “Without the research and the care at St. Jude, where would our children be? What hope would there be?

“I don’t want my child to have cancer, but I’m thankful that she’s here,” Melissa adds. “We’re in awe of what St. Jude has done for us. I want to say, ‘Really? You’re doing all this for our child and our family?’ But they do it not just for Hannah, but for all of these kids.”

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**LEARN MORE**

about the ESFT13 clinical trial:  
stjude.org/ESFT13
What if cures for some of the worst childhood cancers already existed...and nobody knew it?

In fact, researchers at St. Jude Children’s Research Hospital are betting those cures are out there—hidden among the legions of medicines already used to treat adult cancers and other diseases.

“There is a mistaken belief that all of these drugs have been tried for pediatric cancers. The reality is, they haven’t,” says Anang Shelat, PhD, who plays a central role in drug discovery in the department of Chemical Biology and Therapeutics (CBT). “We say, ‘Let’s test everything we can get our hands on.’ That leads to unexpected discoveries.”

Recently, one of these discoveries has given new hope for children with an aggressive form of medulloblastoma, the most common malignant childhood brain tumor.

The story begins in a laboratory, as it often does at St. Jude. After years of research, Martine Roussel, PhD, of Tumor Cell Biology, and her scientific team had perfected a difficult art: producing medulloblastoma tumors in the lab that accurately mimic human disease. With this valuable resource in hand, they set out to find new ways of destroying those tumors.

“ Our focus was to identify drugs that we could move quickly from the laboratory to the clinic, because new treatments are desperately needed for high-risk medulloblastoma patients,” Roussel says.

So, they called a few chemists. And a robot.

Shelat and his colleagues were ready for the call. They used a high-tech robotic system to rapidly test thousands of chemicals for their ability to kill lab-grown tumor cells.

Among the battery of chemicals was a library of more...
than 1,300 existing medicines. This St. Jude collection, one of the best in the world, includes virtually every drug approved for clinical use in the U.S. to treat any disease.

That’s where the scientists uncovered their prize. After careful analysis, two existing medicines stood out, proving especially potent against the tumors when used together. The pair worked even better when combined with existing chemotherapies against medulloblastoma.

The two drugs, gemcitabine and pemetrexed, are commonly used to fight breast cancer and other aggressive adult tumors. But they had never been tested against medulloblastoma. Without St. Jude, they might have remained hidden in plain sight forever.

The process of finding new uses for existing drugs, known as repurposing, has a major advantage: It is much faster than developing a new drug from scratch. Because gemcitabine and pemetrexed have already met strict U.S. government safety standards for clinical use, St. Jude patients may begin receiving them immediately.

Children and teens with high-risk medulloblastoma are now being treated with the drug pair as part of a St. Jude clinical trial.

Amar Gajjar, MD, co-chair of Oncology, leads that trial, called SJMB12. He hopes the drug pair will improve the outlook for high-risk medulloblastoma patients, whose cure rate hovers around 40 percent. Patients with other forms of medulloblastoma are twice as likely to survive.

“We need new chemotherapy agents, because the current treatment often doesn’t cure,” Gajjar says. “The drugs identified in this study will hopefully close that survival gap.”

For Roussel, doing science that has the potential to help cure patients fulfills a longtime aspiration. “As a basic scientist, it is exciting to be able to translate a laboratory discovery into drugs that are now being used in a clinical trial,” Roussel says. “This is one of the most rewarding things that I’ve done.”

The St. Jude campus and culture have been deliberately designed to spark critical connections between physicians and scientists, and across scientific disciplines. “That’s what’s special about St. Jude,” Roussel says. “Everything is in one place, and people are extremely collaborative and willing to be part of big projects.”

Using new scientific findings to improve patient care sounds simple. In practice, the process, called translation, is complex. To be successful, experts across many research fields must first find each other, then work together productively for many months or years.

One key collaborator on this project was Gajjar, who helped guide the laboratory work from the perspective of a physician who sees medulloblastoma patients every day.

“We are not a typical children’s hospital where the research university is five blocks away,” he says. “Our mission, our facilities, our culture, our environment—all of that goes
toward fostering this type of collaboration. It’s a constant
dialogue, with information flowing back and forth.”

Shelat and others on campus also played central roles. Clinton Stewart, PharmD, and his research group in Pharmaceutical Sciences conducted laboratory experiments showing that the drug pair can pass through the blood-brain barrier to target the tumors in the right place. Scientists in Stewart’s laboratory collaborated closely with each other to collect the samples, measure the amount of drug with sophisticated instruments, and then model the drug concentrations to determine the correct doses to use in SJMB12.

Kip Guy, PhD, the chair of CBT, has been the architect of many drug discovery efforts at St. Jude. Like Gajjar, he credits the St. Jude mission with drawing people together to find cures.

“This place is an order of magnitude more mission-driven than anywhere else I’ve ever seen,” he says. “We are here because we care about the pediatric clinic. More often than not, you could ask me about a specific childhood cancer and I could list 10 people at St. Jude who could come together as a team to work on it.”

Saving children with high-risk medulloblastoma is one critical priority. There are many others.

The drug discovery program at St. Jude has been built to find cures for the world’s toughest-to-treat childhood cancers by casting as wide a net as possible.

Researchers on campus have also recently teamed up against another childhood brain tumor, ependymoma, and revealed unrecognized promise in an adult cancer drug called 5-fluorouracil (5-FU).

Guy and Richard Gilbertson, MD, PhD, director of the St. Jude Comprehensive Cancer Center, spearheaded the project, which was the first large drug repurposing screen on campus. 5-FU is now being given to St. Jude patients with relapsed ependymoma in an early-stage clinical trial.

Similar projects homing in on other cancers are blossoming around campus, fueled by the early successes of these teams.

For the researchers leading these projects, repurposing known drugs is simply the first step. The screening process also provides an opportunity to assess tens of thousands of other chemicals that have never been tried in the clinic. These molecules represent uncharted territory; after careful testing and refinement, a select few may one day be shaped into completely novel therapies.

This state-of-the-art drug discovery pipeline would have sounded like science fiction when St. Jude opened in 1962. Yet, it is really just a modern embodiment of what the hospital’s founder first envisioned.

“Our academic mission is to develop new therapies,” Gajjar says. “It’s what Danny Thomas’ dream was—to build an institution where the lab and clinic were interwoven to improve cure rates for these children.”
It is past noon in the Department of Chemical Biology and Therapeutics (CBT) at St. Jude Children’s Research Hospital. Some scientists are bent over experiments, hoping to snatch a quick bite to eat later. Others are down the hall in the lunchroom, taking a much-needed break with their colleagues.

But Billy the Robot is still working. All day long, his arms swing silently back and forth with a single purpose: to discover drugs that can help save kids’ lives.

In a single day, Billy can test tens of thousands of chemicals, seeking a small handful with the ability to kill cancer cells while sparing normal cells. The cancer cells come from some of the most aggressive and hard-to-treat childhood tumors. The chemicals come from, well, everywhere.

“Creating new drugs for pediatric cancers requires discovery on an industrial scale,” says Richard Gilbertson, MD, PhD, director of the St. Jude Comprehensive Cancer Center. “We have chemicals from all over the planet—the bottom of the ocean, the Amazon jungle—and they cover every chemical space you can imagine.”

The St. Jude collection contains more than 800,000 unique, purified molecules and is one of the largest chemical libraries at any academic institution in the world. Thousands of these chemicals have been isolated from natural sources. Others are existing drugs, already used to treat different diseases. More than 50,000 are new molecules, created in-house by St. Jude chemists.

It is no surprise that Billy and his robot colleagues, under the expert direction of Taosheng Chen, PhD, are prized on campus for their ability to rapidly test so many chemicals with outstanding fidelity. (The robots were named by St. Jude patients; others are Saver, Tobor and Clifford.)

The robot-based testing approach, called high-throughput screening, has proven a powerful way to find existing drugs with potential new uses against childhood cancers. It is one of many methods used at St. Jude to identify promising new agents that have never been tested in patients.

However, for truly driving drug discovery, humans still rule. “People see the robots, and they think they’re pretty snazzy,” observes Kip Guy, PhD, who spearheads the St. Jude drug discovery effort as chair of CBT. “But the robots are just one part of a workflow.”

Once a new molecule is identified, it is usually still years away from becoming a drug. Careful refinements must be made and tested to create a safe and effective drug for patients. This process requires untold hours of meticulous lab work and lively discussion among teams of scientists.

“To make a drug, everything has to come together in exactly the right way,” Guy says. “It’s the people, the science, the materials and the equipment; you need all of those things working together in order to be successful.”
Scrutinizing Stress

Children with cancer are tougher than you might assume.

By Anita Houk

RESEARCH SHOWS childhood cancer patients are no more likely than their healthy peers to develop post-traumatic stress disorder.

Three years ago, Mia Troquille expected that getting into fourth grade would be her No. 1 challenge. Then she heard the words acute lymphoblastic leukemia.

“The day my cancer was diagnosed,” says Mia, now 12, “was the last day of the school test to determine if you passed. I finished the test, but I missed fourth grade.”

Mia and her family embarked on a previously unfathomable journey to St. Jude Children’s Research Hospital and to cancer remission. Her last day of treatment occurred in December 2013.

“I think we handled it like professionals,” says her mom, Christie Barnes. “She’s a really strong little girl. As horrible as it was going through, I don’t really think it’s going to affect her future.

“I don’t feel that she has post-traumatic stress.”

This remarkable resilience, often anecdotally noted in childhood cancer patients, was also found in a St. Jude study of stress and adjustment, published in the Journal of Clinical Oncology.

Challenging assumptions

The study showed childhood cancer patients are no more likely than their healthy peers to develop post-traumatic stress disorder (PTSD).

A condition of persistent mental and emotional distress, PTSD can result from injury, terror, severe shock or a life-threatening illness. The disorder may cause flashbacks, detachment, sleep disturbance and other problems. In the past,
investigators at other institutions identified PTSD as widespread, affecting 20 percent to 35 percent of childhood cancer patients.

Now Sean Phipps, PhD, St. Jude Psychology chair, and his colleagues are finding otherwise.

“We suggest that the problem of PTSD in childhood cancer is an example of a ‘perpetuated fallacy,’” reported Phipps in the study.

**Surprising strength**

As part of the research, Phipps and his colleagues talked with 255 St. Jude patients, as well as 101 of their healthy peers between the ages of 8 and 17. Part of a long-term project tracking patient adjustment, the study involved three interviews with each child.

The control group, Phipps says, is key: “How can you talk about elevated stress in children with cancer unless you talk with children who don’t have it?

“It’s an important design issue that we do not identify cancer as the event of interest. If you tell participants, ‘We’re studying you because you have cancer and are traumatized,’ you get a lot more symptoms reported.

“We try to be as neutral as we can to allow the participant to decide what they believe is their most stressful event,” Phipps adds. “In this study, children identified that event.”

Fifty-two percent of current patients identified cancer as the most stressful event in their lives. But only 23.8 percent of children who had passed the five-year mark after diagnosis identified cancer as their most traumatic event. Parent interviews suggest slightly, but not significantly, higher rates of PTSD in their children.

The study is intended to help guide and encourage, Phipps says. “It’s pretty impressive if you assess children in a clinic, and only half identify that cancer is their most traumatic event.”

**Resilience is the rule**

Scientists found that only 2.8 percent of cancer patients met criteria for lifetime PTSD diagnoses. Two of those seven cases were cancer related; others included a drive-by shooting, displacement by Hurricane Katrina, homelessness and unexpected family deaths.

Not only do children with cancer appear to be resilient, but they report benefits and psychological growth as a result of their cancer experiences. In fact, the survivors report closer social connections, a deeper empathy for others and a healthy perspective about their journeys. The young survivors seem to gain more benefit from the cancer experience than they do from other stressful events in their lives.

As for young Mia, her ordeal with cancer pales in comparison to an experience she had in 2011, when she battled a serious respiratory infection.

“I took my mask off for a second,” Mia says, “and I got a fungus in my nose.”

“It was pretty bad,” her mom concedes, noting Mia’s several nasal surgeries and time in ICU. “But now she’s fine.”

“The resilient outcome is the rule,” reports Phipps, who believes the St. Jude findings could apply to children treated at other institutions.

“It’s sort of a miraculous thing,” he says, “a testament to the human capacity to endure and thrive.”

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**NOT ONLY** do children with cancer appear to be resilient, but they report benefits and psychological growth as a result of their cancer experiences.
Recent years have brought an unprecedented number of human infections from animal flu viruses, including H1N1, H7N9 and H5N1,” says Webby, who directs the St. Jude-based WHO Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds. “It’s pertinent for us to keep track of the viruses and provide recommendations, which help guide public health authorities as they prepare the upcoming flu vaccines.”

Flu infections remain a leading cause of illness and death worldwide. During an average U.S. flu season, the virus is linked to approximately 36,000 deaths and 114,000...
Who needs a whiteboard? Richard Webby, PhD, scribbles notes on a window as he and a colleague track the latest movement of influenza viruses.

hospitalizations. The highly contagious disease poses a serious risk to the extremely old and young, as well as to cancer patients and others with compromised immune systems.

The WHO group meets to determine recommendations twice a year—February and September—as it could take up to eight months to produce flu vaccines. Along with looking at the most recent vaccine’s effectiveness, the experts assess flu activity in particularly virulent flu viruses, discuss surveillance and response systems, and “create antigenic and genetic characteristics of current flu strains to develop candidate vaccine strains for flu viruses,” Webby says.

A global leader

For almost five decades, St. Jude has been a global leader in influenza research. The study of diseases such as flu is critical to cancer patients because the treatments they endure diminish their immune systems and put them at risk for infections.

“The question often asked of me is, ‘Why are you working with influenza in a cancer institute?’” says virologist Robert Webster, PhD, who holds the hospital’s Rose Marie Thomas Chair in Infectious Diseases. “It’s the infectious diseases—the simple, everyday diseases like measles and influenza—that pose serious risks to our children. Studying
influenza is a very important component of St. Jude.”

Webster is internationally recognized as an expert in understanding, tracking and combating flu and advancing knowledge of how new flu strains evolve.

“When I started at St. Jude in 1968, we had no idea where these pandemics of influenza came from,” he says. “We started with the WHO studying wild birds, and over the years established firmly that the source of all influenza A viruses in the world comes from the aquatic birds.”

As a result of the initial studies, the WHO approached St. Jude to become a collaborating center in 1975. “We are particularly interested in understanding how some avian flu viruses jump from infecting birds to infecting humans and other mammals while others do not,” Webster says.

St. Jude is also one of five U.S. research institutions designated as a Center of Excellence for Influenza Research and Surveillance by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. The collaboration unites basic and clinical researchers to advance understanding and response to flu, especially pandemic flu strains that pose a global health threat. At St. Jude, the federal funds help support an international flu surveillance network focused on wild birds and domestic animals.

**Recent research**

Within the past year, St. Jude has increased the world’s knowledge about influenza. One study provided evidence that the immune system can help predict which flu patients will develop severe symptoms and become hospitalized. The findings also help explain the reasons infants and toddlers have a higher risk for developing complications from the flu.

“This suggests there is an immune signature that could help doctors identify who needs closer monitoring or maybe more aggressive treatment,” says Paul Thomas, PhD, of St. Jude Immunology. “Clinically, we need to explore targeted therapies to address this problem separately from efforts to clear the virus.”

A study led by Webster found that descendants of the H2N2 avian flu A virus that killed millions worldwide in the 1950s still pose a threat to human health, particularly to those under age 50, because they lack immunity to the virus.

“This highlights the importance of continued surveillance of viruses circulating in animals and additional research to enhance our ability to identify viruses that are emerging health threats,” Webster says.

**The future of flu**

Flu remains a global health threat, from viruses that have been circulating for generations to the first North American case of H1N1 in January 2014.

St. Jude scientists are at the forefront of unraveling this threat—focusing their efforts on emerging flu strains, circulating viruses and global strategy. In addition to surveillance, the researchers are studying the human immune response to flu; risk factors such as obesity, which are associated with flu complications; flu transmission; and ecological factors that help maintain H5N1 avian flu presence in Southeast Asia poultry populations.

“We study such viruses as H5N1 and H7N9—specifically concentrating on the human-animal interface,” Webby says. “We’re trying to understand how much of these viruses are out there and exactly what it takes for them to become human pathogens—to go human to human.”

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**Vaccines and anti-virals**

Given the evolving flu environment, St. Jude scientists remain focused on the ecology and development of influenza, including studies on bird flu and a universal flu vaccine. Research conducted at St. Jude has led to new understandings of how serious flu outbreaks and pandemics arise. The hospital’s scientists have had a vital role in helping develop improved vaccines and anti-viral drugs.

In 2013, St. Jude produced seed stock for a potential vaccine against H7N9 avian flu, critical to dealing with the growing threat posed by the virus. St. Jude was the only non-government center within the World Health Organization system that made this vaccine seed stock. Work in Webster’s lab optimized a technique called reverse genetics, now widely used in flu vaccine development.

Although the seed stock has not yet been used for vaccine manufacture, two seed stocks developed at St. Jude have been used in vaccines currently in the U.S. stockpile in the event of a flu pandemic.

**WATCH THIS VIDEO**

to learn more about the impact St. Jude scientists have on the field of flu:
stjude.org/flu-research
Even though Kaiden Seals weighs only 9 pounds, he is—let’s face it—a chick magnet. When the 4-month-old turns his radiant smile onto women in his proximity, they melt like butter in an oven.

This morning, Kaiden (pictured on next page) works his charms on his mom and Tricia Mamer, RN, as they discuss the best way to care for a tube that protrudes from his tiny chest. Called a central line or central venous catheter, the tube is actually a lifeline through which Kaiden receives the blood products, medications and fluids he needs to battle...
hepatoblastoma, a rare type of liver cancer. Nearly every child undergoing cancer therapy receives a central line, which is surgically inserted into one of the large veins leading to the heart.

Mamer, a line nurse at St. Jude Children’s Research Hospital, meets regularly with Kaiden’s mom to help her master the nuances of caring for the line. Gently, they peel away the tape covering the tube. Mamer tempers her instructions with humor, as Kaiden wriggles and coos, first kicking his feet and then flailing his arms.

“I need to grow another hand,” jokes Kaiden’s mom, as she attempts to restrain her squirming son. “Once I figure this out, the goal is to have me do it by myself.”

Mamer and other St. Jude line nurses give one-on-one instruction to caregivers, offering advice and encouragement, building self-confidence and answering thousands of questions. With each appointment, the parent learns a little more, until finally the caregiver becomes the expert.

“As line nurses, we get to see almost every patient who comes through the hospital,” Mamer says. “We get to empower parents who may feel scared. It’s a wonderful feeling to be able to show them how to take care of their child’s line; to give them the knowledge and the resources to be able to be proficient. It gives them a way to take control during a time when their world seems to be spinning out of control.”

What’s my line?

When it comes to central lines, parents are not the only ones who need education and encouragement. The hospital’s Child Life specialists handle that duty for patients.

“Have you heard the word ‘line’ today?” Child Life Specialist Jessica Goddard asks a young patient. Goddard uses a doll to show the child what a central line looks like, inviting the child to touch the tube extending from the doll’s chest.

“I want them to understand that it’s not going to hurt the doll to manipulate the line, and I want the child to feel as comfortable as possible before they go in for surgery,” Goddard explains.

Medical play unfolds differently, depending on the patient’s developmental level. One little boy asked Goddard if his stuffed dinosaur could have a line, too. After checking with the child’s parents, Goddard performed an operation on the toy.

“The little boy pretended that he was the parent, and I pretended I was the surgeon,” Goddard recalls. “I cut a hole in the dinosaur, poked a line in there and sewed it up.”

Her colleague Jaime Moran uses vastly different techniques to broach the subject with older children and young adults. Today, Moran meets with a 16-year-old boy who is about to receive his central line. To ensure that he understands the upcoming operation, Moran quizzes him on the concepts they discussed during a previous conversation.

“What’s the goal of having the line in your body?” she asks.
“It’s so I won’t have to be stuck or have an IV all the time,” responds the young man, who is eager to demonstrate his knowledge.

“Exactly! You’ll have fewer pokes,” she replies. “The medicine they put into your line travels directly to your heart, where it is pumped throughout your body.”

Moran explains that in addition to giving chemotherapy, fluids, blood and platelets through the line, medical staff can also collect blood samples. At the end of their relaxed banter, the teenager waves goodbye, proud that he has mastered the information and comfortable with the upcoming procedure.

Central lines on trial

Nearly 3 million central lines are used in the U.S. each year. A critical part of cancer treatment, they allow for easy administration of fluids and medications. But these lines also increase the risk of bloodstream infections. Worldwide, about one in four patients with cancer will have at least one such infection.

If a child has a central line-associated infection, the possibility of having a second such infection is significantly higher than it was for their first infection. What can be done to reduce that risk?

Josh Wolf, MD, of St. Jude Infectious Diseases, is trying to answer that question. He is heading a randomized clinical trial to use a new way of treating and preventing central line infections called ethanol lock therapy. “We don’t just want to help kids at St. Jude; we also want to identify a treatment that will help kids everywhere,” Wolf says.

He has developed a clinical trial called ETHEL that involves injecting a small dose of highly concentrated alcohol into the central line, allowing it to remain there for a while, and then drawing the alcohol out of the line.

“The idea is that it’s able to penetrate into the bacteria that stick on the inside of the line and hopefully eliminate them in a way that antibiotics just don’t do,” Wolf says.

As part of standard line care, clinicians and caregivers regularly flush the central line with a sterile solution. This is done to prevent bacteria from accumulating inside the catheter. Once bacteria colonize inside the line, they are able to adapt so that antibiotics are not effective. The standard treatment for an infection is to administer antibiotics through the line for 10 to 14 days. But that treatment has a 50 percent failure rate over six months.

“It takes about 1,000 times the concentration of antibiotics to kill one of those bacterial cells as it does to kill a normal cell in the test tube,” Wolf observes.

ETHEL is open to St. Jude patients who have already had a central line-associated blood stream infection. In studies at other institutions, scientists noted side effects such as dizziness or nausea when they used ethanol in central lines. The researchers at St. Jude have not encountered those problems.

“We measure the dose much more carefully than they did in other studies, so rather than giving a standard dose to everyone, we give a dose that’s determined by the actual volume of the patient’s line,” Wolf explains. “Also, instead of flushing it, we draw it back out.”
Wolf plans to expand the clinical trial to other institutions, so that he can recruit 138 children to the study.

**Study within a study**

Twelve-year-old Angiel Maosa is an imaginative girl whose conversation flits like a butterfly—touching briefly on one topic and then fluttering away to another subject. So it’s no surprise that she takes the same lighthearted and creative approach to her treatment. When Angiel participated in the ETHEL study, she conducted her own “clinical trial,” keeping close track of her data.

“You know how kids taste saline when their line is flushed? I tried to determine whether you wouldn’t taste it if you had something in your mouth,” she explains.

“Angiel did multiple trials of each candy,” Wolf explains. “She tried each one twice and gave it a rating out of 10 in terms of the impact it had on reducing the taste. She created a poster of her findings. I was very impressed.”

And what did the data show?

“The best were mints and Jolly Ranchers,” Angiel reports, adding that bubble gum and jelly beans lacked the robust flavor necessary to mask the saline taste.

When Angiel enrolled in the ETHEL clinical trial, she had already endured two line infections during treatment for the bone cancer osteosarcoma. Her mom, Damaris, recalls that the procedure added only a few minutes to their usual line-care routine.

“An infection compromises a kid whose health is already compromised,” Damaris says. “If there is something that will help other kids in the future avoid line infections, then it was worth it to me.”

**Reducing INFECTION RISK**

St. Jude takes a coordinated approach to preventing central line-associated bloodstream infections. Hana Hakim, MD, infection prevention and control officer, oversees the hospital’s program. She also serves as liaison with a group of other children’s hospitals that work together to decrease the number of central line infections nationwide.

To further reduce its infection rate, St. Jude recently embarked on a line-care initiative that involves every area of clinical care. “Everybody at St. Jude is committed to providing safe care for our patients,” Hakim says.

“The children are already at high risk of acquiring infections, and if they do acquire infections, they can be severe. Because of that, all of our employees understand the importance of doing this project right.”

Instead of ordering blood draws several times a day, physicians now consolidate blood tests, reducing the number of times a child’s central line is accessed. Pharmacists review patient charts to suggest oral medications that may work as well as ones given through the line. Nurses have adopted stricter sterile techniques for line care. During weekly line care rounds, clinical staff members visit inpatient rooms—checking central lines, obtaining parent input and emphasizing the importance of hand hygiene by families, visitors, friends and staff. Administrators, infection experts, nurses and quality management staff also play important roles in the program’s success.

Thanks to this coordinated effort, the hospital’s rate of central line-associated bloodstream infections is low. But Hakim will not rest until it is even better.

“We’re not done, definitely; there’s still more work to be done to get the rate as low as it can go,” she says.
A passion for serving others guides the family of Doug and Holly Brooks to help St. Jude Children’s Research Hospital find cures and save children.

“Service happens to you; hospitality happens for you,” Doug says. “It’s about making people feel special, and St. Jude is amazing at making kids and parents feel special. I call it ‘St. Jude Hospital hospitality.’”

The family’s St. Jude journey stemmed from Doug’s 36-year-career with Chili’s Grill and Bar. Doug worked his way up from restaurant manager to be named chairman of the board and CEO of Brinker International, the parent company of Chili’s, in 2004. Doug and Holly married in 1977, and they both worked at Chili’s in Dallas, where the restaurant originated. When they started a family, Holly became a full-time mom to sons Taylor and Kyle.

The Chili’s partnership with St. Jude began in 2002 when the restaurant was asked to support a Dallas fundraising event for the hospital.

“From that point on, I was able to watch my family and our Chili’s family fall in love with St. Jude,” Doug says. In 2006, Chili’s made a $50 million commitment to build the Chili’s Care Center with proceeds from its highly successful “Create-A-Pepper to fight childhood cancer” campaign held each September.

“The ribbon-cutting ceremony was very emotional,” Doug says, “seeing the name of the company where I spent my entire career on a building that would save children’s lives.”

In 2013, Doug retired, but the family’s personal involvement with St. Jude deepened. The couple and their sons visited St. Jude together for the first time in 2012.

“It was a life-changing experience, seeing how the children and their families equate Chili’s with hope,” Kyle says. Taylor adds, “The personal trip really changed everything in terms of how I think of St. Jude.”

Recently, the family made a generous personal donation to name the Proton Therapy Post Anesthesia Care Unit, which will be located in the St. Jude Red Frog Events Proton Therapy Center now being built on the hospital’s campus.

“My dad’s best friend died of a brain tumor. We were very close, and, unfortunately, that is what made all of this real for us,” Kyle says.

“I also have a good friend who had a brain tumor. Once you are touched by that,” adds Taylor, “everything happening at St. Jude takes on a whole new meaning.”

“We wanted to be part of the proton beam therapy because of how we have been touched by brain tumors,” Holly explains. “We love seeing our boys becoming involved, and we are so proud just to be a part of the work St. Jude is doing.”

Doug sums it up when he says, “It’s one thing to serve someone a meal, but it’s another to be involved with a company that is helping to solve the problem of pediatric cancer. Our success gave us that opportunity.”

By Kerry Healy

Serving Up a CURE

Supporting St. Jude is a family affair for Doug and Holly Brooks
A structural biologist from St. Jude is one of the newest members of the National Academy of Sciences. Brenda Schulman, PhD, is among 84 new members and 21 foreign associates from 15 countries selected to join the academy this year. The organization is a private, nonprofit society of distinguished scholars charged with providing independent, objective advice to the nation on matters related to science and technology. Scientists are elected by their peers based on their outstanding contributions to research.

“Dr. Schulman continues to blaze new paths using structural biology to advance global scientific understanding of how key cell processes are regulated,” said Dr. William E. Evans, St. Jude director and CEO. “Her election to the National Academy of Sciences is a richly deserved honor for her life’s work as well as for St. Jude. We are pleased, but not surprised that her work has attracted this recognition.” Schulman is a co-director of the St. Jude Cancer Genetics, Biochemistry and Cell Biology Program. She is a faculty member in the departments of Structural Biology and Tumor Cell Biology as well as a Howard Hughes Medical Institute Investigator.

Other St. Jude researchers elected to the academy include Nobel Laureate Peter Doherty, PhD, renowned virologist Robert Webster, PhD, and esteemed tumor cell biologist Charles Sherr, MD, PhD. Several St. Jude scientists have also been elected to the Institute of Medicine, a prestigious branch of the National Academy of Sciences. They include Evans, Sherr, James Downing, MD, Mary Relling, PharmD, and Arthur Nienhuis, MD.

For brain tumor patients, age matters

Scientists at St. Jude have more evidence that age matters when it comes to the devastating brain tumors called high-grade gliomas (HGGs).

Researchers knew the genetic makeup of these tumors varied significantly between adults and children. The new findings suggest the same is true for children of different ages. In this study, investigators sifted through billions of pieces of DNA. They discovered specific genetic alterations that occurred most often in the youngest patients.

The discoveries provide clues researchers can use to fashion more effective age-specific therapies. Such treatments are urgently needed. Despite aggressive treatment with surgery, radiation and chemotherapy, fewer than 20 percent of patients with these tumors are alive two years after their cancer is diagnosed.

“This study provides striking new evidence of how high-grade gliomas differ not only between adults and children, but also between older and younger children,” said Suzanne Baker, PhD, of St. Jude Developmental Neurobiology.

The findings, published in the journal Nature Genetics, are from the St. Jude Children’s Research Hospital–Washington University Pediatric Cancer Genome Project.
Scientists discover gene mutated in most childhood bone tumors

Scientists working on the St. Jude Children’s Research Hospital—Washington University Pediatric Cancer Genome Project recently discovered that the tumor suppressor gene TP53 is mutated in 90 percent of osteosarcoma tumors. This finding suggests that the alteration plays a key role early in development of the bone cancer.

Michael Dyer, PhD, Developmental Neurobiology (pictured above, at right), discusses the project with colleagues Armita Bahrami, MD, of St. Jude Pathology (at left), and Xiang Chen, PhD, of the hospital’s Computational Biology department.

The discovery that TP53 is altered in nearly every osteosarcoma helps to explain why, at standard doses, radiation therapy is largely ineffective against the tumor.

“This study identifies numerous mutations in TP53 missed by previous studies that did not include whole genome sequencing,” said Dyer, who is also a Howard Hughes Medical Institute Investigator. Jinghui Zhang, PhD, of St. Jude Computational Biology, joined Dyer, Bahrami and Chen in authoring a paper on this project, which was published in the journal Cell Reports.

Molecule acts as umpire to make tough life-or-death calls

Cells may be small, but they are home to plenty of mystery and drama. Take the enzyme known as RIPK1. St. Jude scientists have just determined that after birth, RIPK1 functions like an umpire in cells, making the tough calls necessary to balance competing signals that determine if cells live or die.

RIPK1 is already the focus of research to develop drugs that limit cell damage following heart attack, stroke or kidney injury. This study suggests the enzyme and the signals it helps to control might be harnessed to kill cancer cells. The results also provide clues about how the disease-fighting immune system curbs the spread of infection.

“This study fundamentally changes the way we think about RIPK1, a molecule that we care about because it is required for life,” said the study’s corresponding author Douglas Green, PhD, St. Jude Immunology chair.

The research appears in the scientific journal Cell.

St. Jude ranked as the No. 1 preferred company to work for by millennials

St. Jude is ranked as the top place students and young professionals wish to work, according to a survey conducted by the National Society of High School Scholars. This is the second year in a row that the hospital leads in the survey.

More than 12,000 high school students, college students and young professionals, ages 15–27, were asked to rank their preferred companies to work for from a list of 220 organizations.

The list of organizations on the survey are generated from FORTUNE magazine’s “100 Best Companies to Work For” and “Global 500” lists, DiversityInc’s “Top 50 Companies for Diversity” list and write-in choices. St. Jude has been on FORTUNE magazine’s “100 Best Companies to Work For” list for four consecutive years.
New twist discovered in Lou Gehrig’s disease

In 1939, a star hitter for the New York Yankees was diagnosed with a rare and deadly disease. The disease, amyotrophic lateral sclerosis (ALS), attacked his nerve cells, gradually weakening his muscles. Two years after ending Lou Gehrig’s baseball career, ALS took his life.

ALS remains incurable, but new insight into its causes gives reason to hope. A research team led by St. Jude revealed that mutations causing ALS have an unexpected toxic effect in human nerve cells.

Investigators found that mutations in a protein called TDP-43 disrupt the delivery of critical factors to the points of contact between nerve cells and muscles. To make the discovery, the scientists developed a new way to track the factors in living human nerve cells.

The research, published in the journal Neuron, opens a novel avenue in the pursuit of treatments for ALS and related disorders such as Parkinson’s and Alzheimer’s diseases. The work was led by J. Paul Taylor, MD, PhD, St. Jude Cell and Molecular Biology chair.

Broken DNA is bad for the brain

DNA may be the cornerstone of life, but the molecule breaks all the time. To read DNA’s code or make more DNA, cells routinely nick and unwind the famous double helix using specialized enzymes. Free radicals and other stresses can also break DNA.

Usually, cells just repair the break and life goes on. But if repair processes fail, the damaged DNA can hurt cells and tissues. DNA damage has been linked to diseases such as cancer and neurodegenerative disorders.

Research from St. Jude has revealed an unexpected cause for the DNA damage in two rare childhood diseases of the brain. In models of these diseases, an enzyme used by cells to nick DNA becomes trapped in the molecule. Because of disease-associated defects in the normal repair process, the enzyme stays trapped, leading to permanent DNA damage.

“We are now working to understand how this newly recognized source of DNA damage might contribute to tumor development or age-related DNA damage in the brain that is associated with neurodegenerative disorders like Alzheimer’s disease,” said Peter McKinnon, PhD, of St. Jude Genetics.

The findings appear in the journal Nature Neuroscience.

Hathaway visits St. Jude

Academy Award-winning actress Anne Hathaway hugs St. Jude patient Tyler West during a recent visit to the hospital. Patients and siblings were treated to an advanced screening of her new animated film Rio 2, in which Hathaway voices the part of Jewel. Hathaway toured the hospital and also visited patients’ rooms. The actress is a longtime supporter of the hospital.
It can be difficult to describe the journey through childhood cancer at St. Jude Children’s Research Hospital. But Katie Bruce and her husband, Ryan, managed to sum it up in a few words inscribed in an 8-inch by 8-inch brick: “Fighting the fight—our little boy, Jack Bruce.”

The brick is one of about 11,000 that adorn a walkway around the St. Jude campus called the Pathway to Hope. These bricks—available for individual dedication—often represent the hopes and dreams of St. Jude families and supporters, and honor the recovery or the memory of beloved children in the fight of their lives.

For the Bruce family, the battle has been a success. “Jack is doing wonderfully well,” Katie says of her son, 7, who was diagnosed with the soft tissue tumor rhabdomyosarcoma just before his second birthday.

“The brick is a constant reminder that Jack will always be fighting his fight and the fact that if anything ever happens to him again, we know that St. Jude will welcome him with open arms,” she says. “It is an honor to have my son’s name on such an amazing tribute.”

Jack suffered a relapse in 2009 and returned to St. Jude for treatment. He has had no evidence of disease for four years, Katie says. The family still travels to St. Jude every six months from their Illinois home so that Jack can get scans to ensure there has been no recurrence of cancer.

Today, Jack is a happy, healthy boy who is “an awesome big brother to his best little buddy, Tucker,” Katie says.

He loves dirt bike riding, fishing, playing with his dog and any activity that involves mud.

“I could never put into words what St. Jude means to our family,” Katie says. “They saved my baby boy not once, but twice. The care, dedication and love that are in the hospital are phenomenal. St. Jude will forever hold a special place in my heart.”

A new section of the Pathway to Hope is being created for the sidewalk surrounding a $198 million tower under construction at St. Jude. The pathway gives supporters and families like Jack’s an opportunity to pay tribute to loved ones. Four types of bricks, ranging in size from 4.5 x 9 inches to 16 x 16 inches, are available for dedication at various donation levels.

The new tower includes the first proton therapy center in the world dedicated solely to children, as well as a state-of-the-art surgery center, intensive care unit and a global education and collaboration center. All proceeds from dedications for the new Pathway to Hope will go toward the tower.

For more information or to order a brick, visit stjude.org/brick-dedications or call 1-800-395-1087.
A Whole **NEW FAMILY**

You’ve just inherited a whole new family who is committed to walk through your journey with you,” Penny Tramontozzi tells incoming patients. It’s a community that includes employees, volunteers…and you.

As a guest services representative at St. Jude Children’s Research Hospital, I have the privilege of meeting many patient families when they walk through our front door for the very first time. “You’ve just inherited a whole new family who is committed to walking through your journey with you,” I tell them. It’s a truth I witness every day at St. Jude.

When I welcomed one young boy on his first day, I told him about our weekly events and pointed out the ice cream counter that was built at the request of our patients.

“I’m never going to want to leave!” he responded.

But the next morning, he was not a happy camper. Because he could not eat until after his MRI, he was hungry. I told him if he couldn’t eat, that I wouldn’t, either. I asked him to let me know when we could have breakfast.

I was called away from my desk for a short time. When I returned, I found a note. “Miss Penny,” it said, “we can eat now.” I smiled at the word “we.” We were now in this together. That’s what it’s all about.

I have watched a generation of patients grow up, graduate from high school and college, get married, start families. Many of those patients have also chosen to work at St. Jude or ALSAC, our fundraising organization. All of this is possible because our medical staff never gives up on our patients.

“I don’t save lives, but I am one of many employees who have the honor of nurturing our patients. It may be making an overhead announcement to get children excited about a special event, offering a cozy blanket, or, most importantly, giving a warm smile.

One of our patients recently burst into the hospital’s lobby and shouted, “Look, Mom, there’s my friend!”

He wasn’t talking about me; he was pointing to one of our housekeepers, who obviously had taken the time to talk with the patient while cleaning his room.

Everyone is invested in our children. We all do our part to create a positive and loving environment for our patients and their families.

To those of you who support our children with your generosity, I want to quote one of our St. Jude mothers who shared these words with me: “Although I may not recognize our donors by face,” she said, “I surely know them by their generosity.”

One of our St. Jude fathers shared with me that he would like to say, “Thank you for choosing to help our children.”

Please remember that when we speak about our St. Jude family, we are including you.

A cancer survivor herself, Alice “Miss Penny” Tramontozzi has worked as a St. Jude volunteer and staff member for 15 years. ■
“What better way is there of guaranteeing a brighter future for so many children?”

—Patricia Susa-Cottage

Her legacy. Their future.

Secure the future for yourself, your family and the children of St. Jude Children’s Research Hospital by preparing or updating your estate plans.

By including St. Jude in her estate plans, Patricia Susa-Cottage will be providing for her loved ones and helping St. Jude work toward a future where no child dies in the dawn of life. Her legacy of compassion will continue to carry her values forward for future generations.

Begin your legacy today. Call 1-800-910-3188 or visit stjude.org/legacy.
Shining a light on Tri Delta

St. Jude patient Bailey Parker plays with two members of Tri Delta. Members of the sorority visited the hospital to celebrate their successful campaign to raise $15 million for St. Jude in five years. They achieved their goal 1.5 years ahead of schedule and recently announced a new goal to raise $60 million in 10 years to name Tri Delta Place, the hospital’s on-campus residential facility.