DNA points the way
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Scientist discovers origins of soft-tissue tumor

Hospital mobilizes resources for refugees with cancer
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Inherited mutations can lead to a childhood brain tumor.
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A fun, informative cooking class offers a delicious smorgasbord of benefits for patients and families.

By Elizabeth Jane Walker

Twelve-year-old Marley Harris loves to paint and color and draw. So it’s no surprise the sixth-grader embraces the tactile pleasures of creating beautiful and delectable foods. Clad in a colorful apron, she brandishes a spatula during a recent cooking class at St. Jude Children’s Research Hospital.

“I absolutely love this class,” she tells her mom. “I love it, I love it, I love it!”

Led by dietitians in St. Jude Clinical Nutrition Services, the twice-weekly Nutriolicious class is designed to help improve the nutrition of patients and their parents while instilling knowledge about healthful food choices. Parents say the activity helps their children regain a sense of normalcy, hone valuable skills, meet new friends and have fun.

Participants have prepared dishes ranging from fish tacos and pancakes to vegetable quesadillas and pasta.

“The best way to eat right is to learn to cook,” says St. Jude Registered Dietitian Karen Ringwald-Smith. “If we can teach patients healthful behaviors while they’re cooking in a fun, hands-on way, it might stick. If they enjoy the experience, they’re less likely to choose fast food and more likely to cook wholesome food at home. And if we involve the parents in the class, then we teach both the parents and the children.”

Although open to all St. Jude patients, the class is also being incorporated into the hospital’s newest clinical trial for acute lymphoblastic leukemia (ALL) and lymphoma.

According to St. Jude oncologist Hiroto Inaba, MD, PhD, children with ALL are at high risk for weight gain because of the steroids required to eradicate their cancer. Unhealthy eating habits, combined with excessive weight gain, could place them at high risk of long-term medical problems. The 12-week cooking class for new patients in the Total 17 clinical trial is aimed at breaking that cycle before it begins.

Marley and her mom say the sessions offer a break from the proton therapy treatments required to treat ependymoma, a brain tumor.

“I like to bring her so that she can learn techniques of the kitchen,” Marley’s mother explains. “The classes teach her to be self-sufficient, help her gain organizational skills and teach her about healthy food alternatives.”

For Marley and her mom, those benefits are like icing on the lowfat cupcake.
“That funny cat video is amazing. I’m going to email it to my aunt,” you say.

Five minutes later, your email has crashed, and the cat video is forever stuck in limbo. And you are slapping yourself for trying to send such a huge file.

Now imagine that the file is 2 million times larger. And instead of a video, it holds information about the genetic code of thousands of childhood cancers. That data is like gold to researchers all over the world who are seeking new cures.

But how on earth are you going to send it to them?

Jinghui Zhang, PhD, has an answer—don’t send it to them. Put the data in the cloud instead.

A newly unveiled cloud storage and computing portal called St. Jude Cloud holds the world’s largest public collection of pediatric cancer genomics data.

Sharing resources worldwide

In the past, downloading one of these datasets could take six months, and that’s even before the scientist could start analyzing it.

“Occasionally, users of our data would run into technical problems in the data transfer process.
“Through St. Jude Cloud, researchers can use our data and analysis tools even if they don’t have the infrastructure at their home institutions.”

– Keith Perry

At times, we even had to ship hard drives to share the data,” says Zhang, who chairs the St. Jude Department of Computational Biology. “Now, you don’t have to download it at all. We put all of the data where scientists can access it directly.”

Once researchers are approved for access, they can see it in just minutes.

“Instead of six months, it can take just a weekend to do the analysis,” Zhang says, “because you bypass the downloading step.”

Faster, easier, more productive

Speed matters, because these analyses can reveal the genetic changes that cause a child’s cancer. Although St. Jude Cloud was launched as a tool for researchers, the hope is that one day it will allow clinicians and researchers to rapidly identify and target a cancer’s molecular weaknesses—an approach known as precision medicine.

That’s why it was important for St. Jude Cloud to be accessible to as many researchers as possible.

“We had a strong emphasis on making it easy for anyone to use,” Zhang explains. “This data is not only helpful for cancer geneticists and computer scientists, but for researchers who may not have computation backgrounds.”

Zhang and Keith Perry, chief information officer at St. Jude, co-led the development of St. Jude Cloud in a partnership with Microsoft and DNAnexus, to create a secure, easy-to-use platform to share data and unique analysis tools.

“With St. Jude Cloud, we hope to break down entry barriers for researchers around the world,” Perry says. “Scientific discovery, especially in the field of cancer genomics, requires sophisticated technology. Through St. Jude Cloud, researchers can use our data and analysis tools even if they don’t have the infrastructure at their home institutions.”

The two-year project involved extensive collaboration among teams of scientists, software engineers and web specialists.

“There has been a lot of synergy among the teams,” says Clay McLeod of St. Jude Computational Biology. “Our group developed the genomics tools and data because that is our specialty. Microsoft and DNAnexus brought their own specialized expertise to the project. And Keith’s team is really focusing on the next steps. There’s an attitude that everyone truly is working together toward the same goal of curing kids.”

No strings attached

The public launch of St. Jude Cloud occurred in April 2018 at the American Association for Cancer Research annual meeting.

“We had an overwhelmingly positive response,” Zhang says. “We met a lot of young scientists who were really enthused about being able to access data. And people were truly impressed by the ease of the navigation through the datasets.

“One surprising reaction we saw was disbelief,” she continues. “People asked, ‘Are any strings attached to this data sharing?’ They almost thought it was too good to be true. To see that we are making such an impact on the research community is satisfying.”

And one day this cloud may yield another type of gold—new therapies.

“Our interest is in removing obstacles to sharing the data so it will be usable by others as quickly as possible,” Perry says. “Once you put St. Jude data in the cloud, and others begin to share their data, then meaningful conversations can occur.

“We hope those conversations will lead to new cures.”
In the race to increase survival rates for a soft-tissue cancer, one researcher surges ahead with an exciting discovery.

When she’s astride her favorite horse, Brieanna Elmer exudes a deep sense of joy and exhilaration. Eyes sparkling, she caresses Apollo’s velvet nose, listens to the music of his hooves, and inhales the pungent aroma of stable and corral. Yet, the 11-year-old has had to put horseback riding on hold while undergoing treatment for rhabdomyosarcoma, the most common type of soft-tissue cancer in children.

The cancer diagnosis came as a surprise to Brieanna, who was irritated when her mom insisted she visit the doctor to check out mysterious bumps on her neck. “I’m not sick!” insisted the high-spirited equestrian, who also loves to hike and fish.

Sure enough, Brieanna’s blood work looked perfect. To be on the safe side, the doctor prescribed an antibiotic to head off a possible infection. But she and her medical team soon discovered things are not always as they appear.

When the lumps persisted, tests showed Brieanna had cancer. Originating in her sinus cavity, the disease had spread to lymph nodes in her neck and shoulder.

Within a couple of days of diagnosis, she and her parents were on their way to St. Jude Children’s Research Hospital.
Taking the reins

Meanwhile, in a lab in the Danny Thomas Research Center at St. Jude, oncologist and researcher Mark Hatley, MD, PhD, was having a “eureka” moment.

When it comes to the origins of rhabdomyosarcoma, he discovered, appearances can be deceiving.

For decades, scientists worldwide had assumed rhabdomyosarcoma developed from immature muscle cells. But Hatley and his fellow researchers at St. Jude proved the cancer can originate in the inner surface of blood vessels tucked into the spaces between muscle fibers. Identifying the cell where rhabdomyosarcoma begins may help scientists improve the diagnosis and develop new treatment approaches for the disease.

“Under the microscope, rhabdomyosarcoma looks like muscle cells,” Hatley explains. “But just because someone lives in Memphis doesn’t mean they’re from Memphis. Similarly, just because rhabdomyosarcoma looks like muscle cells doesn’t mean it arises from muscle cells.”

Although this type of cancer often occurs in the muscles, it also can develop in tissues that lack skeletal muscle, such as the bladder, prostate, salivary gland, abdominal fat and liver. Until now, no one had been able to fathom why that happened.

“Rhabdomyosarcoma occurs all over the body, and the location of the tumor is pivotal to how patients survive,” Hatley says. “The tumors that arise around the eye are much different than tumors that arise in the arm, and clinically they behave completely different and their survival is much different.”

Unbridled enthusiasm

Brieanna and her family say they were drawn to St. Jude because of its world-class reputation for both research and clinical care.

“We had to find the best place for her to receive treatment,” explains her mom, Amanda.

Brieanna enrolled in a clinical trial that combines chemotherapy, surgery and proton beam radiation. St. Jude has the world’s first proton therapy center designed solely for children. The hospital is also home to a cadre of dedicated experts such as Hatley.

As a physician-scientist, Hatley spends most of his time in the lab working to better understand the biology of cancer. But he also cares for children in the hospital, which allows him to hone his clinical skills while sharing knowledge gleaned from his research.

“By spending most of my time in the lab, I can really focus and ultimately help more kids,” he explains.

Hatley says he marvels that one institution can house many of the world’s top experts in science and medicine.

“The depth and breadth of the researchers here is absolutely amazing,” he says. “These scientists are independently giants in their field.”

St. Jude is also home to such distinguished clinicians as Alberto Pappo, MD.

“He literally wrote the book on sarcomas,” Hatley says. “He’s one of the main reasons I came to St. Jude. It was the coupling of all this amazing science, these resources, and the ability to work with the leading sarcoma doctor in the world.”

Changing horses midstream

The trail to discovering the origins of rhabdomyosarcoma has been long and circuitous. Years ago, Hatley approached the problem by activating certain proteins known to play a role in the disease. He then deleted tumor suppressor genes at various stages of muscle development. But the tumors that formed were not the ones he sought.

“We would never get the cancers we were looking for,” he says.

Then a researcher at another institution made an unexpected discovery while investigating cellular machinery called the hedgehog pathway. Activating the pathway caused tumors to form. Hatley and his colleagues realized that the tumors were rhabdomyosarcoma.

He has spent the past six years trying to figure out which cells were giving rise to those tumors.
“We knew it wasn’t muscle,” he says, “but I always thought it was a type of metabolic fat called brown fat.”

He ultimately proved his hypothesis wrong. But in the process, he discovered the answer that had eluded scientists for decades: Rhabdomyosarcoma begins in cells that would normally develop into the cells that line the inside of blood vessels.

“That could explain why these tumors occur in places that aren’t skeletal muscles,” Hatley says. “Every part of the body has blood vessels.”

Galloping ahead

In addition to learning the cell of origin for rhabdomyosarcoma, the research team found evidence that the disease process begins before birth. They also suspect that tumors occurring in different parts of the body have diverse sources.

By understanding the origins of rhabdomyosarcoma, Hatley hopes to uncover new ways to eradicate the disease.

“We’re still using the same therapy that was used over 40 years ago,” he says. “In leukemia, we’ve made landmark changes, pushing survival from 4 percent to 94 percent. But for rhabdomyosarcoma, we’re still sitting at about 70 percent survival. And for kids who have the highest-risk disease, the survival is around 20 percent. We need to do better.”

Now that researchers have figured out where rhabdomyosarcoma comes from they’re trying to figure out how it happens.

“A pie-in-the-sky idea would be if we could determine how those early transformations occur, we could give them a drug to inhibit that process in patients with a predisposition to rhabdomyosarcoma,” Hatley says. “If we could win the scientific lottery, that’s what we’d want.”

Chomping at the bit

During the past couple of years, Brieanna has completed many chemotherapy treatments, followed by surgery and six weeks of proton therapy. Her mom says the care has been exemplary.

“It was surprising to me to realize that the main concern at St. Jude is to do what’s best for her—regardless of what the insurance is going to approve,” Amanda Elmer says. “To me, that’s huge.”

As she finishes her maintenance chemotherapy, Brieanna spends much of her time reading books and dreaming about horseback riding.

An avid reader since age 3, she attained a high school or higher reading level when she was in the third grade. She enjoys books about animals, especially horses. She also likes to reminisce about her favorite horse, Apollo.

“He’s a chestnut roan,” she explains. “He’s brown with bitty, bitty little speckles that are like blue roan colors. He’s really pretty. I miss him a lot.”

Thanks to St. Jude, Brieanna is convinced she’ll be back in the saddle again soon.

Surprise finding

For decades, scientists had assumed that rhabdomyosarcoma developed from immature muscle cells. But St. Jude oncologist and researcher Mark Hatley, MD, PhD, and his colleagues proved the cancer can originate in the inner surface of blood vessels tucked into the spaces between muscle fibers.
“Just because someone lives in Memphis doesn’t mean they’re from Memphis. Similarly, just because rhabdomyosarcoma looks like muscle cells doesn’t mean it arises from muscle cells.”

– Mark Hatley, MD, PhD

Back in the saddle...soon
Eleven-year-old Brieanna Elmer has put horseback riding on hold while undergoing treatment for rhabdomyosarcoma, the most common type of soft tissue cancer in children.
Ed Sibis was a quiet man with a soft place in his heart for children. And, according to his friend Rick Putnam, he loved the work of St. Jude Children’s Research Hospital.

Sibis and Putnam met on a golf course in Southern California more than 35 years ago.

“Ed had a strong connection with St. Jude, both philosophically and emotionally,” Putnam says.

When Sibis died last year, just shy of his 90th birthday, Putnam became executor of his estate.

“He had no family I was aware of,” Putnam says, “and he left everything to me, with instructions in his will that I’d do what I could to maximize the value of the estate for the children of St. Jude.”

At the suggestion of their financial adviser, Putnam and his wife, Lynne, purchased a life insurance policy with St. Jude as the owner and beneficiary. For 10 years, the couple will receive a tax deduction for their contribution to cover the cost of the premiums. After their lifetime, St. Jude will receive a much larger gift than the original value of Sibis’ estate.

“I thought about what Ed might do,” Putnam says. “A gift of a life insurance policy allowed me to take advantage of a tax break, benefit from paying over time, and most importantly, maximize his gift for St. Jude.”

Sibis grew up in an orphanage in Pennsylvania coal country during the Great Depression. After joining the Navy and then traveling the country with his brother, he worked for years at the University of California, Los Angeles.

“Ed was an introverted, somewhat gruff man,” Putnam says. “But get him around children, and it was amazing to watch.”

Both West Coast natives, the Putnams have been married more than 50 years and live in the same town as their children and grandchildren. They say they hope to visit St. Jude, to see firsthand the hospital that meant so much to their friend.

“Thanks to Ed, we’ve learned about the great work St. Jude does,” Putnam says. “It’s a great resource for children going through such a difficult time.”

To learn more about gifts of life insurance or other ways to support St. Jude, call 1-800-910-3188 or email giftplanning@stjude.org.
Gratitude is the reason Team Griffin hits the pavement during the St. Jude Walk/Run to End Childhood Cancer.

By Lynda Nance

In 2016, when Shannon and Bill Goold noticed bruising on the ankles of their son Griffin, it was easy to chalk it up to roughhousing. Griffin has an identical twin, as well as an older brother and sister.

“With three boys, it’s rough and tumble all the time,” Shannon says.

The bruises lingered on Griffin’s ankles, and he began to complain of knee pain. Then, during church one Sunday, Shannon noticed dark bruises beneath Griffin’s eyes. The next day, lab tests revealed a rare type of leukemia called acute promyelocytic leukemia, which is a subtype of acute myeloid leukemia.

Griffin and his family arrived at St. Jude Children’s Research Hospital in the middle of the night.

“It was terrifying,” Shannon says, “but the moment we walked through the doors, they took care of us.”

Griffin’s treatment included five rounds of chemotherapy. He’s now done with treatment and visits St. Jude for checkups every three months.

From the start of their St. Jude journey, Griffin’s family has been dedicated to giving back to the hospital that helped save his life. In September 2016, two months after Griffin became a St. Jude patient, a host of family and friends took part in the St. Jude Walk/Run.

“We thought, ‘OK, we can all walk and we can pull Griffin in a wagon,’ so we formed a Walk/Run team,” Shannon says.

Every September, supporters from across the nation come together for the St. Jude Walk/Run to End Childhood Cancer during Childhood Cancer Awareness Month to raise money for St. Jude.

Team Griffin walked in 2016 and 2017, raising approximately $5,000 for St. Jude. They plan to walk again in 2018.

“All our kids participate. From the very get-go, our family has been touched by all the hope and love and care we’ve received at St. Jude,” Shannon says. “We’re going to do whatever we can to give back. It’s our mission. I don’t take for granted that Griffin is doing well today. We know how quickly that can change.”

Take part in the 2018 St. Jude Walk/Run to End Childhood Cancer: visit stjude.org/together.
In satellite images, the Middle East can look serene—fertile green vegetation along the coastlines; white, snow-capped peaks in the mountains; orange desert sand; the deep blue waters of the Mediterranean Sea. But natural beauty cannot hide the humanitarian crisis that besets this region.

Since 2011, images taken on the ground in Syria have been tragic—bombs exploding, smoke billowing, and the wrenching and all-too-familiar photographs of children suffering the consequences of those atrocities.

Millions of Syrians have fled their embattled homeland.

Soon after the war began, refugees started pouring across the border into Lebanon. Today, Lebanon has, per capita, more refugees than any other country in the world. With the war entering its eighth year, this migration continues to tax Lebanon’s strained resources.

“The number of refugees in Lebanon rapidly grew from 300,000 to over 1.5 million,” says Sima Jeha, MD, of St. Jude Children’s Research Hospital. “That’s one-third of the population in Lebanon. 

“It would be like 100 million refugees coming to the U.S. over two years,” Jeha continues. “You can imagine how straining that would be to our infrastructure.”

Jeha, a leukemia expert who earned her medical degree at the American University of Beirut, works in the Oncology and Global Pediatric Medicine departments at St. Jude and directs St. Jude Global efforts in the region.
Offering hope and help
Sima Jeha, MD, of the St. Jude Oncology and Global Pediatric Medicine departments, directs St. Jude Global efforts in the East and Mediterranean Region.

“We were able to save the lives of children who would have otherwise died just because they happen to have cancer when their families were displaced.”

—Sima Jeha, MD

Joining forces to save lives
Among the refugees entering Lebanon are children with cancer.

St. Jude founder Danny Thomas—the son of Lebanese immigrants—once said that “No child should die in the dawn of life.” That belief sustains the hospital’s mission today.

For the past 16 years, St. Jude has been helping improve cancer care for children in Lebanon through a partnership with the Children’s Cancer Center of Lebanon (CCCL) at the American University Beirut Medical Center. This partnership grew stronger in response to the humanitarian crisis.

Between 2011 and 2017, CCCL staff evaluated 575 displaced children for cancer. Of that number, 311 received treatment through the CCCL network. The remaining 264 patients received medical consultations, which included accurate diagnoses, treatment recommendations and referral details.

A total of 159 patients have completed their treatment and remain in remission. The likelihood of treatment complications, premature treatment termination or missed appointments for follow-up care was comparable to patients who were not refugees.

A blueprint for success
When refugees began arriving in Lebanon, St. Jude and its fundraising and awareness organization, ALSAC, shared knowledge, resources and best practices in a coordinated approach. The CCCL and the medical center provided staff, medical infrastructure, funds and other support.

This international team demonstrated how treatment for childhood cancer can be delivered effectively in a crisis.

“If you have a network that includes everyone—from dedicated people on the ground to international oversight supporting the people on the ground—then you can effectively mobilize a network when there’s a disaster,” Jeha says.

She and her colleagues point to three lessons for the rest of the world about providing treatment for refugees with chronic medical conditions: establish networks before a crisis, re-examine priorities as needed, and mobilize advocates at the regional and international level. Results of the efforts were recently published in the journal Cancer.

“We were able to save the lives of children who would have otherwise died just because they happen to have cancer when their families were displaced,” Jeha says.

Reaching out to others
St. Jude and ALSAC are now working to develop a strategy to treat displaced children with cancer in Jordan. That country is second only to Lebanon in its per capita population of refugees.

Jeha plans to propose a wider network of care that includes not only Lebanon and Jordan, but also Turkey, Syria, Iraq and Palestine. The project involves public and private entities, including health care workers, social scientists, advocacy groups and international agencies, who work together and maximize the impact of ongoing efforts.

At times of crisis, Danny Thomas turned to St. Jude Thaddeus, the patron saint of hopeless causes. With his prayers answered, Thomas kept his vow to build a shrine to St. Jude.

Today, that hospital continues to seek cures for life-threatening diseases in the U.S., the Middle East and around the world.
SHADOW HUGHES describes himself as a “lazy person,” a perception seemingly at odds with his pursuit of energetic hobbies such as swimming, snowboarding and hunting. But the straight-A student’s mellow manner came into sharper focus when he was diagnosed with the brain cancer medulloblastoma last year.

During six months of treatment at St. Jude Children’s Research Hospital, Shadow soaked in the serene approach he noticed in everyone involved in his care, appreciating the peaceful port in a storm.

“They were all at ease and calm. No one was rushing around,” recalls the 14-year-old, whom his mother calls “everybody’s favorite” in his family of six. “I knew if they were calm, I should be calm.”

The Oklahoma boy’s family has also drawn comfort from the hospital’s aggressive approach to treating Shadow, whose initial MRI scans showed nine tumors in his brain. Within hours of his arrival in Memphis in April 2017, surgeons performed complex brain surgery and told Shadow’s parents that a cure is possible.

“That was the first instance of hope we had in all of this,” says his mom, Jennifer. “It was a game-changer for us.”

New awareness

New international research co-led by St. Jude, the European Molecular Biology Laboratory and German Cancer Research Center in Heidelberg, and the Hospital for Sick Children in Toronto, has transformed our understanding of the inherited risks for medulloblastoma.

Until now, scientists believed most cases of medulloblastoma occurred by chance and did not run in families. But in the largest study yet of genetic susceptibility in a pediatric brain tumor, scientists learned that inherited gene mutations often play a role in its development.

The discovery has prompted new recommendations for genetic testing and counseling of medulloblastoma patients and their families.

The massive effort, co-authored by St. Jude cancer biologist and medulloblastoma expert Paul Northcott, PhD, revealed germline variations—typically inherited and carried in cells...
Despite the fact that medulloblastoma is the most common malignant childhood brain tumor, it is diagnosed in only about 400 children in the United States each year. The cancer’s odds of appearing due to inherited genes vary depending on the disease’s four subgroups. These subgroups are named WNT, sonic hedgehog, Group 3 and Group 4.

St. Jude scientists discovered that inherited gene mutations often play a role in medulloblastoma’s development.

Assigning risk
Each subgroup carries different characteristics and treatment outcomes. Northcott’s paper, published in the journal Lancet Oncology, looked for gene variations related to each subgroup.

Among the most striking findings: As many as 20 percent of sonic hedgehog medulloblastoma cases stem from germline mutations in five out of six of the implicated genes. This places these patients and possibly their siblings not only at a higher risk of developing medulloblastoma, but also of having other cancers later in life.

Additionally, inherited genes account for about 10 percent of patients with WNT medulloblastoma.

“When we break this down, we clearly see different risks according to the subgroups,” says Northcott, who works in St. Jude Developmental Neurobiology. “Somewhere between one in five and one in six sonic hedgehog medulloblastoma patients have a clear hereditary predisposition based on mutations in these six genes. That’s an important finding for parents and doctors alike.”
Monitoring risk

“When we break this down, we clearly see different risks according to the subgroups,” says Paul Northcott, PhD. The findings have important implications for the treatment and surveillance of patients and their families.

that has significant implications for patients’ treatment and their surveillance—as well as for their siblings and parents.”

Discoveries and more discoveries

Northcott and his colleagues published another major international study in 2017 that revealed the genomic changes responsible for more than 75 percent of medulloblastoma tumors. The scientists also discovered two new suspected cancer genes found only in the least-understood disease subgroups.

Combined, the pair of efforts help round out scientists’ understanding of the genes at play in this brain tumor.

“In the earlier study, we focused on the medulloblastoma tumors themselves, describing their molecular landscape and the genes that were mutated,” Northcott says. “In this case, we’ve studied the germline—the normal DNA that’s present in every cell of these patients.”

Compelling comparisons

In their most recent study, the researchers analyzed germline DNA samples from 1,022 patients with medulloblastoma and 58,000 individuals with no history of cancer.

The scientists used next-generation gene sequencing—a process that deciphers the exact makeup of a DNA molecule—to compare how often variants in 110 cancer predisposition genes occurred in the medulloblastoma patients and the healthy subjects. These methods teased out six high-risk gene variants that show up in medulloblastoma patients far more often than in healthy people.

The findings, Northcott notes, are especially compelling because the healthy comparison group was so large.

“We focused only on the strong predisposition genes, where there’s plenty of evidence that mutations in these genes are known to cause cancer,” he says.

“When we see a variant that is much more prevalent in medulloblastoma patients compared to 58,000 normal, healthy controls,” Northcott adds, “we can be pretty confident that this gene is playing a role.”

Risky business

The study spotlights an urgent need to make genetic counseling and testing the standard of care for many medulloblastoma patients, particularly those in the sonic hedgehog and WNT subgroups.

Northcott and his team have created detailed
Collaborators around the globe are encouraging the World Health Organization to incorporate the St. Jude guidelines into its recommendations for managing and diagnosing brain tumors.

**PROPOSED GUIDELINES**

for medulloblastoma genetic counseling and testing

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| Absence of somatic CTNNB1 mutation | Test for: PTCH1, SUFU, TP53, BRCA2, and PALB2 | Family history of BRCA-associated cancers Test for: BRCA2 and PALB2 | Recommendations guiding clinicians on which types of other cancers to watch for in medulloblastoma patients—and in some cases, their relatives—based on genes and family history. For example, between 5 and 10 percent of WNT subgroup patients have an inherited mutation in the APC gene, which is tightly linked to the development of colorectal cancer and other malignancies. “These medulloblastoma patients might assume they’re free and clear because they’ve survived their brain cancer, but they’re certainly at risk for other cancers,” Northcott says. “They also have to be careful with the treatments they’re given for their medulloblastoma, because that could make them more prone to develop second cancers.”

**Sharing guidelines worldwide**

Among patients in the sonic hedgehog subgroup, Northcott points to five genes—including p53, a prominent cancer driver—commonly mutated in their inherited DNA. “We’re proposing that these patients are all screened for these five genes up front,” he explains.

Just a few years ago, almost no medulloblastoma patients would be referred for genetic testing or counseling unless a rare companion syndrome was suspected, according to study co-author Giles Robinson, MD, of St. Jude Oncology. “The screenings can help patients and families understand and manage their lifetime cancer risk,” Robinson says. But the new research greatly broadens the scope of patients who will be pegged for such consideration.

Already in use at St. Jude, the new guidelines fill a great need and should be adopted widely, Northcott says. His collaborators around the globe are encouraging the World Health Organization to incorporate the advice into its own guidelines for managing and diagnosing brain tumors. “That’s the advantage of working together as a community,” Robinson says. “This isn’t something that will just stay at St. Jude. It will spread quickly.”

**Total care**

Shadow’s mom, Jennifer, says she’s grateful for the St. Jude efforts to uncover the genetic underpinnings of medulloblastoma. While the family’s Native American heritage isn’t specifically linked, the mother of four has certainly wondered if her son’s case stemmed from something in their DNA.

Ever the bookworm and smitten with adventure novels and outdoor-themed magazines, Shadow has “bounced back completely” from his treatment, which he finished in October 2017 with no evidence of disease. He undergoes imaging scans every three months at St. Jude to confirm he’s still cancer free. “It’s a complete and total mystery to us, and we would love to find out more about where this has come from,” Jennifer says. “Every bit of research is building toward finding a better way to treat this. It’s just total care, all the way around.”

“Every bit of research is building toward finding a better way to treat this.”

—Jennifer Hughes

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Reflections on Connections

Encouraging news gleaned from new St. Jude tool measures quality of young survivors’ social connections.

By Maureen Salamon
from their disease and treatment,” Huang explains. “They have a lot of late effects and chronic conditions stemming from independence from parents and starting college or a job. Pursuing good social connections and social integration because they are not St. Jude patients. This St. Jude index was further tested using survivors recruited from a community survey panel who are not St. Jude patients. It’s critical to be aware of those struggles in order to have a positive outcome in your survivorship.”

A new St. Jude study offers crucial insight into young adult cancer survivors’ social networks—the collection of family members, friends, coworkers, neighbors, and others surrounding them. Unlike previous research, the effort is the first to measure not just the number of these connections, but their value to adolescent and young adult survivors moving into the next phase of their lives.

Unique challenges

Led by I-Chan Huang, PhD, of St. Jude Epidemiology and Cancer Control, the study found that many cancer survivors from ages 18 to 30 actually have more high-quality social connections than peers who haven’t had the disease. But, survivors of brain malignancies have significantly fewer social connections compared to survivors of other types of cancers. Huang and his colleagues developed a new method, called the St. Jude functional social network index, to quantify the transition from cancer patient to cancer survivor can be fraught. After treatment, she worked to build a new base of friends—many of whom had also been through the experience—and embraced the ever-present support of her family and many doctors, nurses and others at St. Jude Children’s Research Hospital.

“Cancer never exits your life once it enters.” Having weathered the shifting sands of friendships after her diagnosis at 13, Vivian quickly recognized the transition from cancer patient to cancer survivor can be fraught. After transitioning to post-cancer lives typically involves becoming independent from parents and starting college or a job. “The problem is that cancer survivors are at a disadvantage to pursue good social connections and social integration because they have a lot of late effects and chronic conditions stemming from their disease and treatment,” Huang explains.

Even though a decade has passed since she was successfully treated for the bone cancer osteosarcoma, 23-year-old Vivian Laws has swallowed a sobering truth: “Cancer never exits your life once it enters.”

Exploring further

The St. Jude index proved a better predictor of survivors’ ability to cope with challenges than did traditional indicators. Instead of gauging just the structure of social networks—as in who knows whom—and including only marital status or membership in church or community groups, the St. Jude method explores further. It also measures social connections as a source of practical and emotional support from friends and relatives, along with advice about weight management and physical activity.

This part is key because adolescent and young adult cancer survivors are more likely than their non-cancer peers to be physically inactive and carry extra pounds. And survivors’ supporters tend to step up to the task, providing more advice and help than what’s available to others, according to the study, published in the journal Cancer. Among survivors, higher social network index scores were linked with better coping skills, including less denial, less destructive behavior and more planning for the future.

“St. Jude patients absolutely have more of those connections than any of our non-cancer survivor peers,” says Vivian, who sings the praises of her ongoing visits to St. Jude psychologist Valerie Crabtree, PhD. “That’s because we’ve been set up for success in that sense, especially at St. Jude. We have a million resources here.”

Holistic view

St. Jude scientists are still trying to reveal the link between survivors’ social networks and their health outcomes, as well as identify promising therapies to help patients thrive. The researchers are also streamlining their new tool to enable clinicians elsewhere to measure support for survivors of any age, such as seniors.

Now a marketing coordinator at ALSAC, the hospital’s fundraising and awareness organization, Vivian says she has found “empowerment and strength” in connecting with others by sharing her survivorship story. She’s heartened that St. Jude scientists are examining all aspects of the cancer experience, not just the physical.

“It’s so important that we’re doing research on finding cures for cancer, but it’s also important that St. Jude is doing these studies to find out how to create a better quality of life for cancer survivors—not just at St. Jude, but around the world.”

– Vivian Laws

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“It’s so important that we’re doing research on finding cures for cancer, but it’s also important that St. Jude is doing these studies to find out how to create a better quality of life for cancer survivors—not just at St. Jude, but around the world,” Vivian says. “The care St. Jude provides doesn’t just end at your No More Chemo party. It carries on for the rest of your life, and if we can share some of these findings and interventions, it’s a huge step forward.”
St. Jude partners with the community to bring cutting-edge HIV prevention research to youth.

By Mike O’Kelly

It’s not uncommon for one of DeMarcus Jones’ two cell phones to ring as early as 4:30 a.m. or as late as 11 p.m. Jones, who works at St. Jude Children’s Research Hospital, knows the importance of being accessible—he’s part of an international effort to prevent the spread of the human immunodeficiency virus (HIV).

St. Jude has been making progress against HIV/AIDS since 1987, when hospital founder Danny Thomas declared AIDS a catastrophic disease of children. In the decades since, the St. Jude HIV program has become a well-respected clinical care and research program with a strong community outreach component.

The hospital’s latest effort involves a worldwide clinical trial to test the effectiveness of a long-acting, injectable HIV prevention and treatment drug called cabotegravir.

St. Jude is one of 27 U.S. institutions in the study and one of only three pediatric institutions. The clinical trial, called HPTN 083, plans to enroll HIV-negative, at-risk individuals around the globe.

Research suggests that one injection of cabotegravir every eight weeks can prevent HIV infection. HPTN 083 is the largest study to date to confirm this. Clinicians will track participants for four-and-a-half years.

Changing attitudes, saving lives

“Participants’ feedback about how the study has changed their lives and their decision-making is encouraging and energizing,” says Aditya Gaur, MD, of St. Jude Infectious Diseases.
“We’re trying to change the course of the HIV epidemic in the U.S. as well as locally, and it’s looking promising with these emerging prevention options.”

– Andrea Stubbs

Worth a shot
Currently, people at risk of contracting HIV have only one medication option for prevention, a daily pill.

“The Food and Drug Administration licensed one pill once a day for prevention several years back,” says Aditya Gaur, MD, of St. Jude Infectious Diseases, the project’s principal investigator at St. Jude. “That drug works well for those who take the pill regularly, but taking a pill daily falls back to a commitment, and not everyone can do it consistently.”

A long-term injection is a welcome option.

Community focus
Part of Jones’ role at St. Jude involves working with community partners to promote the study as well as building rapport with study participants to ensure retention. Since many enrollees come from low-income backgrounds, Jones also ensures they have transportation to the hospital.

“We provide education so they understand and feel empowered about making informed decisions and becoming a part of the study,” Jones explains.

“Once they enroll, they spread the word to their peers. From there, it’s a chain reaction of much-needed education in the community.”

Jones’ colleague Andrea Stubbs has spent more than a decade at St. Jude, working with schools, government officials, health agencies and HIV/AIDS organizations to spread the word about the hospital’s HIV clinical trials, activities and ongoing efforts.

“We’re trying to change the course of the HIV epidemic in the U.S. as well as locally, and it’s looking promising with these emerging prevention options,” she says.

Kickball and clinical trials
Stubbs and Jones coordinate local events that cater to the study’s target population. At dances, fashion shows, karaoke nights and kickball games, individuals interested in HIV testing, education or study enrollment can learn more in private sessions with St. Jude staff members.

At first, study participant Jessie Claudio was skeptical of taking part in the clinical trial. After learning more, he felt a sense of empowerment and enrolled in July 2017.

“Participating in this study is important to me, because I get to be one of the first to try something new and revolutionary that can possibly save the lives of hundreds from contracting HIV,” he says.

Claudio also shares his experience with others, stressing the study’s benefits and the importance St. Jude places on care and education.

Local epidemic
HPTN 083 allows St. Jude to make an even stronger contribution to HIV education and prevention.

The Memphis metropolitan area ranks 41st in population nationally, but ranks eighth in the rate of new HIV cases and 12th for newly diagnosed AIDS cases. To date, 78 youth have joined the study at St. Jude, making the hospital the trial’s highest enrolling center worldwide. This shows the enthusiasm among youth for research and the strong relationship St. Jude has with community partners engaged in HIV prevention.

Study participants have shared stories of changing behaviors and reconsidering risk-taking actions.

“Working with youth can at times be frustrating,” Gaur says. “They’ll be no-shows for appointments, or they may take ongoing risks despite being cautioned. Participants’ feedback about how the study has changed their lives and their decision-making is encouraging and energizing. It keeps the team going.

“Our staff’s experience working with youth, our resources, and our track record as a high-performing HIV prevention and treatment center uniquely position St. Jude to take cutting-edge HIV prevention research to the community,” he says.

Serving up prevention
St. Jude Infectious Diseases employee DeMarcus Jones (center) uses many tactics—including community kickball games—to spread the word about HIV prevention.
The Year Everyone FINISHED FIRST

By Gary Bridgman

When they arrived at the St. Jude Children’s Research Hospital Graduate School of Biomedical Sciences last year, many of the students already had connections to the hospital through internships or fundraising activities.

“We’ve all been affected in some way by St. Jude since long before we even knew about the graduate program,” says Brennan Bergeron, who is also a former St. Jude patient. Bergeron was preparing to attend medical school when he heard about the new graduate school, whose faculty included some of his former doctors.

“Why would I skip a chance to be taught by them?” he says.

The first year has transformed the lives of Bergeron and his classmates—and their presence has injected new energy and excitement into the hospital’s clinics and labs.

“The students have matured rapidly as independent thinkers,” says Stephen White, DPhil, Graduate School dean. “They’ve each completed three six-week rotations, and are now well known among the research community at St. Jude.”

From student to scientist

University of Kansas graduate Mackenzie Bloom says the year of study and research has helped focus her interests.

“I already have an idea of what type of affiliation I want to have with a primary investigator, and what type of lab dynamic will be my best fit,” she says.

One of Bloom’s classmates is pursuing a PhD from St. Jude and an MD from the University of Tennessee.
The scope and impact of the science here is tremendous.”
– Rahul Kumar

Rahul Kumar says St. Jude is the best place to prepare for that role.
“The scope and impact of the science here is tremendous,” Kumar says.

Progress report
The school’s dean says he has enjoyed watching the students flourish at St. Jude.
“The students were quite nervous and reserved last summer, and lectures and classes were relatively quiet affairs,” White says. “Fast-forward 10 months, and the transformation has been astonishing. They’ve grown in confidence, ask many questions and are unafraid to challenge their lecturers. These are all qualities that are paramount in academia and research, and providing this training is a hallmark of any premier graduate school.”

Bloom remembers her own turning point.
“I was sitting in class where they were talking me through a process, and I thought, ‘What happens if you knock out that protein?’ or ‘What would happen if I did this with a different model?’
“You start to think about how to design experiments and how everything you learn applies to whatever you’re interested in researching.”

As they learn to bridge the gap between the lab and clinic, students benefit from dedicated advising and mentorship by world-class biomedical researchers. The faculty includes leading scientific and clinical investigators from many fields. The model tends to erase barriers between scientific disciplines.
“This diversity creates a program in which everyone brings a different strong suit, and that’s really the essence of St. Jude,” Bergeron says.

Crawfish and camaraderie
The student body has already developed into a close-knit community. Near the end of the school year, Bergeron’s family planned to bring crawfish from Louisiana and host a dinner for the school’s students and faculty. For Bergeron, it was a hectic week that included a major exam. To make the situation more complicated, he had already planned to propose to his girlfriend the day before the crawfish boil.

As Bergeron’s stress levels increased, his classmates went to work on his behalf.
“They got my parents’ phone number,” he says, “and they told me, ‘You just ask her. That’s it. Don’t worry about anything else.’”

Bergeron passed the exam. His proposal was accepted, and the crawfish boil was a success.
“We are definitely a family now,” Bergeron says, “a large, extended, random family.”

Thanks to the St. Jude Children’s Research Hospital Graduate School of Biomedical Sciences, the scientists of tomorrow have a new training ground at St. Jude, a new academic family and a bright future in biomedical research. ■

For information about applying to the St. Jude Children’s Research Hospital Graduate School of Biomedical Sciences, visit stjude.org/graduate-school.

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BRAIN TUMOR subtype discovered that responds to less-aggressive treatment

Medulloblastoma patients under 5 years of age are among the most challenging patients to treat. That’s because their developing brains can be harmed by brain and spine irradiation. Intensive chemotherapy regimens have become the surrogate treatment option, but this also brings toxicity.

However, in a recent study, St. Jude researchers and their colleagues discovered a new subtype, which does well without brain and spine radiation and with less aggressive chemotherapy. About a quarter of infants with medulloblastoma have this subtype, called infant SHH-II. Seventy-five percent of patients with the subtype did not have their disease return for five years or more after receiving therapy that included only chemotherapy. The rates were even higher, 91 percent, for those whose tumors had been completely removed and had not spread.

The discovery identifies a group of patients who can be spared the life-long side effects of more aggressive treatment.

Giles Robinson, MD, of St. Jude Oncology led the research, which appeared in The Lancet Oncology.

‘LONE WOLF’ protein offers new pathway to cancer treatments

Just as a lone wolf leaves the pack to operate on its own, a key protein named BOK goes rogue to trigger cell suicide, or apoptosis.

Tudor Moldoveanu, PhD, of St. Jude Structural Biology, and his colleagues discovered how that happens. Their findings offer the potential for new drugs to more selectively kill cancer cells.

Usually, our bodies use a process called apoptosis to get rid of cells that are no longer needed or faulty, such as cancer cells. But cancers mutate to survive by switching off apoptosis. The goal of many cancer drug treatments is to switch on apoptosis in cancer cells.

The findings pave the way for a new approach to anti-cancer drugs.

“This is exciting, because it opens the way to develop new drugs that would stabilize BOK and enable it to effectively trigger apoptosis in cancer cells,” Moldoveanu said.

A report on this study appeared in the journal Cell Reports.
Fourth ALL predisposition gene discovered

St. Jude researchers have discovered a fourth gene that can predispose carriers to childhood leukemia. The finding expands the list of genes clinicians should include in cancer screening.

The gene, *IKZF1*, can increase an individual's susceptibility to B-cell acute lymphoblastic leukemia (ALL). The discovery comes a decade after Charles Mullighan, MBBS, MD, of St. Jude Pathology, and his colleagues reported that *IKZF1* was often mutated in leukemic cells and was a sign of poor treatment outcomes.

In the recent study, scientists analyzed data from almost 5,000 young ALL patients and found that 0.9 percent of patients with B-cell ALL had inherited variations in *IKZF1*. The researchers also learned that inherited gene variations can affect how well leukemia cells react to chemotherapy drugs. Results of the study will help genetic counselors as they educate families about cancer risks.

A report on the findings appeared in the journal *Cancer Cell*.

WHO expands partnership with St. Jude

The World Health Organization has named St. Jude as its first WHO Collaborating Centre for Childhood Cancer. The designation represents a new push to expand efforts that will advance pediatric cancer survival rates worldwide.

"With this partnership, we have a unique opportunity to accelerate progress against the disease and change how childhood cancers are treated everywhere in the world," said James R. Downing, MD, St. Jude president and chief executive officer.

St. Jude is also a WHO Collaborating Centre for Influenza and has worked with the organization to support pandemic preparedness efforts since 1975.

Special thanks

St. Jude patient Matthew Fulcher presents a gift and scrapbook to oncologist Ching-Hon Pui, MD, to recognize Pui’s 40th anniversary at St. Jude. The scrapbook included photos, drawings and handwritten notes from patients.
DNA Day
In celebration of National DNA Day April 25, the Division of Cancer Predisposition “Gene Team” demonstrated how to extract DNA from strawberries. From left: Jamie Maciaszek, PhD, and Stacy Hines-Dowell, DNSc, both of Cancer Predisposition, assist Christian Trey Hall with the DNA extraction.

NEUROCOGNITIVE risk may begin before treatment

Leukemia itself, not just side effects related to its treatment, may increase the risk for long-term problems with attention, organization and other neurocognitive skills in survivors of the most common childhood cancer, according to recent St. Jude research.

Scientists analyzed the cerebrospinal fluid of 235 St. Jude children with acute lymphoblastic leukemia (ALL). Even before treatment began, some patients’ fluid contained proteins that suggested injury to cells that make up the brain’s white matter. These cells help the brain function correctly.

RESEARCH pinpoints crucial flu mutation

St. Jude scientists have identified a mutation that would enable the influenza virus to become resistant to a promising new class of drugs.

The most advanced of these drugs were recently approved for use in Japan and are in late stage-clinical trials in the U.S. These drugs will be the first new approved class of influenza therapeutics in nearly 20 years.

“Before this study, there was limited information on the resistance pattern of this new class of drugs,” said Elena Govorkova, MD, PhD, of St. Jude Infectious Diseases.

By better understanding the resistance mutation, scientists may not only be able to engineer drugs that avoid resistance by the flu virus, but also identify and track drug resistance in treated influenza-infected patients.

A report on this research appeared in the journal mBio.

Kevin Krull, PhD

“This was a surprise. Until now, we had not suspected that leukemia, by itself, or the inflammatory response to the disease, may lead to changes that leave ALL survivors at risk for long-term problems with executive functioning and processing speed,” said Kevin Krull, PhD, of St. Jude Epidemiology and Cancer Control. He and his colleagues also found that genetic variation may make patients vulnerable to such treatment-related problems.

The study appeared in the journal JAMA Oncology.
‘SECURITY chief’ sounds alarm against infections

St. Jude scientists have identified a key molecule that serves as a “security chief” to help the immune system recognize and fight infections with dangerous bacteria such as *Salmonella* and *Burkholderia*.

The key molecule is called IRF8. Researchers showed that in immune cells, IRF8 functions like a building security chief to make sure there are enough guards on duty to spot burglaries and alert authorities.

IRF8 regulates proteins that detect bacteria and activate the NLRC4 inflammasome. Then the NLRC4 inflammasome helps launch a response to fight the infection and trigger inflammatory cell death.

“This advances our understanding of how our bodies sense infectious agents, particularly toxic agents like *Salmonella*, *Burkholderia* and *Pseudomonas*,” said Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology. “Such knowledge is essential for finding new ways to block infections.”

The research appeared in the journal *Cell*.

One enchanted evening

Patients and siblings ages 15 to 19 enjoyed a special night of dancing and fun at the 2018 St. Jude Teen Formal at the Enchanted Garden. Child Life sponsors the annual event, which allows teens to experience one of the most anticipated events in a teen’s life: prom.
My Legacy

“I’m joyful and happy and appreciative—never regretting for one moment that I had cancer. It’s been an unbelievable journey and a privilege to look back and know I had a second chance at life.”

By Ryan Maranto

Everybody has a story that makes them who they are—a legacy they’ll leave behind. Mine started the day I found out I had leukemia.

At age 8, it was hard to comprehend what the world of cancer really meant. I just knew I was sick, and I was going to a place that would help make me better: St. Jude Children’s Research Hospital.

I remember the chemotherapy, the bone marrow and spinal tap procedures, and the nervous feeling of waiting for my name to be called. St. Jude is where I took my first communion and where I saw snow for the first time. My childhood revolved around the hospital.

Ching-Hon Pui, MD, is a legend in the field of leukemia treatment. He was my doctor: the man who made it happen for me. I have nothing but love and admiration for Dr. Pui. How can you express thanks to someone who not only gave you a second chance at life, but who has also done the same thing for so many other kids?

When I was a boy, I had two friends who watched me progress through treatment. Those friends eventually married and had a daughter who is now undergoing treatment for the same cancer I had. I was able to explain to that couple what their daughter was about to experience.

And her oncologist? It’s Dr. Pui.

My greatest joy is when I can provide some level of hope for parents who are just starting on this journey. Today, I lead an active and fulfilling life: attending football games in the fall, wakesurfing and wakeboarding in the summer. I never take life for granted. I’m joyful and happy and appreciative—never regretting for one moment that I had cancer. It’s been an unbelievable journey and a privilege to look back and know I had a second chance at life.

I’m living proof of what St. Jude can do, and I want to continue to carry that legacy, spreading a beacon of hope to other patients.”
His future starts with your legacy.

Meet your financial needs and help children like Keeton.

Receive regular, fixed payments for life, and see the impact you are making on our lifesaving work with a St. Jude Charitable Gift Annuity (CGA). A St. Jude CGA could help you supplement your income, save on taxes and give the gift of a lifetime to help the children.

Begin your legacy today.

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Taking St. Jude to the World
St. Jude is expanding its reach around the world with the launch of St. Jude Global. At a recent press conference, James R. Downing, MD, the hospital’s president and chief executive officer (pictured), unveiled a bold new initiative to improve access to care for children with cancer and other life-threatening diseases in every corner of the world.

The hospital’s goal is to influence the care of 30 percent of children with cancer worldwide within the next decade. St. Jude Global will leverage the resources and expertise of the hospital and its partners around the world.

The initiative will create a network of interactive programs and institutions, forming a global alliance that will improve access to care, enhance the quality of care children receive, and provide better options for cures.

Learn more: stjude.org/global