A NEW APP FOR PATIENTS AND FAMILIES

BIOSTATISTICS: THE POWER BEHIND THE PROTOCOLS St. Jude

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A NEW DIRECTION

FOCUS ON CHILDREN'S NEUROLOGICAL DISORDERS

featuring

DATA-DRIVEN DISCOVERY AT ST. JUDE

THE ST. JUDE GLOBAL ALLIANCE



ONE VACCINE PREVENTS 6 TYPES OF CANCER

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06/05

HPV PREVENTION

Portrait of a Scientist

A new painting has appeared in a venerable portrait gallery at St. Jude. Molecular oncologist Martine Roussel, PhD, is the first woman to receive this honor.

Roussel has made landmark findings in molecular oncology, cell cycle control, and the translational development of treatment strategies for pediatric medulloblastoma. She played a pioneering role in identifying several important oncogenes and made key contributions to the understanding of receptor signal transduction, cell cycle control and tumor development.

NN-MARGARET HEDG

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By Erin Podolak

Conversations that Connect

Virtual lecture series fosters community.

SHARING SCIENCE fuels progress by enabling researchers to hear about others' work, swap suggestions, and apply new findings and methods to their own efforts. But communicating through conferences and other large in-person gatherings has not been possible during the COVID-19 pandemic.

Scientists at St. Jude haven't allowed the pandemic to keep the cancer research community apart. Instead, they are using technology to find ways to connect virtually.

INTERNATIONAL AUDIENCE

One of these ways is the Science of Childhood Cancer virtual lecture series hosted by the St. Jude Comprehensive Cancer Center. The initial 15-week series last fall attracted 3,700 registrants from more than 1,000 institutions, representing 97 countries worldwide. The program was so successful that a second series launched in January 2021.

"Scientists frequently travel to conferences and to other institutions to share ideas and learn about the latest discoveries," says Charles Roberts, MD, PhD, director of the St. Jude Comprehensive Cancer Center and executive vice president. "However, the COVID-19 pandemic brought travel to a halt. As the nation's only NCI-designated Comprehensive Cancer Center dedicated solely to children, we saw an opportunity to facilitate engagement among scientists on a wide variety of topics relevant to pediatric cancer research."



(点) 【久間 The Science of **Childhood Cancer**

SPARKING COLLABORATIONS

Scientists from leading research institutions, including St. Jude, are invited to present their work at the weekly lectures. The speakers are experts across the fields of basic, translational, clinical and population science. Each presentation is followed by a robust question-andanswer session, where participants can use the digital platform to interact with the speaker. Attendees often stay past the lecture's formal end to continue their conversations.

CREATIVITY AND COOPERATION

The sessions have attracted investigators across the full career spectrum ranging from students to senior professors, lab technicians to physicians.

Fostering connections

In pre-COVID-19 days, Charles Mullighan, MBBS, MD (left), and Charles Roberts, MD, PhD, could collaborate in person. When the pandemic hit, they worked with other St. Jude scientists to host a lecture series that reaches the world.

Watch the lectures: stjude.org/socc

Two-thirds of the initial series attendees hailed from organizations other than St. Jude, re-creating a sense of global community that had been lost to the pandemic.

"This series has driven home how with a little creativity and cooperation we can still come together and connect over a shared passion for science," says Charles Mullighan, MBBS, MD, deputy director of the St. Jude Comprehensive Cancer Center.

"Pediatric cancer hasn't stopped during the pandemic," he continues, "and neither have we."

In Search of Hidden Gems: Data-Driven Discovery

With the world's top talent and technology in place, St. Jude is using data-driven discovery to better understand childhood cancer and to identify promising drug targets.

IMAGINE SEARCHING for a sparkling diamond amid a beach of glittering sea glass. Scientists today face a similar task as they comb vast amounts of data in pursuit of lifesaving discoveries.

The data generated as part of one scientific project can be mind boggling – exceeding the capacity of multiple computers. How does a researcher find one elusive gem among terabytes of data?

"What fascinates me the most about big data is that we now have more information than any one person can really think about," says M. Madan Babu, PhD, who holds the endowed chair in Biological Data Science in the Department of Structural Biology and directs the new Center of Excellence for Data-Driven Discovery at St. Jude Children's Research Hospital.

"The key to navigate this complex landscape of data is to ask the right scientific questions and bring multiple disciplines together," he says. "With clinical scientists, chemists, physicists, statisticians, biologists, structural biologists and computer scientists united under the same mission, there's no better place than St. Jude to take on a task of this magnitude."

As a boy growing up in India, Babu was captivated by computer science and biotechnology. He went on to build a distinguished career in computational biology and bioinformatics. In fact, he was one of the pioneers to establish data sciencebased approaches to reveal the basic principles of biological systems.

Babu was inspired to use his knowledge and skills to change the lives of children with catastrophic diseases, including cancer. So, in July 2020, he accepted a position where his work might reveal deep biological insights that could one day lead to new treatments and cures.

SHAPE DETERMINES FUNCTION

Most of the work inside our cells is performed by proteins. The shape of a protein determines how it functions. Some proteins change shape in response to messages received from other molecules through receptors. These receptors, a group of proteins that sit on the cell membrane, change shape themselves in response to messages received from outside of the cell, and they transmit those messages to make changes inside the cell.

G-protein coupled receptors (GPCRs) are the largest family of protein receptors in the human genome. More than 800 GPCRs are expressed throughout the body. They play essential roles in our immune, hormone, cardiac and respiratory systems,

By **Jane Langille**

as well as in our ability to smell and taste and other functions.

Each GPCR binds to one or very few specific molecules, fitting together like a lock and key. Scientists must determine the shape of these receptors and learn how other molecules interact with them. Only then can the scientists design drugs that alter the commands affecting the proteins' shapes and functions.

GPCRs are excellent drug targets because they sit on cell membranes. One-third of all approved drugs target GPCRs, but scientists have studied only about 150 of the 800 that are known.

Surprisingly, just a few of the FDAapproved cancer drugs target GPCRs. Why are they not targeted?

The answer, Babu says, is that the role of GPCRs in cancer has only been looked at in the last few years. He and his colleagues are using data-driven approaches to reveal how GPCRs drive cancer.

A CLOSER LOOK

St. Jude structural biologists can see farther into cells than ever before. They use the world's most advanced tools to reveal once unknown molecular structures. Those tools include X-ray crystallography, single-molecule imaging, mass spectroscopy and highresolution nuclear magnetic resonance spectroscopy.

Now, Babu brings data science approaches to St. Jude, providing new insights into variations in molecular structures.

He and his colleagues have integrated information on protein structures with human genetics and transcriptomics data. They found multiple GPCR gene variants that give rise to slightly altered shapes of the same receptors — changing the nature of the signaling messages. The findings may explain why side effects occur with currently available targeted therapies that address only one variant. The findings may also explain why some "Together, we are taking **big steps** to advance the field of pediatric cancer —working on **longterm, complex problems** that can't be solved with quick fixes."

– M. Madan Babu, PhD



drugs work well in cell models but fail in animal models — hence, never making their way to patients.

At St. Jude, Babu aims to understand how different families of GPCRs may play a role in pediatric cancer, because many GPCRs are key players in the immune system.

He is investigating a family of GPCRs called chemokine receptors. They regulate how immune cells travel to cancer cells and interact with them. Targeting chemokine receptors with drugs could help the immune system better identify and attack the cancer cells.

DIAMONDS AND DEPENDENCIES

"Initiatives such as the Pediatric Cancer Genome Project [led by James R. Downing, MD, president and CEO of St. Jude] have provided an unparalleled view of the landscape of where things have gone wrong with cancer," Babu says.

St. Jude researchers are capturing these — and other — massive amounts of data and are making that data available to researchers across the world through the St. Jude Cloud.

"This presents unprecedented opportunities to discover mechanisms and events that lead to altered behavior at the molecular level, eventually paving the way to fix them," Babu says.

That's where big data science comes in. Babu and his team develop new methods to analyze and mine data from many sources, including DNA sequences, gene expression profiles, proteomics, protein structures and details about the shapes of compounds that could lead to drug candidates.

VIRTUAL DRUG DISCOVERY

St. Jude researchers are using 3-D computer modeling techniques to screen billions of chemical compounds to see if one might lock into proteins of interest. Recent advances in computing power have made it possible to whittle that list to a manageable size.

"Once you know the shape of the molecule, you want to discover a compound that will bind and perturb its function. That compound will eventually become a drug," Babu explains. "But the chemical space is vast. There are many different compounds, and we don't know which one is going to be able to bind to it.

"We can't do an experiment to test a billion compounds," he continues. "How could we even test that many?"

That's where, again, computers come in handy.

"At St. Jude, we have the technolog-



ical expertise and computing power to do just that," he says.

Babu is particularly interested in revealing the unique biological weak points in cancer cells that are not present in normal cells. These weaknesses are known as dependencies. His team strives to discover mechanisms involving previously unstudied GPCRs, also called orphan receptors, that are dependencies in pediatric cancers.

"We don't know yet what messages many of these orphan receptors respond to," Babu says. "We aim to identify which ones play important roles in cancer. For this, we use our analysis methods in combination with the thoughtfully set-up core facilities and other resources within St. Jude to investigate them further."

Babu says he hopes his discoveries about dependent GPCRs can drive virtual screening efforts to reveal such compounds.

Data science approaches can also iden-

tify drugs already approved for other health conditions that affect the same dependencies cancer cells use to survive. That means it may be possible to repurpose drugs already approved for other health conditions to treat pediatric cancers driven by the same variants.

COLLABORATIVE CULTURE

Babu says he's excited to be working alongside other world-class experts from diverse fields, united under the hospital's inspiring mission. St. Jude is paving the way for world-leading research in data science.

Scientists from the departments of Biostatistics, Chemical Biology and Therapeutics, Structural Biology, Cell and Molecular Biology, Developmental Neurobiology, Immunology, Infectious Diseases, Pharmaceutical Sciences, Cancer Biology, Genetics, Computational Biology, and Bioinformatics are uniting to share their knowledge and define the data science culture.

"This culture that breaks down scientific silos is remarkably rare," Babu says. "It creates a diverse and unique intellectual ecosystem that enables us to tackle some of the most fundamental problems in biomedical data science."

Babu says he recognized St. Jude was exceptional during his first visit in 2012, when he delivered the Danny Thomas Lecture, a prestigious lecture series named after the hospital's founder.

"Its world-class core facilities, shared resources and commitment to cutting-edge science foster collaboration across multiple departments," he says.

"Together, we are taking big steps to advance the field of pediatric cancer working on long-term, complex problems that can't be solved with quick fixes. There is no better place than St. Jude to do this."

By Keith Crabtree, PhD

A DECADE OF ACHIEVEMENT Family, Home and Hope

The St. Jude Global Alliance empowers its members to improve care worldwide.

IN SEPTEMBER 1962, the same year St. Jude Children's Research Hospital opened its doors, President John F. Kennedy went to a football stadium in Texas to reiterate the United States' commitment to put a man on the moon.

"We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard," Kennedy said.

Before the address, the president underlined the last word in blue ink. (The Apollo 11 astronauts set foot on the moon July 20, 1969.)

Curing cancer is harder than putting a man on the moon. In the 1950s, only 10% of children with cancer survived. Yet, progress is clear.

In the U.S. today, more than 80% of children with cancer survive. The prognosis, however, for children with cancer in low- and middle-income countries where more than 80% of all children with cancer live — remains grim.

Most of them will die because of their disease.

St. Jude Founder Danny Thomas believed that no child should die in the dawn of life. James R. Downing, MD, St. Jude president and chief executive officer, expands upon that sentiment.

"Our mission is to find cures and save children — regardless of where they live," he says. Carlos Rodriguez-Galindo, MD, executive vice president and director of St. Jude Global, puts the monumental task into perspective. "This is our moonshot," he says.

THE GLOBAL ALLIANCE FAMILY

The St. Jude Global Alliance gives St. Jude Global its full meaning—uniting institutions, foundations, doctors, nurses and other partners who are committed to improving care for children with cancer and other life-threatening diseases.

"We want to build a family," Rodriguez-Galindo says. "This is how we will succeed."



The Global Alliance offers its partners collaboration opportunities that provide the evidence-based knowledge they need to make significant and long-lasting progress against pediatric cancer.

"We empower people," Rodriguez-Galindo says.

Building capacity — the workforce and resource development necessary to create a durable response — is crucial. St. Jude Global takes a tiered approach that encompasses individuals, institutions, countries, regions, and ultimately, the globe.

But the alliance is more than just an initiative. It's a global family.

"We all share the dining table, if you wish," Rodriguez-Galindo says.

Soon, they may need to lift the table's drop leaf to make room for additional chairs.

In December 2018, the first St. Jude Global Alliance meeting drew more



than 200 people from more than 50 countries. Two years later, more than 800 people spanning 71 countries joined the first day of the virtual St. Jude Global Alliance convening.

Without a doubt, the face-to-face model of engagement yields dividends.

When St. Jude Global staff travel to other countries, they attend hospital rounds. They spend days embedded in local health care systems. They look doctors and nurses in the eye. They talk to ministers of health and ministers of finance.

They want to convey a simple message: "We're here to help."

A PANDEMIC PIVOT

Throughout 2020, the pandemic's destructive effects — shortages of supplies, equipment and staff, to name a few — unfurled across Asia Pacific, Central and South America, China, the Eastern Mediterranean, Eurasia, Mexico and Sub-Saharan Africa, the regions that form the St. Jude Global Alliance.

In moments of uncertainty, Rodriguez-Galindo is likely to say, "Cancer doesn't wait, and neither do we."

As a result of the pandemic, he and his colleagues pivoted.

"Now we have a whole different way of working," he says.

The face-to-face model of engagement



"We have **a better chance** in fighting cancer in children when we are together."

- Allen Yeoh, MBBS, of Singapore



"With this alliance with you, **we definitely feel that we have a partner;** that we are not on our own."

- Gita Naidu, MD, of South Africa

ceded to a virtual one. The St. Jude Global Alliance Online Community, the newly created Global COVID-19 Observatory and Resource Center for Childhood Cancer, and other web-based tools made it possible for Global Alliance members to continue their work.

VIRTUAL CONVENING

December's gathering of alliance members — with the theme "We are complete when we are together" — was an entirely virtual event.

"The goal of the convening was to give people an opportunity to connect, to focus on our members after a difficult year and to ignite momentum for 2021," says Whitney Foster, program manager for St. Jude Global Operations.

The event included a panel discussion about resilience and teamwork. Alliance members attended workshops, took part in live Q&A sessions and learned about new tools. Participants also interacted with staff from the St. Jude Global Regional and Transversal programs and education teams; ALSAC, the hospital's fundraising organization; and Together, an online resource for childhood cancer created by St. Jude. Along the way, participants learned about remarkable global partnerships, such as the World Health Organization Global Initiative for Childhood Cancer.

"I think people felt at home," Rodriguez-Galindo says. A video called *Inspiring Hope* debuted at the event. In the video, Global Alliance members convey an optimistic message.

"With this alliance with you, we definitely feel that we have a partner; that we are not on our own," says video participant Gita Naidu, MD, of South Africa.

"We have a better chance in fighting cancer in children when we are together," adds Allen Yeoh, MBBS, of Singapore.

"I found a family," says Luis Fernando Mendoza-Moreno, MD, of Mexico.

UNIFIED BY FAMILY AND HOPE

"We have more than 500 projects around the world right now from education to operations to quality improvement," Rodriguez-Galindo says.

He's understandably hard-pressed to select one top achievement.

"There are many examples," he says. "In each region, you would find them."

But it may be possible to rank one project high on the list — the growth of the alliance family, who work tirelessly together to achieve a lofty goal.

Monika Metzger, MD, director of the Central and South American Region, asked members attending one convening session a question: "What motivates you to get out of bed each morning?"

A doctor from Nicaragua, a developing country with a history of civil war and economic hardship, spoke up.

"How much time do I have?" she said. Ears perked, Rodriguez-Galindo listened in. He recalls her words: "I just have hope," the doctor said. "I keep working for that hope — to give hope and to receive hope."

Watch Inspiring Hope: global.stjude.org

Photos for this article were taken pre-COVID-19.



"I found a **family."** – Luis Fernando Mendoza-Moreno, MD, of Mexico







By Maureen Salamon

St. Jude at Your Fingertips

The Our St. Jude mobile phone app guides patients and families, easing their load.

THE FRANTIC, frightening, frazzled first weeks at St. Jude Children's Research Hospital are still etched in the minds of Jason and Felicia Winkle six years later.

Overwhelmed with details about their son's diagnosis of Ewing sarcoma, a rare bone and soft tissue tumor, the couple could barely track what day it was – much less their list of appointments and travel, housing and meal arrangements.

"In the first month, Micah's appointments changed constantly, and we'd sign in to the St. Jude patient portal every couple of hours to keep up," Jason recalls. "It's also easy for parents to forget the names of doctors, nurses and other staff members because you meet so many, especially at the beginning."

This keen insight fueled Jason — now co-chair of the St. Jude Patient Family Advisory Council — to provide inspiration and guidance as St. Jude created its new patient and family app, called Our St. Jude. Launched in late 2019, the award-winning mobile phone application offers patients and caregivers quick and easy access to personalized, real-time updates on clinical appointments, campus events and myriad other pivotal details.

KEY COLLABORATIONS

Among other major features, the colorful Our St. Jude app lists each child's care team and contact information and provides step-by-step walking directions to every campus building. With all this crucial information at families' fingertips, St. Jude aims to lighten their load – whether their child is newly diagnosed or years out from active treatment, says Diane McGarry, administrative director of the Patient and Family Experience Office.

"The idea for the app came from our patients and families," says McGarry, whose office spearheaded the project. "Why now? It's staying relevant with where the world is going. It's common to use your mobile device as a resource for planning your day, tracking the things you need to do and researching unknowns.

"We know that when our patients are new to St. Jude, they're also likely new to a pediatric catastrophic disease, and that alone is enough," she adds. "But many may also be new to the city of Memphis. At St. Jude we have so much information to give them. Our hope with the patient app is that we provide some peace of mind and a resource that helps them navigate many new and unknown things."

PLUGGING IN, LOGGING ON

The app's creation — incorporating photos, maps and other splashy visual touches — spanned several years, McGarry explains. Along with the St. Jude Mobile Development Team, her office collaborated with patients and families at

every step, interviewing them about their needs and ideas and asking them to test preliminary versions.

When users — who logged in more than 150,000 times in 2020 — open Our St. Jude, they first see what's on their calendars, including appointments, social events and any travel or housing reservations. Up-to-the-minute alerts tell them how their schedule might have shifted, a common issue at a hospital as busy as St. Jude.

"Nothing else would have provided these kinds of notifications to our families," McGarry explains.

"With COVID-19 constantly changing things, the app has been so useful. We've been able to send our families updates regarding changes to campus. Prior to the app, there wasn't a great way to do that type of targeted communication."

MEETING FAMILIES' NEEDS

Several tweaks to app features are still planned, McGarry says, including

"...we provide some **peace of mind** and a resource that helps them **navigate** many new and unknown things."

- Diane McGarry



Menus and more

Jason Winkle and his son Micah say the Our St. Jude app makes the hospital more accessible to families.

offering it in Spanish and adding a personalized medication list and symptom tracker. She notes that those who are less tech savvy or don't wish to use the app can still obtain all the same information in other formats.

But Micah Winkle is more than satisfied with what it offers him when he comes back to St. Jude for periodic follow-up scans. Five years after Micah's treatment ended, a seemingly minor feature of the app — the daily cafeteria menu — is a big deal for the growing 15-year-old.

Small touches like this epitomize how well St. Jude shepherds its patients and families through an all-consuming experience, Jason says.

"It makes St. Jude that much more accessible to families," he says. "Getting a cancer diagnosis is life-changing, but the way St. Jude meets the whole needs of the family is also lifechanging. The app is a game-changer in that sense."



By Maureen Salamon Direction

St. Jude expands its mission to embrace children's neurological disorders **AFTER DECADES OF FRUSTRATION** watching seemingly healthy babies lose their power to roll over, sit up or eat, Richard Finkel, MD, was amazed.

A new drug was changing everything for children with spinal muscular atrophy (SMA). This previously untreatable neurologic disease withers nerve cells in the brain and spinal cord.

"We started seeing one child after another sit up and roll over – things these babies never, ever achieve," he recalls. "Several years later, we see these children continue to improve. Now we're starting to think about them growing up and becoming teenagers and young adults and facing the world, where none of this was ever possible before."

Finkel played a vital role in testing what eventually became three successful drugs for SMA, which often killed affected babies by their second birthday. Now he's bringing that lifechanging insight to St. Jude Children's Research Hospital as he creates a model for treating SMA and scores of other neurologic diseases that affect babies and children.

TRUE NORTH

Finkel is director of the Center for Experimental Neurotherapeutics, the clinical component of a new St. Jude program called the Pediatric Translational Neuroscience Initiative (PTNI). Unlike other pediatric neurological programs, the PTNI joins lab and clinical research, local and international collaborations, and partnerships with drug companies to bring promising treatments to children with neurological diseases.

Launched in 2020, the PTNI will also test current treatments to gauge their safety and effectiveness in children at St. Jude and beyond. This initiative joins the hospital's renowned programs for catastrophic childhood diseases such as cancer, sickle cell anemia and HIV. Neurologic diseases are just as big a burden, even though therapies had been limited until recently by poor understanding of their causes.

"We're moving in a new direction, perhaps, but staying true to the core



"We're moving in a new direction, perhaps, but staying true to the core values and mission of St. Jude." values and mission of St. Jude," Finkel says. "It's a chance to be bold in steering St. Jude toward other catastrophic diseases affecting children where there's a high unmet need and opportunity to hopefully find cures and save lives."

THE TIME IS NOW

About 1 in 6 children have some form of neurological disability, ranging from seizures to movement disorders to neuromuscular diseases. Some of those disorders can thwart a child's ability to talk, see or hear. Like SMA, almost all of these diseases are driven by a mutation or change in a single gene. This trait makes them ripe for drug treatments that have recently emerged to target wayward genes and block the disease process.

For most of these conditions, current treatments either don't work or only manage symptoms without fixing the underlying problem.

"These are substantial disorders that limit the ability of these children to function independently or become adults who can function effectively in society or at home," Finkel explains. "They're often unable to get jobs, they struggle with relationships, and in the most severe conditions, these children have reduced survival. Unfortunately, with some of the conditions I've dealt with, more than half the babies don't make it through infancy."

CHART THE COURSE

PTNI started as a St. Jude-funded blue-sky project of bold ideas to transform science and medicine. But the program was years in the making. The vision of J. Paul Taylor, MD, PhD, chair of St. Jude Cell and Molecular Biology,

"We want to map out the conditions where we can have the most impact because of critical gaps, or because the companies developing those therapies don't know what to do once they have the therapy in hand."

J. PAUL TAYLOR, MD, PHD

the initiative comes in an era when key developments have merged: Not only have scientists cracked the genetic cause of many pediatric neurologic conditions, but promising treatments have surfaced to target those genes.

Taylor, director of PTNI, was an integral part of research that pinpointed the genes responsible for children's neurologic syndromes and figured out how they cause illness. Today, next-generation gene sequencing is helping researchers find the genes that cause individual conditions. Meanwhile, drugs have been developed that can deliver their effects straight to the brain through innovative techniques.

DISCOVERIES IN THE LAB

The basic research component of the PTNI is called the Center for Pediatric Neurological Research. Led by Peter McKinnon, PhD, of St. Jude Genetics, scientists in this program will make discoveries that can be translated into cures.

"It's always been clear that the mission of the hospital has been to tackle catastrophic diseases. If you want an example of a catastrophic disease, you need look no further than inherited neurologic diseases," McKinnon says. "Our work will have a really profound impact on families affected by these disorders."

He explains that treating children with neurological diseases is fundamentally different than treating those with cancer.

"With cancer, you basically want to get rid of the cancer by killing it," he says, "so the strategies are to develop agents that target and destroy the cancer. To some extent, it's the opposite with neurodegenerative diseases. You want to prevent symptoms from occurring; you want to save the tissue. It's important to intervene as early as possible before anything bad has happened."

McKinnon has conducted extensive

research into movement disorders associated with the cerebellum, the part of the brain that affects muscular activity. One of his newest colleagues, Heather Mefford, MD, PhD, studies the genetic causes of childhood epilepsy. Another team member, Andy Kodani, PhD, focuses on the development of the cortex, a brain region that plays a key role in activities such as attention, perception and memory. McKinnon is currently recruiting additional scientists who will add breadth and depth to the program.

HIGHEST CHANCE FOR CURES

Hoping to speed new and different treatments from the lab to the clinic, Finkel and his St. Jude colleagues are launching several clinical trials this year.

Children in these studies will be treated by a dedicated team of doctors, physical and occupational therapists, and specialists such as pulmonologists and surgeons.

The first such study will take a closer look at one of the drugs already approved for children with SMA, but in an age group that hasn't been studied — newborns. These babies will be screened at birth with a test that reveals SMA before symptoms such as muscle weakness occur.

"Treating them before they show symptoms offers them the highest chance of a cure," Finkel says. "We know this drug works well in infants and children who show signs of weakness, but it doesn't cure them. Hopefully this study fills that gap."

Other clinical trials will focus on Duchenne muscular dystrophy, the most common and severe form of muscle-weakening disease; and another genetic condition called Friedreich's ataxia. There are currently no effective medications for Friedreich's ataxia, which causes problems with speech, swallowing, hand control and walking.

Some trials will also include children who have been left out of prior research, whether because of age or disease severity, but who still might benefit from therapy, Taylor says.

"We want to map out the conditions where we can have the most impact because of critical gaps," he adds, "or because the companies developing those therapies don't know what to do once they have the therapy in hand."

A CENTER WITHOUT WALLS

Partnerships and collaborations are crucial to the success of this new venture. Local partners include the University of Tennessee Health Science Center and Memphis-based Le Bonheur Children's Hospital, whose neurology department has expertise in epilepsy and disabilities related to brain development.

Input and efforts by drug manufacturers, global experts, patient foundations, outside institutions and other St. Jude departments will create a "center without



"If you want an example of a catastrophic disease, you need look no further than inherited neurologic diseases. Our work will have a really profound impact on families affected by these disorders."

walls" to ensure all goals are met.

"It's impossible to do all of this at St. Jude," Taylor says. "There are so many diseases and so many ways one could develop therapies. The smartest thing to do is make this a global effort."

Finkel hopes in the next five years to recruit more physician-scientists to the program and explore a dozen or more neurologic diseases. To Taylor, bigpicture success requires "systematically churning out effective therapies for kids with neurological diseases."

Success might mean providing proof that current treatments also work for other age groups or can be stopped after a certain age without patients getting worse, Taylor says. It also means creating treatments that never before existed.

"I want to see us change the standard of care for kids who are currently just supported with things like slings, braces and surgery," Taylor says. "If this initiative is successful, we will see kids treated differently than they are today."

"This is clearly at the very center of our mission to address catastrophic diseases of childhood," he says. "There is no other place that's stepping up to fill this unmet need."

By Elizabeth Jane Walker Power Behind the Protocol

Who provides fuel for the engine of medical research – helping design studies, analyze data and report results? *Biostatisticians*.

LET'S PLAY THE WORD ASSOCIATION GAME: What springs to

mind when you hear the phrase "clinical trial"?

Perhaps you think of doctors and nurses. Of tests and treatment. Of chemotherapy and surgery.

If your answer is "biostatistics," you're in good company. Medical research begins and ends with biostatistics – the branch of statistics that deals with biological data.

At St. Jude Children's Research Hospital, Motomi Mori, PhD, leads a staff of 60 individuals who support all the institution's clinical trials.

"We help design the research studies," says Mori, chair of Biostatistics. "How many patients must be enrolled to answer a particular research question? What kind of statistical analysis should be used? What kind of data needs to be collected?

"After the study is complete, we are the ones who get the data, analyze it, help the scientists prepare their manuscripts and share the results."

RESOURCES AND RESEARCHERS

Mori's team supported 274 projects from 122 investigators in the last six months alone. More than 140 of those projects were clinical studies, many of which extend across multiple years.

For decades, scientists at St. Jude have turned to the Department of Biostatistics as a shared resource — their secret weapon for designing, running and reporting the results of their research.

Mori, who joined the institution two months before the COVID-19 pandemic

hit, is committed to maintaining that robust level of support. Simultaneously, she aims to build an environment where biostatisticians can perform independent research that will increase the stature of St. Jude and enhance the knowledge base for the entire field.

HOT COMMODITY

In 2009, the chief economist at Google surprised a *New York Times* reporter by predicting that the "sexy job in the next 10 years will be statisticians."



"We help design the research studies. After the study is complete, we are the ones who get the data, analyze it, help the scientists prepare their manuscripts and share the results."

– Motomi Mori, PhD



Eleven years later, biostatisticians indeed became a hot commodity, as news outlets clamored for experts to help explain the scope and threat of COVID-19.

"I have never seen so many biostatisticians on the national news," Mori's husband marveled.

The media sought answers when people around the world began asking how the pandemic would affect them. How many individuals would be infected? How many would be hospitalized? How many would die? How would data modeling influence policy decisions?

"Everybody was looking at the data," recalls Mori, who wonders whether the recent media attention might cause a spike in the number of children who one day enter the field. "People were looking at the shapes of the curves and how many cases we had. They were watching the trends. They were also changing their behavior in response to predictions — which meant the predictions would then change, as well."

On the local level, she and Greg Armstrong, MD, of St. Jude Epidemiology and Cancer Control assisted with the local pandemic response through participation in a data monitoring group and a joint task force. They helped individuals from Mid-South universities, law enforcement, emergency services, governments and school districts better understand and appropriately respond to national, regional and local data.

Throughout these crisis-planning interactions, Mori says, the collaborations have been overwhelmingly positive.

"The pandemic brought together people from the city, the county, the health department and our St. Jude Infectious Diseases department — people I would probably never have interacted with under normal circumstances," she says. "It's been an interesting year."

CONNECTED TO THE MISSION

Individuals in the Department of Biostatistics hail from 11 countries, speak 16 languages and are fluent in 15 computer languages. Mori says this disparate group is united by the hospital's mission, even though most patients and families are unaware of their existence.

Through their work on research projects and clinical trials, St. Jude biostatisticians are helping to increase scientific knowledge and save young lives.

"We don't treat the patients, but we see them on campus," Mori says. "That's a daily reminder to us. Going into work each day, we pass by the statue of St. Jude Thaddeus. And every time we walk across campus, we see the children and their families — and we remember why we're here."



"I knew the HPV vaccine helps prevent against a number of adult cancers," says Rachael Murray about her daughter, Annabelle. "She has been through so much already. I don't want her to experience something later in life that could have been prevented."

By Mike O'Kelly

Prevention is Key

The new St. Jude HPV Cancer Prevention Program seeks to increase HPV vaccination rates to help reduce the number of deaths from six types of cancer.

YOU'VE PROBABLY SEEN the brochures tucked inside the plastic sleeves that hang on the wall of the pediatrician's office. Or you've seen a few TV ads and wondered if the topic was relevant to yourself or your children.

Human papillomavirus (HPV) is more common than you might think. Nearly 80 million people in the U.S. are infected with the virus. That's 1 in 4 Americans. More than 36,000 of those will be diagnosed with one of six HPV-related cancers this year. But the brochures and ads have a simple call to action: "HPV vaccination is cancer prevention."

Ten-year-old Annabelle Murray has been a patient at St. Jude Children's Research Hospital since she was 3 months old. Annabelle has spent much of her life undergoing treatment for severe chronic neutropenia. When her mother, Rachael, learned that Annabelle could receive the HPV vaccine at St. Jude, her decision was easy.

"I knew the HPV vaccine helps prevent against a number of adult cancers," Rachael says. "She has been through so much already. I don't want her to experience something later in life that could have been prevented."

ON THE MAP

Heather Brandt, PhD, cringes when she looks at two maps of the United States.

The first shows regions with the highest incidence and deaths from HPV-related cancers. The second displays HPV vaccination percentages. Together, the maps reveal a grim picture for states in the Mid-South and Southeast. Those states rank last on both maps. St. Jude sits in the heart of that region -a major factor in Brandt's decision to join the hospital to direct the new HPV Cancer Prevention Program.

"Part of our work is raising awareness about the HPV vaccine. It is safe, effective and durable," says Brandt, a social and behavioral scientist. "Our goal is to reduce HPV-associated cancer deaths locally and nationally by driving up vaccination rates."

Much of that work occurs through education, awareness and partnerships. Andrea Stubbs, who has worked at St. Jude for 14 years building community partnerships in the hospital's HIV Prevention and Care Program, will use



that experience in her new role as administrative director of the HPV program.

"I plan to invite parents, administrators, clinicians and community partners to have a conversation," Stubbs says. "We can discuss the risks associated with HPV and the impact of HPV vaccines to prevent cancer."

The Centers for Disease Control and Prevention routinely recommends HPV vaccination for both girls and boys at age 11 or 12. Children as young as 9 and up to 14 can receive two doses of the vaccine. Adolescents and young adults ages 15 to 26 receive three doses. Adults age 27 to 45 should discuss HPV vaccination with their health care provider to determine if it is right for them.

"We want to make sure people have the right information but also ensure they know how to act on it," Brandt says.



BLUE SKIES ON THE HORIZON

Part of the hospital's Comprehensive Cancer Center, the St. Jude HPV Cancer Prevention Program stemmed from the hospital's blue-sky process. This program encourages employees to submit novel proposals that could transform science and medicine.

The question asked was, "What if we could prevent adult cancers by vaccinating children?" The initiative received support and approval, using the St. Jude platform to help increase HPV vaccination rates.

In 2018, St. Jude joined other National Cancer Institute (NCI)-designated cancer centers in the American Cancer Society's effort to eliminate HPV-related cancers. St. Jude aims to increase the number of children who are vaccinated and reduce HPV-related cancers in the region.

"At St. Jude, we use every tool at our disposal — including chemotherapy, radiation, surgery and immunotherapy — to strive to cure each child's cancer. But in the case of HPV-related cancers, the need for these therapies could be avoided because these cancers can be prevented in the first place with HPV vaccination,"

Our goal is to reduce HPV-associated cancer deaths locally and nationally by driving up vaccination rates." - Heather Brandt, PhD

says Charles Roberts, MD, PhD, St. Jude Comprehensive Cancer Center director and executive vice president.

BUILDING BRIDGES

Brandt and her St. Jude team work with partners to strengthen existing efforts, implement programs and increase vaccination rates.

"HPV-related cancers are recognized as the most preventable cancers," says Rochelle Roberts, co-facilitator of HPV Cancer Free Tennessee. "With targeted efforts to increase the vaccination rates for children, teens and adults, we can

Lofty goals

States in the Mid-South and Southeast have the highest incidence and deaths from HPV-related cancers – and the lowest HPV vaccination rates. Heather Brandt, PhD (at left), and Andrea Stubbs aim to change those statistics.

decrease HPV-related cancer mortality rates in Tennessee. We are excited about our partnership with the St. Jude HPV Cancer Prevention Program."

St. Jude is also working with a coalition called ImmunizeTN.

"Our goal is to get every eligible person in the state vaccinated with the HPV vaccine to prevent cancer," says Dee Sinard, MD, co-chair of that organization. "Having St. Jude on board to assist our efforts strengthens our messages across Tennessee."

Brandt serves on the National HPV Vaccination Roundtable, a collaboration of 70 organizations coordinated by the American Cancer Society. St. Jude will take a leading role in the Southeast.

"We are excited to work with Dr. Brandt and St. Jude," says Debbie Saslow, PhD, managing director of HPV and GYN Cancers for the American Cancer Society. "With St. Jude taking on a leadership role, this allows the great work in the southeastern region to continue."

THE ROAD AHEAD

The St. Jude HPV Cancer Prevention Program faces many challenges vaccine hesitancy, misinformation and the effects of the COVID-19 pandemic. Brandt is realistic yet optimistic about these hurdles. She says the hospital's commitment to the program mirrors her optimism.

"I am inspired by the possibilities that become reality at St. Jude," Brandt says. "It is a great privilege to have the opportunity to lead this new program focused on preventing HPV cancers."



Joseph V. Simone, MD



St. Jude mourns the loss of pioneers, leaders

ST. JUDE RECENTLY lost two extraordinary leaders and giants in the research and treatment of pediatric catastrophic diseases: Joseph V. Simone, MD, who served as the third director of St. Jude; and Arthur W. Nienhuis, MD, the hospital's fourth director.

Simone helped lead the first curative treatment for childhood leukemia, the legendary Total 5 clinical trial. During his tenure, the hospital instituted an HIV/AIDS clinical program, elevated its research to unprecedented heights, and created the world's largest long-term follow-up clinic for childhood cancer survivors.

Nienhuis, a gene therapy pioneer, contributed to research that led to a cure for X-linked severe combined immune deficiency and to gene transfer that transformed life for men with a severe form of hemophilia B. Nienhuis oversaw the "billion-dollar expansion," one of the most dramatic eras of growth in the hospital's history.

The legacy of Simone and Nienhuis will live on through the students, scientists, clinicians, academicians and survivors who benefited from their genius, their vision, their passion and their leadership.



Challenging dogma about a relapsed **brain tumor**

ST. JUDE SCIENTISTS are studying a childhood brain tumor called medulloblastoma. It is among the most common malignant pediatric brain tumors. The work provides a new way of looking at relapses.

This study looked at clinical trial data alongside pairs of new and relapsed tumor samples. Ten percent of those classified as relapses were actually secondary cancers.

Most tumors stay in the same molecular group from diagnosis to relapse. But the research showed this is not always the case. The scientists also found that the genes involved in cancer largely stay the same between the primary and relapsed tumors. The findings help us understand molecular features related to relapse.

"These findings show the need to include detailed molecular analysis with the diagnosis and treatment of these tumors," said Paul Northcott, PhD, of St. Jude Developmental Neurobiology.

"Understanding the molecular mechanisms responsible for treatment failure and recurrence is important, since children who relapse have few effective treatment options."

The Journal of Clinical Oncology published this work.



SFTH DIXO

COVID-19 poses risk to **transplant** recipients

PHYSICAL DISTANCING.

Wearing a mask. Frequent hand washing. All are important ways to prevent COVID-19.

A new study suggests children and adults who receive bone marrow transplants should make prevention a priority.

Researchers studied 318 transplant recipients worldwide who developed COVID-19. These patients were more likely than the general public or cancer patients to develop severe COVID-19 and die. Even recipients whose transplants occurred more than one year earlier were at increased risk.

COVID-19 survival is 95–99% in the general population. It was about 68% among transplant recipients in this study.

"Transplant recipients should take the utmost precautions to avoid exposure to the virus that causes COVID-19," said Akshay Sharma, MBBS, of St. Jude Bone Marrow Transplantation and Cellular Therapy.

Lancet Haematology published a report on this study.

Genetic variants linked to heart health in Black childhood cancer survivors

ST. JUDE SCIENTISTS have

found genetic variants that increase the risk of heart problems in childhood cancer survivors who are Black. The finding could affect how their health is monitored.

Scientists used the St. Jude Lifetime Cohort (St. Jude LIFE) study to evaluate risk factors. Black participants had a higher risk of developing cardiomyopathy than whites did. Cardiomyopathy is a chronic disease of the heart muscle. Scientists found two genetic variants linked with that disease in Black survivors.

Details from this study can be used to guide follow-up and treatment for these individuals.

A report on the study appeared in the journal **Cancer Research**.



Researchers offer new strategy to stop COVID-19

Chirumala-Devi Kanneganti, PhD

ST. JUDE SCIENTISTS may have figured out how the pandemic virus kills and how to stop it.

COVID-19 has killed more than 2.5 million people worldwide. Current treatment may include extra oxygen and breathing support.

The virus responsible for COVID-19 can cause life-threatening inflammation and breathing problems. The virus can also damage the heart, kidneys and other organs. Until now, the process causing the inflammation and tissue damage was uncertain.

Scientists identified how the virus activates inflammatory cell death pathways. Based on this discovery,

they found that drugs already used to treat some inflammatory diseases could be repurposed for use in COVID-19.

The drugs protected against death in mice with COVID-19, as well as sepsis and other inflammatory disorders that every year kill millions worldwide. This includes hemophagocytic lymphohistiocytosis (HLH), in which the immune system does not work right.

"The understanding that we gained in this study of how SARS-CoV-2 causes COVID-19 and inflammation helped us identify a promising therapy that relies on available drugs," said Thirumala-Devi Kanneganti, PhD, of St. Jude Immunology.

Cell published a report on this work.



Massive cloud eases genomic data sharing

IMAGINE A CLOUD-BASED datasharing platform with 1.25 petabytes of genomic data along with apps to make the most of those details. That is St. Jude Cloud, which was created and launched by St. Jude scientists in 2018.

The cloud makes data sharing faster and easier for researchers. Its goal is to advance diagnosis, treatment and outcomes for children with cancer and other life-threatening diseases.

St. Jude Cloud is the world's largest pediatric cancer genomic data resource. It includes data from more than 10,000 childhood cancer patients and survivors. It also holds genomic



Jinghui Zhang, PhD, and Clay McLeod

details of more than 800 sickle cell disease patients.

The cloud's content grows larger each day. Its apps and design help those who are not computing experts do complex analyses.

"Data sharing is especially important for making progress in childhood cancer, which is driven by many different and distinct genetic alterations," said Jinghui Zhang, PhD, St. Jude Computational Biology chair. "We created St. Jude Cloud as a resource and data-sharing model for researchers worldwide."

Cancer Discovery published a report on this work.



Protecting the lungs after flu and other respiratory infections

THE GREATEST THREAT

for flu patients often comes as the infection winds down. That's because the immune response that kills the virus can also trigger inflammation that damages the lungs.

St. Jude scientists have found cells that play a key role in regulating inflammation. Evidence suggests the system is at work in children and adults with the flu.

Now researchers are working to develop drugs to tame the inflammation.

"There are no effective therapies for this life-threatening complication of flu and other respiratory infections," said Paul Thomas, PhD, of St. Jude Immunology. "The goal is to develop a drug that would help protect lung function in the wake of flu and other viral respiratory infections, including the COVID-19 pandemic virus."

Nature published a report on this work.

Machine learning gives research **a leg up**

ST. JUDE SCIENTISTS have added deep learning to their cancer research toolkit. Deep learning is part of a family of machine learning methods that use artificial neural networks. It boosts the computational side of science.

MethylationToActivity (M2A) is a machine learning approach for epigenetic research. Created at St. Jude, M2A allows researchers to infer more from a single type of test.

"M2A is a method for integrating DNA methylation information to make it easier to interpret," said Xiang Chen, PhD, of St. Jude Computational Biology. "Using M2A, we can learn about promoter activity changes and gene expression changes by DNA methylation in different types of tumors."

Scientists around the world can use M2A through St. Jude Cloud. The analysis is fast, cheap and reliable.

Genome Biology published this work.





Results published on medulloblastoma **clinical trial**

SJMB03 was an international, phase 3 clinical trial for children with a brain tumor called medulloblastoma, one of the most common malignant childhood brain tumors. The study enrolled patients from 2003 to 2012.

"This was a large clinical trial that really incorporated biology into the analysis," said Amar Gajjar, MD, St. Jude Pediatric Medicine chair. "It allowed us to interpret the outcomes based on clinical and molecular risk features."

Previous research classified this tumor into four molecular groups: WNT, SHH, Group 3 and Group 4. The trial findings confirm outcomes previously linked to these molecular groups. The study also offered new insights into subgroups within those groups.

The researchers found that all WNT, and some SHH and Group 3/4 are low risk. These groups could possibly be cured with less-intensive therapy. Scientists also found that some SHH and Group 3/4 are high risk. Those high-risk groups need new treatments to improve cure rates.

This new understanding can help doctors design the next generation of treatment.

The Journal of Clinical Oncology published this work.

By **John Rose**

Life after St. Jude: Faith, Life, Laughter

Cancer survivor offers support and advice.

IN 1994, after finishing my senior year of high school, I felt pain and a lump in my neck that I assumed was a pulled muscle. The pain persisted all summer, ending in a diagnosis of mononucleosis.

After rounds of prescription steroids, the lump persisted. One Friday night early into my freshman year of college, I chose to stay in instead of attending a fraternity party. The next morning, I felt worse. My best friend said, "We're going to the ER." I was so scared that he had to pick me up kicking and screaming.

It was a good thing he did—I would've died within three days if he hadn't. Tests revealed I had high-risk T cell acute lymphoblastic leukemia, which at the time had only a 73% survival rate.

While trying to attend college, I was sick from the chemotherapy and radiation. At the time, I couldn't appreciate St. Jude because I was angry about missing out on my friends and college life.

I came to realize, though, that to make it through, I'd need faith in God, a sense of humor and trust in St. Jude. Without Danny Thomas — a man I never met — and his hospital, I would not be here now.

St. Jude continually researches what does and doesn't work. Having scientists down the hall from patients means that, as a patient, you get the immediate benefits of the latest, greatest results of research and





"To make it through, I'd need faith in God, a sense of humor and trust in St. Jude."

Then and now

Back in 1994, John Rose didn't know what the future held. Today, he appreciates spending time with his wife, Dawn, and son, Matthew.

clinical care. That is also why I participate in the St. Jude LIFE long-term follow-up study. It's one way I can help patients now and those in the future.

Today, I have a wife, an 11-year-old son, a home and a job. I still believe laughter is an important part of life. I think when you laugh so hard that you can't breathe, you add years to your life.

If you're a parent or a childhood cancer patient or survivor, look at the things that make you laugh. If you're a faithful person, take time to thank God for the things you have. Don't worry about what you're missing out on. A positive outlook is important!

Cancer doesn't **DEFINE** you.

Teens&20s is an online resource created to meet the unique needs of teens and young adults, ages 13-25, who are dealing with childhood cancer.

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Together





VISIT US! together.stjude.org/teensand20s Scan QR with a smartphone.





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The Domino's Village

Construction has begun on a new six-story housing facility for St. Jude patients and families. The Domino's Village will offer 140 units for both short-term and long-term stays, as well as an underground parking garage, an outside courtyard and play area, and a pedestrian bridge across North Third Street. The facility is scheduled to open in spring 2023.