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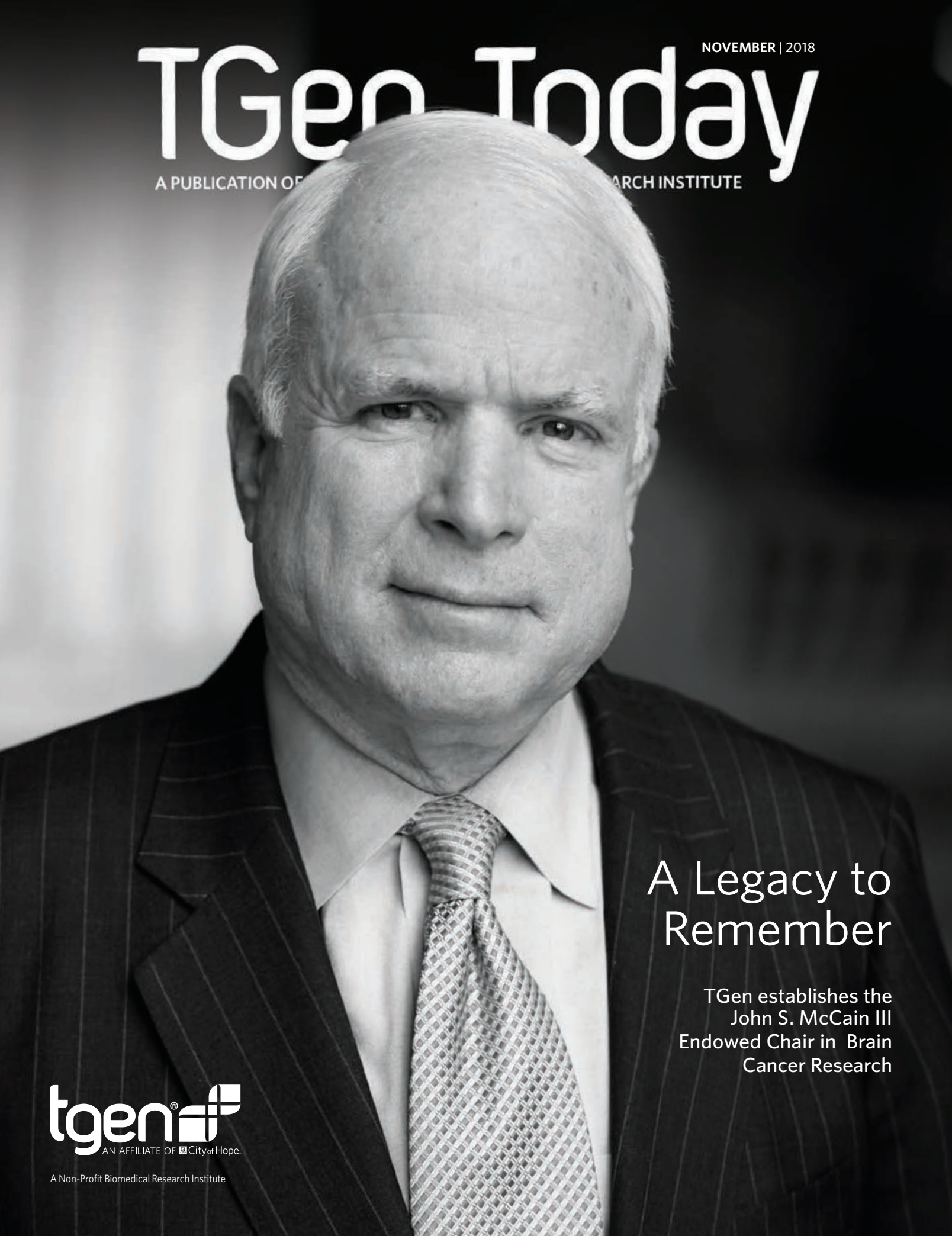
TGen Today

A PUBLICATION OF ARCH INSTITUTE



A Legacy to Remember

TGen establishes the John S. McCain III Endowed Chair in Brain Cancer Research

tgen®
AN AFFILIATE OF City of Hope.

A Non-Profit Biomedical Research Institute

A Look Inside...

Dear Friends,

Our precision medicine efforts with City of Hope are enabling TGen's scientists to impact patients faster than ever before. Together, the world-class physicians at City of Hope and the groundbreaking scientists at TGen are transforming the lives of individual patients today, and revolutionizing the practice of medicine for years to come.

Our friend, Sen. John S. McCain III, embodied this sense of a shared mission to advance the greater good. The late senator, recognizing the power of the human genome to transform medicine, actively recruited Dr. Jeffrey Trent to return to Arizona to establish TGen. He was an enthusiastic supporter of our work, and it is only fitting that the John S. McCain III Endowed Chair in Brain Cancer Research at TGen carry his name and further his legacy of service forward, impacting patient care and scientific discovery for generations.

In this edition of *TGen Today,* you will also meet a TGen researcher, Dr. Sampath Rangasamy, whose diabetes defined his career path and allowed him to meet the doctor behind the human synthetic insulin that changed his life forever. Today, Dr. Rangasamy leads a research project into diabetic retinopathy, which causes blindness in up to 24,000 Americans annually.

As you read these and the other stories, I hope you will more clearly understand the power of precision medicine and how City of Hope and TGen are saving lives through advanced research, treatment and compassionate patient care.

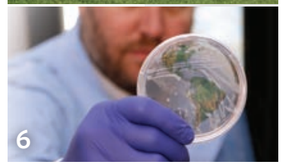
By transforming one patient's life, together, we can impact thousands.

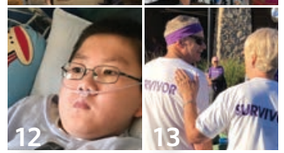
With gratitude,

Erin Massey
Chief Development Officer, TGen Foundation
Vice President of Development, City of Hope

TGen Today

A Publication of The Translational Genomics Research Institute





Back Cover

On #GivingTuesday, November 27, you can be an angel for TGen's Center for Rare Childhood Disorders as all donations will be matched. Make your donation at www.tgen.org/givingtuesday

TGen, the Translational Genomics Research Institute, is an affiliate of City of Hope. We are an Arizona-based, nonprofit medical research institute dedicated to conducting ground breaking research with life-changing results. We work to unravel the genetic components of common and complex diseases, including cancer, neurological disorders, infectious disease, and rare childhood disorders. By identifying treatment options in this manner, we believe medicine becomes more rational, more precise and more personal.

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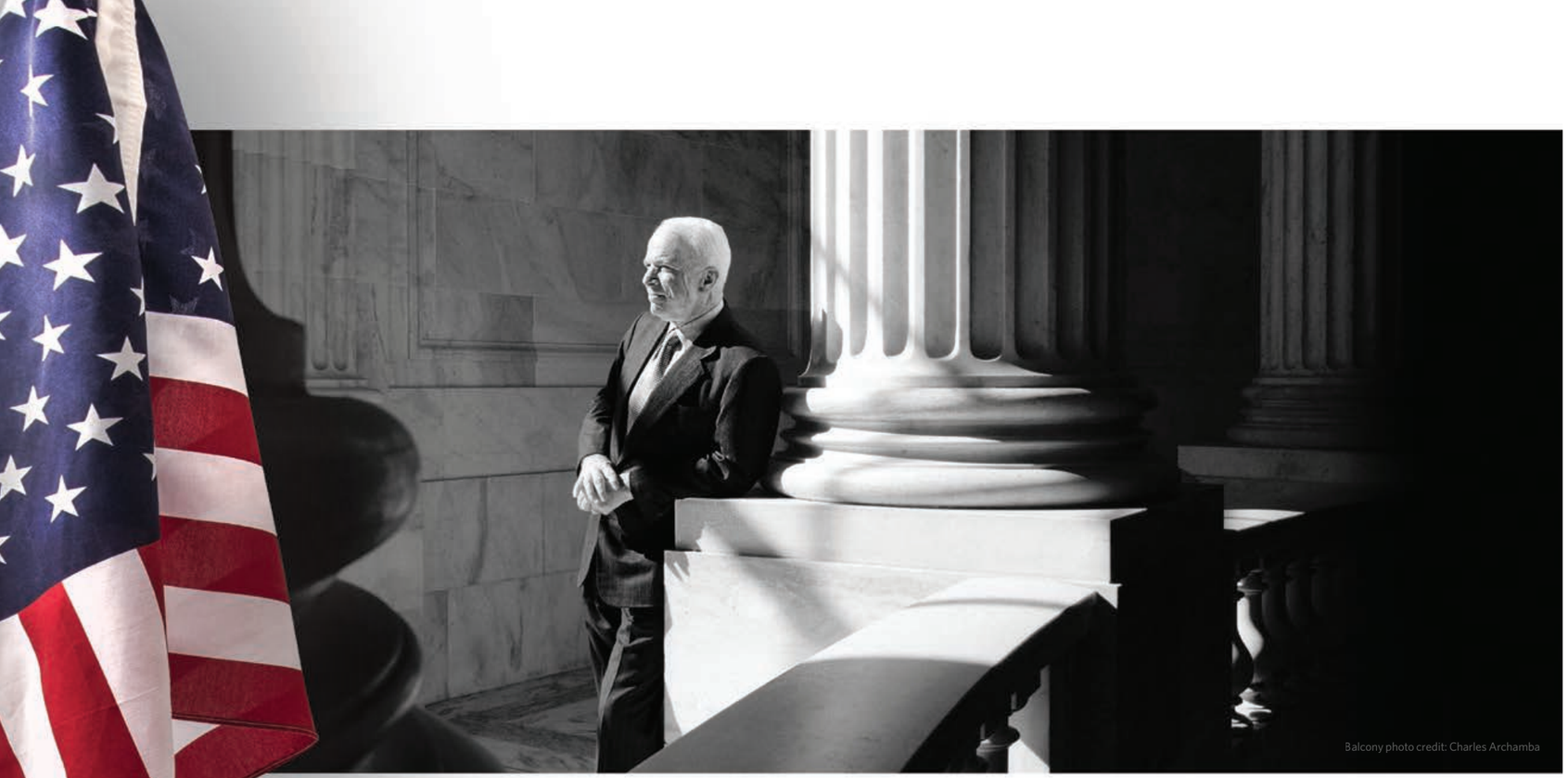
TGen Talks is a monthly podcast that explores the latest science and discoveries in cancer, neurological disorders, rare disease and infectious outbreaks. Meet our scientists and hear news you can use to help you understand precision medicine. Find *TGen Talks* on the tgen.org homepage or through iTunes or SoundCloud.



Balcony photo credit: Charles Archamba

A Legacy to Remember

TGen establishes endowed chair to honor Sen. John McCain

U.S. SEN. JOHN MCCAIN'S remarkable record of leadership embodies his unwavering lifetime commitment to service. With his passing, TGen lost a friend, supporter and advocate.

In 2002, the senator called on Dr. Jeffrey Trent to meet with him in his Washington Office. Once there, the Senator convinced him to return to Arizona and bring this new knowledge with him, establishing TGen in an effort to turn breakthroughs in genetic research into medical advances.

Today, TGen is poised to take that knowledge and transform brain cancer research in honor of Senator McCain through the establishment of the John S. McCain III Endowed Chair in Brain Cancer Research — TGen's first endowed faculty position.

"The establishment of this endowed chair is a fitting tribute to a man who worked determinedly to help TGen take root in Arizona. We have wanted to recognize Senator McCain for many years, and have worked closely with the family and close friends in creating something special, something appropriate, and something that speaks to the Senator's impact on our work," said Dr. Trent, TGen President and Research Director.

In its inaugural phase, the John S. McCain III Endowed Chair in Brain Cancer Research will recruit a nationally acclaimed scientist recognized for trailblazing leadership and innovation in brain cancer research, who also actively promotes excellence in training the next generation of leaders within the field.

The holder of the chair will be an innovative clinical investigator who, much like the Senator, embodies a "maverick" spirit to drive unconventional, outside-the-box research. This individual will be part of a world-class translational brain cancer research program in our community committed to pursuing effective clinical applications that set new standards of patient care for brain cancer.

"Our family is honored that TGen has agreed to pay tribute to John through this endowed chair. It shows the world our commitment to fighting this disease, and lets brain cancer patients know that they are not alone," said Sen. McCain's wife, Cindy McCain.

The chair will also focus a significant percentage of time on education and training, recognizing that to fully realize TGen's mission of delivering precision medicine to patients, it is important to invest in the development of the next generation of researchers and physicians.

While TGen continues to be successful in attracting quality researchers, it is this pairing of established faculty with up-and-coming talent that allows the institute to remain at the forefront of biomedical research in the field of neurogenomics. The Chair holder will elevate training to a new level, and with a focus solely on brain cancer. Transferring knowledge in this manner will ensure work in the Senator's honor continues for generations to come.

The Moment is Now

An endowed chair is the highest honor TGen can bestow upon a member of its faculty. The title recognizes the efforts of a premier scientist while pairing the name of Senator McCain with an innovator in the field of brain cancer research. Supporting the John S. McCain III Endowed Chair in Brain Cancer Research ensures that TGen remains at the forefront of progress against this disease while transforming patient care.

In receiving the Liberty Medal in 2017 at the National Constitution Center in Philadelphia, Sen. McCain reflected on his 60 years of public service: "I've tried to deserve the privilege as best I can, and I've been repaid a thousand times over with adventures, with good company and with the satisfaction of serving something more important than myself."

Donors interested in supporting the John S. McCain III Endowed Chair in Brain Cancer Research are encouraged to visit **www.tgen.org/mccainchair**.

"Our family is honored that TGen has agreed to pay tribute to John through this endowed chair. It shows the world our commitment to fighting this disease, and lets brain cancer patients know that they are not alone."

— Mrs. Cindy McCain

The Bark Story

HOW CANINE CANCERS MAY LEAD TO GENE-BASED TREATMENTS FOR BOTH DOGS AND HUMANS

Dr. Duregger and Parker...

CAROLYN DUREGGER, D.V.M., has known her dog Parker since his birth. The veterinarian witnessed the Wheaten terrier's birth while visiting a breeder, and took the fluffy-soft pup home a few weeks later, after weaning.

Her family had two good reasons to name the puppy Parker — husband, Dan, is a devotee of jazz saxophonist Charlie Parker while son, Dylan, is a big fan of comic superhero Spiderman, aka Peter Parker.

For nearly 10 years, Parker has generated a lot of love. So, it came as a shock to Dr. Duregger when, during a routine oral exam, she saw the telltale signs of melanoma in Parker's upper right gums.

"My stomach dropped. I literally gasped," she said, recalling the moment she noticed the 1-centimeter-diameter discolored lump, and suddenly realized Parker might be in big trouble. "It's an aggressive cancer with poor prognosis that I've seen many times."

Dr. Duregger surgically removed the cancerous node, and started Parker on radiation and an immunotherapy drug: "We're hopeful he'll get to live his normal lifespan."

Current therapies don't always last, but Dr. Duregger sees hope in the molecular-level research into canine cancers led by TGen. She's intrigued by the notion that the similarities in dog and human cancers may lead to discoveries in human cancer research that could also help pups like Parker.

"The genetic research is so promising for fine-tuning the disease treatments and understanding the disease process," she said.

In the most comprehensive study of its kind, TGen and its collaborators from across the nation recently used multiple genomic analysis techniques to identify several gene mutations that could be the keys to what drives melanoma in dogs. Following the path from human melanoma, the findings of recurring molecular changes in canine melanoma can help veterinary physicians pinpoint potential new treatments for dogs. Likewise, human physicians will view these changes in light of the type of melanoma that occurs in non-sun exposed areas (as in the case of Parker) in the mouth, or other mucosal surfaces.

In August, following a multi-year study, researchers reported identifying mutations in the PTPRJ gene —a tumor suppressor gene— in the open access journal *PLOS Genetics*.

A Genomic Bridge Between Dogs and People

"This mutational landscape of canine melanoma resembles that seen in human melanoma subtypes found in sun-shaded areas of the body, such as the nose and mouth, which remain difficult to treat. This similarity means that we have a genomic bridge across which understanding of the disease in either species can inform the other," said Dr. Will Hendricks, a TGen Assistant Professor of Integrated Cancer Genomics, and the study's lead author.

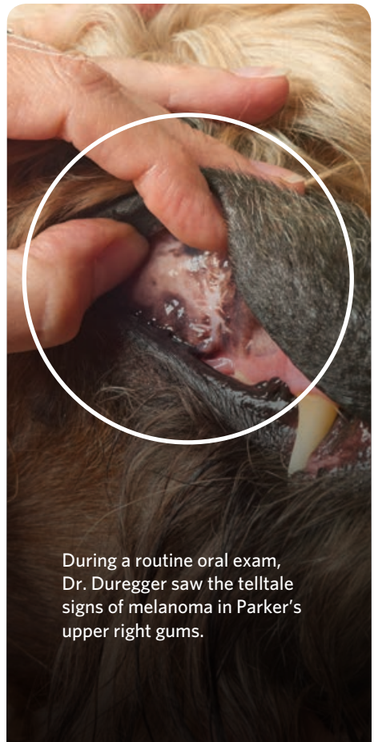
While melanoma is commonly associated with skin cancer, different types of melanoma can originate in different parts of the body, and it often spreads to the lungs, lymph nodes, bones and brain.

The study examined several dog breeds with a propensity for melanoma, including Cocker Spaniels, an English Cocker Spaniel and a Labrador retriever. The paper — *Somatic inactivating PTPRJ mutations and dysregulated pathways identified in canine malignant melanoma by integrated comparative genomic analysis* — notes that an expanded study of breed-specific groups will be critical for further understanding of melanoma among dogs.

New Treatment Promising for Canine Lung Cancer

Now, TGen and The Ohio State University are leading a new study of lung cancer in dogs, funded in part by the Petco Foundation.

The study, which could have implications for people who have never smoked, builds on previous findings by TGen and Ohio State that neratinib — a drug that has successfully been used to battle a type of human breast cancer — may also work for many of the nearly 40,000 dogs in the U.S. that annually develop the most common type of lung cancer, known as canine pulmonary adenocarcinoma, or CPAC.



During a routine oral exam, Dr. Duregger saw the telltale signs of melanoma in Parker's upper right gums.

Neratinib inhibits a mutant cancer-causing form of the gene HER2, which is common to both CPAC and certain types of human breast cancer.

"With our colleagues at Ohio State, we have found that this novel HER2 mutation occurs in nearly half of dogs with CPAC, which presents an immediate therapeutic opportunity for a large proportion of dogs with this type of lung cancer," Dr. Hendricks said.

As part of the study, a clinical trial using neratinib is planned for dogs with naturally occurring lung cancer that have the HER2 mutation.

First Precision Medicine Canine Lung Cancer Trial

"This study is groundbreaking because it not only identified a recurring mutation in this canine cancer that had never been found before, but it actually led directly to a clinical trial. This clinical translation from dog to human and back is the holy grail of comparative cancer research — findings in the dog helping people and findings in people helping dogs," said Dr. Jeffrey Trent, TGen President and Research Director.

CPAC is an aggressive disease that clinically resembles human lung cancer among never-smokers. There is no standard-of-care treatment for CPAC and — prior to the work performed by the TGen-Ohio State team — little was known of the disease's genetic underpinnings. While more than 30,000 human cancer genomes have been sequenced, fewer than 300 canine cancer genomes have undergone similar profiling.

"This is the first precision medicine clinical trial for dogs with lung cancer. That is, the selection of cancer therapy for a particular patient is based on the genomic profile of the patient's tumor and matched with agents that are known to specially target the identified mutation," said Dr. Wendy Lorch, an Associate Professor in the Department of Veterinary Clinical Sciences at The Ohio State University College of Veterinary Medicine, who also will run the study's clinical trial.

Studying how lung cancer can be better treated among dogs could provide insights into better treatments for humans with lung cancer, the leading cause of cancer death in the U.S., annually taking the lives of more than 154,000 Americans.

What in the World?

TGen One Health Collaborative connects human health to the health of animals and our environment

HUMANS AND ANIMALS have coexisted for millennia, though it's only been a few centuries or so that scientists have given any thought to the nexus between the two in terms of health and sickness. Toss in the environment and you have a global ecosystem that, when scientists dig in, exposes the complexities of the world and the upside of gaining a better understanding of what it all means and how it all works together.

Dr. Calvin Schwabe coined the phrase One Medicine in 1964 to highlight the similarities between human and veterinary medicine. Forty years later, the Wildlife Conservation Society convened a group of human and animal health experts who developed 12 priorities, known as the Manhattan Principles, to combat health threats among animals and humans under the banner One World, One Health.

Three years after that the American Medical Association and the American Veterinary Medical Association passed a resolution promoting collaboration between human and veterinary medicine. Soon after, a number of medical professions joined the ranks of One Health proponents along with a number of Federal agencies including the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, and the U.S. National Environmental Health Association.

Fast forward to today and you find TGen North, the Pathogen and Microbiome Division of TGen in Flagstaff, Arizona, applying genomics to many of today's leading One Health questions by adding a depth and breadth unfathomable less than a decade ago. Seeking to gain greater value from their genomic capabilities, TGen North recently partnered with the Flagstaff-based non-profit NARBHA Institute to advance human health through the recently launched TGen One Health Collaborative, an initiative that recognizes the interdependence of people, animals and plants in both the human-built and natural environments.

Sharing a Microbial Universe

Microbial pathogens — the bacteria, viruses, fungi and parasites that can make you sick and even kill you — often know no particular biological boundaries.

Understanding that all living systems share the microbial universe, the TGen One Health Collaborative, funded through the NARBHA Institute, leverages the expertise of TGen North scientists to address today's health challenges in a holistic manner.

These challenges include tracking the cause and source of disease outbreaks, antibiotic resistance, hospital-acquired infections, microbial evolution, pathogen dispersal, and emerging infections.

"Our One Health initiative seeks to understand the larger medical concerns of today through a comprehensive approach to studying human health, both in clinical medicine and public health," says Dr. David Engelthaler, Director of TGen North and the TGen One Health Collaborative.

"Of course, to fully understand the impact requires examination of our relationship to the environment, including water systems, agriculture and natural ecosystems, and animals, whether pets, livestock, or wildlife," he adds.

The NARBHA Institute — formerly known as the Northern Arizona Regional Behavioral Health Authority — has been a major community force in Northern Arizona for more than half a century. It changed its name in 2015 to reflect its expanded mission of promoting human health and wellness, and addressing chronic disease, hunger, homelessness, housing, work force development, and sustainable economic development.

"NARBHA is thrilled to be working with TGen on this important initiative. We know that health is not just about the human condition, but rather a complex set of interactions with the world around us. The TGen One Health Collaborative is an innovative strategy to be more holistic in our understanding of the health ecosystem," says Mary Jo Gregory, NARBHA Institute President and Chief Executive Officer.

Into the Great Wide Open

Through the TGen One Health Collaborative, Dr. Engelthaler and his colleagues at TGen North are focusing on areas of increased health concern, such as antimicrobial resistance caused by the indiscriminant or inefficient use of antibiotics in healthcare facilities and agriculture. To gain a clearer picture of how this impacts health, they're devising systems to track antibiotic resistance in hospitals, communities, ranches, farms, grocery stores and various water sources.

"Coming from an epidemiology background, it's exciting to exploit our genomics capabilities to have an impact on our understanding of health and to really advance the One Health concept," says Dr. Engelthaler, "and perhaps most gratifying is that our work in a number of areas has direct application to the health of Arizona."

Working closely with public health, veterinarians and wildlife professionals, TGen North researchers recently identified an infection known as Canine River Blindness (CRB) in wild coyote populations in northeastern Arizona's Navajo and Apache counties. The parasitic worm known as *Onchocerca lupi* triggers CRB in wild and domestic dogs, and recently caused a handful of human infections. They've collaborated with other academic researchers and public health and mosquito experts to track the continual movement of the potentially deadly West Nile Virus throughout the Southwest — which since its spread to Arizona by birds and mosquitoes in 1999 has become endemic, infecting wildlife, domestic horses and humans. They also track the Valley Fever fungus in humans, dogs and in the air to help public health agencies better understand the connection between the fungus' ecology and human exposure.

"A hallmark of TGen is collaboration," says Dr. Engelthaler. "We know that, if we bring together the right teams with a diverse array of expertise, we can design studies and create the tools necessary to provide answers to many of today's leading One Health questions."

Learn more at: tgennorth.org

IT'S PERSONAL

How Diabetes set Dr. Sampath Rangasamy on a Lifetime Crusade Against the Disease

GROWING UP ON A FARM in rural India, Sampath Rangasamy practiced every morning for his beloved cricket matches.

Then in seventh grade, he dropped 10 pounds from his lanky frame within a week. Insatiably hungry and thirsty, he started urinating frequently.

Two weeks later, he slipped into a coma. His father rushed him to the hospital on the back of his motorcycle.

"The diagnosis of Type 1 diabetes was very devastating for my family," explained Dr. Rangasamy, now a Research Assistant Professor at TGen, an affiliate of City of Hope. "In Asians, Type 1 is a rare disease, compared to Caucasians, and there is even a little taboo around it. In my community, the doctors had never seen it."

The young Sampath set out on a lifetime crusade against the disease that would define his career but not his character: He sent letters to the British Diabetes Association (BDA) to request educational pamphlets in the mail. He made "pen friends" with patients in Europe, whom he found through the BDA magazine. Though his family did not want to share the news of his diagnosis due to stigma, Sampath wanted to learn as much as he could.

"My doctor had trained in the U.S. and wanted to serve in a rural community — and that was the biggest thing for me because he not only treated me, he also educated me, and in turn, I tried to educate him, and my school friends, and my school teachers," Dr. Rangasamy explained. "In two years, I thought I was an expert in Type 1 diabetes."

In 1985, in rural India, he was: Sampath self-administered up to four animal insulin shots daily in his legs, using a glass syringe with a steel needle that he sterilized every time. The family did not have a glucose meter, so his Mom boiled Benedict's solution with his urine to determine his glucose levels by sight. Sampath had an allergic reaction to the animal insulin, which caused lipoatrophy, or a localized loss of fat tissue that left behind scars he carries to this day.

"When I finished high school, I went to a big town in India to talk to a specialist in diabetes, and I learned that there were disposable syringes and testing strips and recombinant human insulin," he said. "After that, I started taking recombinant insulin and didn't have an allergic reaction. It gave me more control. This motivated me to research diabetes."

Last year, Dr. Rangasamy met the man behind his motivation, Dr. Arthur Riggs, Samuel Rahbar Chair in Diabetes and Drug Discovery and Director of the Diabetes and Metabolism Research Institute at City of Hope. Dr. Riggs is renowned for his work on synthesizing the first man-made gene and using synthetic genes to produce human insulin, work which transformed Dr. Rangasamy's life more than 30 years ago and sparked his career in diabetes research.

In September, the National Institutes of Health (NIH) awarded a $2.8 million grant to a consortium led by TGen and the University of New Mexico in a groundbreaking effort to discover new treatments for diabetic retinopathy, one of the primary complications of both Type 1 and Type 2 diabetes, and one of the leading causes of blindness in America, affecting as many as 24,000 patients each year. Dr. Rangasamy is the study's Principal Investigator at TGen.

"Diabetic retinopathy, with loss of vision, is a serious, common and debilitating problem associated with the complications of diabetes," Dr. Riggs said. "This study is an exciting approach to understanding the molecular and genetic mechanisms involved, and it makes use of the extraordinary technology and expertise available at TGen and City of Hope."

The study will use genomic sequencing to identify genes associated with the condition and establish a molecular profile that can predict the severity and treatment of the disease for each patient.

"Why does this occur? Is it because of high glucose or is there a genetic factor that plays a role? Why is it that some people get this complication early despite having good control of their diabetes, while others are not compliant with care but don't get these complications for a long duration?" asked Dr. Rangasamy. "We need to look at specific factors that protect against or predispose patients to developing this complication. Every two years, I have to go for a diabetic retinopathy check, so I am very focused and excited to identify those factors."

As a teen, Dr. Rangasamy was discouraged from playing cricket due to the stigma associated with Type 1 diabetes. As a young man, his parents feared he might not be able to marry if he disclosed his condition, or he might die if he left India to continue his studies in the United States. Though the taboos of his home country have faded, he still battles very real effects from the disease.

"Even with an insulin pump and a continuous glucose monitor, I have to put in an extra two hours each day to take care of myself," he said. "I am prone to infections. I have to get flu and pneumonia vaccinations without fail. So far, I don't have any recognizable complications — I have pretty good control — but for people with long duration, there is always some complication, and so I am always anxious."

But Dr. Rangasamy is also hopeful to see how his work can contribute to the legacy of leadership in diabetes research at City of Hope.

In 2017 City of Hope announced the Wanek Family Project to Cure Type 1 Diabetes (*sidebar story*). This ambitious project seeks to reawaken insulin-producing cells and to harness immunotherapies to cure the disease in six years.

"After living with Type 1 for a long time, it is very important for me to have a cure," Dr. Rangasamy said. "Even though I am a scientist and I know it may take a long time, I am dreaming for a day when I can have a cure and lead a diabetes-free life."

The National Institutes of Health (NIH) awarded a $2.8 million grant to a consortium led by TGen and the University of New Mexico in a groundbreaking effort to discover new treatments for diabetic retinopathy. These images give an impression of what someone with diabetic retinopathy may see compared to someone with normal vision.

THE WANEK FAMILY PROJECT TO CURE type one diabetes AT CITY OF HOPE

City of Hope Seeks to Cure Type 1 Diabetes in 6 Years

by Dory Benford, Senior Content Producer at City of Hope

IN FEBRUARY 2017, TGen's parent organization — City of Hope — introduced its groundbreaking Wanek Family Project for Type 1 Diabetes, which seeks to cure type 1 diabetes within six years.

In the first year, City of Hope launched 16 projects cutting across multiple disciplines, including immunology, endocrinology, cellular therapeutics, nutrition and metabolism. Now, 18 months in, they are pleased with their progress and more optimistic than ever about finding a cure.

Progress to Date

The Wanek team hit the ground running by redefining the disease itself. Textbooks have always described diabetes as a flaw in the immune system, but this may not be correct. Our researchers have found that diabetes is actually a disease of the beta cell. Beta cells, when stressed, send faulty signals to the immune system, and immune cells then read these signals as a threat and attack the beta cells just as they would cancer cells or infection..

Even in patients with advanced disease, beta cells can be hibernating in pancreatic islets to escape the immune system's notice. City of Hope researchers are figuring out ways to jump start these beta cells and improve their function, longevity and resistance to attack.

Additionally, researchers are working to build beta cells from scratch so that doctors no longer have to rely on the short supply available for transplantation.

Another Wanek Project team is validating a biomarker that signals when transplanted beta cells start to die after a transplant. This would alert doctors to suppress the immune response to rescue remaining cells.

City of Hope is planning a clinical trial with a procedure that has shown potential to cure established type 1 diabetes by combining the immune systems of a patient and donor and stabilizing them to avoid an attack on transplanted insulin-producing cells.

The Wanek Project is also working on metabolic memory, a complication where cells still act as if they are in a diabetic state, even when blood glucose is normal. Researchers created and tested a drug that may be able to correct it.

Scientists also succeeded in identifying immune signatures that can predict complete and sometimes long-term remission of type 1 diabetes by bone marrow transplantation, as well as immune signatures that signal the prospect of failure. This breakthrough will ultimately serve as the first evidence that the disease can be cured by precision medicine.

Learn more at *cityofhope.org*

They Are

Bullish on TGen

Ambassadors Energize Community about TGen

JUST 3 YEARS OLD, and already TGen Ambassadors has recruited its 100th member.

TGen Ambassadors, a network of working professionals and emerging leaders, serve as community advocates who help support the biomedical advances made by TGen.

Reine Yazbeck, a Vice President and Non-Profit Business-Banking Manager for Wells Fargo, recently became the 100th TGen Ambassador.

"I joined TGen Ambassadors because I wanted to learn more about all the tremendous, groundbreaking research happening right here in Arizona. My hope in joining the TGen Ambassadors is to help make a deeper impact in the lives of others," Yazbeck said.

The most recent TGen Ambassadors' event was a Nov. 15 tour of the personal collection of classic cars owned by Craig Jackson, Chairman and CEO of Barrett-Jackson, The World's Greatest Collector Car Auctions. Jackson, recipient of TGen's 2014 Collaborative Spirit Award, has helped raise more than $2 million for TGen, and in 2010 established the Barrett-Jackson Cancer Research Fund at TGen as a salute to his father, Russ, and brother, Brian, whose lives were cut short by colon cancer.

Examples of other recent TGen Ambassadors events include:

- A private tour in September of the recently renovated ASU Sun Devil Stadium, where members learned about TGen's efforts to quickly and precisely diagnose head injuries and brain disease, and TGen's leadership in the emerging field of genomics-guided exercise.
- In March, members got to meet Luis "Gonzo" Gonzalez, who made the game-winning hit that won the 2001 MLB World Series for the Arizona Diamondbacks. Gonzo appeared at a D-backs spring training game that ambassadors enjoyed from the exclusive outfield patio at Salt River Fields at Talking Stick. Graham Rossini, D-backs Vice President of Special Projects and Fan Experience, and an inaugural member of TGen Ambassadors, organized the event.

In 2002, visionary Arizona leaders in science, business and government united through networking, advocacy and philanthropy to establish TGen, making The Grand Canyon State a frontier in biomedical technology.

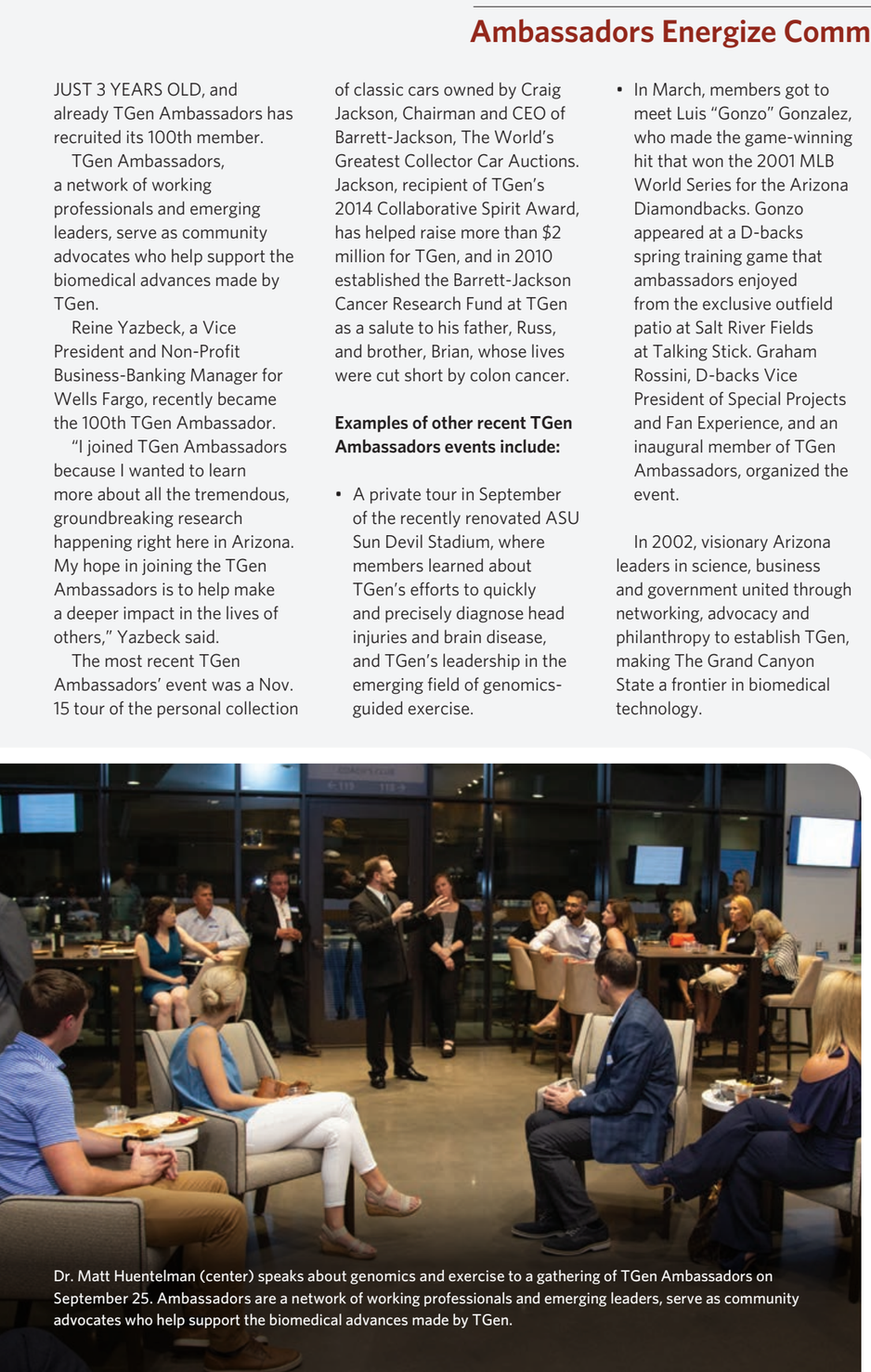
"Through TGen Ambassadors, we look to a new generation of advocates to take up the mantle of leadership and propel TGen's vision forward," said Dean Ballard, Development Director for the TGen Foundation.

Today, TGen is a leader in genomic science and precision medicine, which is the process of taking laboratory discoveries and quickly turning those breakthroughs into new therapies that immediately benefit patients with disorders such as Alzheimer's, diabetes, infectious diseases and many types of cancer.

"The TGen Ambassadors' support of TGen's efforts in unraveling the genetic components of common and complex diseases helps save lives and enhance our community. It also provides our group a unique opportunity to interact with some of the best and brightest in genomics research. I would encourage anyone who has a desire to help others to join us and learn about the amazing research taking place at TGen," said Brian Bogert, Employee Benefits and Risk Management Consultant at Lockton Companies, who became an ambassador soon after the group was established in 2016.

Members of TGen Ambassadors annually make a gift of $1,000 to the TGen Foundation, and extend their financial commitment to advocacy within their professional networks and beyond.

To learn more, contact Dean Ballard at DBallard@tgen.org or 602-343-8543.



Dr. Matt Huentelman (center) speaks about genomics and exercise to a gathering of TGen Ambassadors on September 25. Ambassadors are a network of working professionals and emerging leaders, serve as community advocates who help support the biomedical advances made by TGen.

'Key' Advances Women's Health Research

SAKS FIFTH AVENUE'S 2018 Key to the Cure fashion show, held October 5 at Biltmore Fashion Park, raised more than $100,000 in support of TGen research. The event pushed the 9-year total for donations past the $1 million mark — all in hopes of defeating cancers that affect women.

These funds become the seed money that TGen uses to launch promising lines of research. TGen leverages successful pilot programs in pursuit of larger federal grants in support of additional studies and clinical trials.

2018 Key to the Cure co-chairs Lisa Portigal, Jan Lewis and Mary Ellen McKee (pictured above center from left to right) led a highly supportive planning committee that left attendees with a newfound appreciation for the research conducted at TGen and its life-changing impact on the lives of patients.

"We are so proud to support TGen's efforts toward developing new and better treatments for breast, ovarian and other cancers that afflict women the world over," Lewis said.

Hundreds of dedicated volunteers and caring members of greater Phoenix have now experienced this highlight of the fall social season, an emotionally uplifting morning of fun and friendship. These energized participants become community ambassadors for TGen, spreading the word about what the institute does and how patients benefit.

Erin Massey, Chief Development Officer at TGen, and Vice President of Philanthropy at City of Hope, thanked Saks Fifth Avenue at Phoenix's Biltmore Fashion Park for hosting the event and raising critical research dollars.

"We are truly honored to be a community partner and beneficiary of Saks," said Massey, who also recognized the contributions of the women leaders who have graciously chaired this event for TGen and Saks over the past 8 years: Robyn DeBell, Jacquie Dorrance, Bijen Dyrek, Grace Edgar, Penny Gunning, Carole Moreno, Katie Mueller, Amy Thurston, Vicki Vaughn and Christine Watson.

Key to the Cure proceeds help launch promising lines of research that, if successful, enable TGen to pursue larger federal grants in support of additional studies and clinical trials.

Serendipity Lends a Hand

A typo led to a cold case diagnosis, the story inspires the *Trends Gala* audience

A TYPING MISTAKE SOLVED one of TGen's first medical mysteries.

Alex Yiu was an energetic, bubbly boy, who loved playing with his Power Rangers action figures and bounding around the park, but in 2010, around age 5, he began to stumble when he walked.

He entered first grade in a wheelchair.

Slurred speech, painful muscle spasms, and seizures came next. On New Year's Eve 2014, he had emergency surgery to place a G-tube so he could eat. Palliative and hospice care followed.

But no one had an answer — including the genomics experts at TGen's Center for Rare Childhood Disorders.

"When over 30 of the best medical centers around the world look at your child's genome, and no one finds an answer, that's incredibly scary for a parent," explained Keri Ramsey, Clinical Co-Director for the Center. "They can't name the disease and they don't know what is happening to your child."

TGen sequenced Alex's genome in 2012, and while they identified a handful of mutated genes, they could not pinpoint the exact cause of his neurodegenerative disorder. Fast-forward six years, and everything changes due to a typo.

This past September, a different patient was due in the Center for a follow-up and Medical Director Dr. Vinodh Narayanan asked Keri to re-analyze that patient's data. Except a typo on the medical ID-number led her to Alex's file.

"Because of that innocent error, I looked at Alex's data instead," Keri recalled.

She re-ran Alex's file on new software that pulls the latest findings from the scientific literature, and a mutation in one of Alex's genes — IRF2BPL — popped up in relation to a recently identified disorder, which had been described in an August 2018 scientific journal.

"Alex is now one of 19 patients worldwide with this disorder," Keri said. "This disorder is so new that there is currently no cure, but with this diagnosis, we were able to refer Alex's family to the world's leading authority on this gene. They know they're not alone."

There are more than 300 children like Alex who have undergone genomic testing at the Center, but have not received a diagnosis. When funding permits, the Center will apply new methods and technology to reanalyze these "cold cases." Typically it costs about $1,000 to reopen a case.

TRENDS WEIGHS IN

Inspired by Alex's story and the serendipitous discovery of his diagnosis, the Trends Charitable Fund set an audacious goal of clearing the "cold cases" at its annual Evening of Trends Gala, held on October 12 at the Omni Montelucia Resort in Paradise Valley, Ariz. The evening honors 10 Trendsetters, a group of dynamic women who support causes throughout Arizona.

An innovative "paddle raise" auction generated $67,200 to fund the re-analysis of cases like Alex's. Proceeds from the paddle raise were matched dollar-for-dollar by the Anton's Challenge Fund, enabling the re-analysis of almost half of the Center's backlog.

"The Evening of Trends is about honoring women who are leaders in philanthropy and leaders in our community," said Vicki Vaughn, chair of the Gala, "So it was no surprise to see the Trendsetters and their supporters answer the call to help other children like Alex find the answers they are desperately looking for."

The Evening of Trends raised more than $300,000 for TGen's Center for Rare Childhood Disorders and also its ovarian cancer research, as the Trends Charitable Fund is committed to causes that help women and children.

To learn more, visit *www.trendscharitablefund.org.*

TGEN'S
STEP-N-OUT
5K FUNDRAISER

IN MAY 2017, KAY VERGAMINI learned she had pancreatic cancer after undergoing an emergency appendectomy. In 1974, her mother died from the same disease, just four weeks after learning her diagnosis.

"When the surgeon told me, she had an incredibly sad look in her eyes," Ms. Vergamini recalled at the STEP-N-OUT 5K FUNdraiser on November 4. "And I thought, in 44 years, surely there was something that could be done to extend my life."

Her doctor referred Ms. Vergamini to HonorHealth in Scottsdale where she enrolled in TGen's Grand Slam clinical trial. Her cancer responded immediately to the drug cocktail developed by TGen Physician-in-Chief and Distinguished Professor Dr. Daniel D. Von Hoff.

"I am living my life with this disease," Ms. Vergamini said. "I am 72 years old and recently went back to my job teaching yoga. My life is good."

Helping more pancreatic cancer patients live fully is why more than 750 runners, joggers and walkers turned out on a crisp morning to kick off Pancreatic Cancer Awareness Month. Led by Team Lee and their captain Nancy Hanley, STEP-N-OUT raised more than $115,000 and counting for TGen's pancreatic cancer research.

Upcoming Events

Pints & Pups [Scottsdale, AZ]
January 5, 2019
Bring your favorite four-legged friend and join us for a "yappy" hour benefiting TGen's canine cancer research program.
www.tgen.org/events

Barrett-Jackson Collector Car Auction [Scottsdale, AZ]
January 12-20, 2019
Plan to attend the World's Greatest Collector Car Auction. Barrett-Jackson CEO Craig Jackson has raised over $2 million for TGen's colon and prostate cancer research through this event.
www.barrett-jackson.com

Swing Fore The Kids [Scottsdale, AZ]
February 28, 2019
Come out to Topgolf Scottsdale for a star-studded evening to benefit rare disease patients. Hosted by the Crain Family Foundation.
www.crainfamilyfoundation.org

Casey's Cup 3v3 Ice Man Charity Hockey Tournament [Irvine, CA]
April 13, 2019
For all ages and levels, this 3v3 Cross Ice Tournament is held in memory of Casey Strale, a youth hockey player whose life was cut short by Adrenocortical Carcinoma (ACC). Proceeds benefit TGen's ACC research program.
www.tgen.org/caseystrale

Drive for Diagnosis Golf Classic [Tarzana, CA]
April 22, 2019
This event benefits the C2NK2A1 and TGen's Center for Rare Childhood Disorders in their collaborative efforts to diagnose and cure Okur-Chung Neurodevelopmental Syndrome. Held at El Caballero Country Club.
www.tgen.org/events

To see all current events, please call the TGen Foundation at 602-343-8411 or visit: **www.tgen.org/events**

445 North Fifth Street, Suite 600
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11.27 Be An Angel on #GivingTuesday

COREY COULD NOT SEE or hear his little sister, Cassandra, but he smiled whenever she reached for him. He liked to cuddle beside her when they napped. Though he was five years older than Cassandra, Corey was smaller and more fragile.

Both children struggled with physical and intellectual disabilities.

In a desperate search for answers, Corey and Cassandra's mom, Bridget Damm, sought out researchers at TGen. Dr. Vinodh Narayanan and the team at TGen's Center for Rare Childhood Disorders used genomic testing to discover that Corey and Cassandra had BPAN, a genetic disorder that causes developmental delays, seizures and Parkinson's-like symptoms. It is always worse in boys than girls, and most boys don't survive.

Sadly, that was the case for Corey.

When he passed away in October 2014, Ms. Damm donated his body to science so doctors could study his brain and find ways to help Cassandra and other children.

"Knowing exactly what we're up against has made a huge difference for Cassandra, but it's only the beginning," Ms. Damm said. "We cannot see or hear Corey today, but we feel him watching over his little sister like an angel."

Tuesday, November 27, is #GivingTuesday — a global movement built by individuals, families, nonprofit organizations, businesses and communities in all 50 states and around the world to inspire generosity.

On #GivingTuesday, you can be an angel for children like Corey and Cassandra: All donations to TGen's Center for Rare Childhood Disorders on #GivingTuesday will be matched. On November 27, **make your donation at tgen.org/givingtuesday**.

#GIVINGTUESDAY