OF DOG AND HUMAN

For nearly a decade, TGen scientists have worked toward taking the guesswork out of veterinary treatment for complex diseases with benefits for people and pets.
Dear Friends,

Since our founding, TGen has relied on grateful patients and generous donors to share our story with the world. Informally, these word-of-mouth ambassadors have attracted others to our cause with a message of early detection, smarter treatments and better outcomes for patients.

This year, we are creating a more formal network of ambassadors to share our story: The TGen Ambassadors leverages the passion and energy of a new generation of leaders to engage their networks and bring more supporters into the TGen fold.

In this issue, you'll meet the charter members of the TGen Ambassadors. We also take time to salute one of our greatest ambassadors, Mr. Craig Jackson, the Chairman and CEO of Barrett-Jackson Auction Company. Through his collector car auctions and television presence, Mr. Jackson has tirelessly used his influence to raise awareness about early detection of colon and prostate cancer and raise funds for that critical research at TGen.

Sometimes the mightiest voices come in the smallest packages: 10-year-old Campbell Faulkner brought the house down with his address to 200 guests at our Roaring for Research fundraiser for TGen's Center for Rare Childhood Disorders. Another special patient at the Center, Mylee Grace, inspires generosity in others, even after her passing.

Giving voice to the voiceless, our National Advisory Council for canine research is preparing to take its message of hope for people and pets public. TGen is one of a handful of institutes studying canine DNA for insights into cancer, inherited disorders and Valley Fever in both man and man’s best friend. We have a comprehensive update on this critical work, as well as breakthroughs in glioblastoma and pancreas cancer treatment and the discovery of a gene that contributes to "Broken Heart Syndrome."

As you read this “Ambassadors” issue of TGen Today, we hope that you will take a moment to share our story with your family, friends and colleagues. Because of your advocacy, support and ambassadorship, TGen continues to make inroads in early detection, smarter treatments and better outcomes for patients.

With gratitude,

Michael Bassoff
President, TGen Foundation
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About TGen
The Translational Genomics Research Institute (TGen) is a non-profit organization dedicated to conducting groundbreaking research with life changing results. Research at TGen is focused on helping patients with diseases such as cancer, neurological disorders and diabetes. TGen is on the cutting edge of translational research where investigators are able to unravel the genetic components of common and complex diseases. Working with collaborators in the scientific and medical communities, TGen is making a substantial contribution to the efficiency and effectiveness of the translational process. For more information, visit: www.tgen.org
“Because they are not randomly mating, the genetics in purebred dogs is controlled and simplified, so it should be easier to find the genes that are causing disease.”

— Dr. Matt Huentelman, Professor of Neurogenomics
Rod the boxer greets patients at Dr. Bryan Tran’s dental practice with a wiggling tail and a friendly sniff. His mellow disposition and slight stature puts patients at ease before they climb into the dental chair.

Diagnosed with valley fever as a puppy, Rod’s previous owners did not keep up with his treatments and ultimately surrendered him. The unchecked fungal illness progressed, compromising his left hind-leg. He got his name from the “rod” implanted in his broken bone.

“We were at an adoption event and saw those big brown eyes,” Dr. Tran explained. “He was laying quietly in the back of the cage, and we couldn’t understand why no one wanted him. My wife knew he was the one.”

The Trans spent months working with their veterinarian to get Rod’s illness under control – first with canine antibiotics and finally with human fluconazole, the standard treatment for people with valley fever. Now 9, Rod weighs only 55 pounds – his growth stunted from his ordeal – and still receives a maintenance dosage of fluconazole, which requires a yearly check-up for his liver function.

Doctors know how Rod got valley fever, a fungal disease indigenous to the Southwest. He did what dogs do: sniff everything in sight. All that sniffing led to his inhaling the Coccidioides spores that cause the disease. What they don’t know is why certain dogs like Rod and humans get valley fever.

“There’s such a huge variation in the disease,” explained Dr. Bridget Barker, an Assistant Professor at TGen North. “Some people and some dogs get really sick. Some don’t respond to the medicine. It might be something about the host – the human’s or dog’s genetics – or it might be variability in the fungus itself. We just don’t know.”

To find out, Dr. Barker has started an online registry called Valley Fever P.A.W.S. (Prevention, Awareness, Working for Solutions) at tgen.org. She is asking owners to volunteer saliva samples from healthy dogs and those affected by valley fever to determine if there is a genetic susceptibility in certain breeds.

“I’ve heard a million times that boxers are susceptible to valley fever, but then I’ll talk to a vet who says they’ve never seen a boxer with it, and that it’s the age of the dog or their immune function,” Dr. Barker said. “The fact is, we have to prove it.”

Dr. Barker’s project is part of TGen’s Dog and Human Precision Medicine Initiative. Launched in 2009, the program uses less-invasive saliva, blood and tumor samples from dogs to help diagnose and treat cancer, neurological disorders and infectious disease like valley fever.

Its mission is to help people and their pets.

With an estimated 83 million pet dogs living in 40 percent of U.S. households, there are three main reasons studying dog DNA helps inform human treatment:

- **More than Man’s Best Friend:** Canines and humans have roughly the same numbers and types of genes, so naturally occurring conditions in dogs, like cancer and epilepsy, more closely resemble the same in humans.

Continued
Dog Days, Dog Years: Because dogs age faster than humans, canine clinical trials can be completed more quickly than those in humans, providing a faster and more cost-effective pathway to treatment and discovery.

Purebred Plus: Because of selective breeding, dogs have greater genetic uniformity so locating disease-causing genes is easier.

Unfortunately, treatment options for these types of complex diseases are limited. That’s where TGen steps in.

CANCER

“Comparative oncology” is the study of cancer in both humans and pets, but people have a leg up on their four-legged friends. More than 30,000 human cancers have been genetically sequenced and profiled, compared to less than 300 canine cancers. Because half of all dogs over age 10 will die from cancer, this dearth of information poses serious problems.

“There is a huge need to help these dogs in the first place, because the standard of care tends to be less developed than for humans,” explained Dr. Will Hendricks, Assistant Professor in the Integrated Cancer Genomics Division at TGen. “Compared to the amount of time and money invested in the human cancer space, only a small fraction of those resources have been deployed in canine cancer research.”

TGen’s comparative oncology research currently focuses on four areas:

Melanoma – About half of human melanoma patients have an altered BRAF gene. A new drug that targets this alteration has generated the first significant melanoma survival gains in decades, Hendrick explained, but for patients who lack the altered BRAF gene, no targeted therapies exist. The most common malignant melanoma in dogs, mucosal melanoma, lacks the broken BRAF gene, so the team is studying canine tumors to determine possible targets for cancer in both species.

Lung Cancer – Dr. Timothy Whitsett, Assistant Professor in the Cancer and Cell Biology Division at TGen is collaborating with Dr. Hendricks and Drs. Wendy Lorch, David Carbone and Carlos Alvarez at The Ohio State University on a pilot study of the genetic underpinnings of canine lung cancer. Only a portion of human cancers are smoking-related, so canine lung cancer can help us understand it in nonsmokers.

Osteosarcoma – A relatively rare cancer that attacks children and young adults, osteosarcoma has a high prevalence in dogs. In December, Brooke’s Blossoming Hope for Childhood Cancer Foundation made a $30,000 donation to TGen’s cancer research in memory of Brooke Hester, who wanted to be a veterinarian but succumbed to a rare cancer. “She was an incredible little girl who inspires all we do in canine and pediatric cancer,” Dr. Hendricks said. “This gift provides a great opportunity to help the dog and also translate it to a rare cancer in humans.”

Early Diagnosis – The Center for Non-invasive Diagnostics at TGen under Dr. Muhammed Murtaza is working to develop a canine cancer gene panel that would allow us to create an affordable rapid test for the genetic underpinnings for canine cancer. This test could be used first in a research setting, but ultimately in veterinary practices.

In February, TGen President and Research Director Dr. Jeffrey Trent co-authored a review published in Science Translational Medicine and conducted by the Institute of Medicine of the National Academy of Science. The report’s findings underscore our scientists’ concerns about canine cancer:

• Comparative oncology can help accelerate drug development and FDA approval, as well as save time, costs and risks to patients by providing early assessments of clinical trials.

• Scientists should prioritize development and biomarkers in circulating blood to guide decisions about optimal drug combination strategies.
• There is a need to include veterinarians in clinical practice, the pharmaceutical industry, physician and veterinary medical associations, industry partners and philanthropic organizations.

NEURO

Dogs have evolved alongside humans for thousands of years, but it’s only been a few centuries since humans started breeding dogs for appearance, behavior, and other traits. This has created what are called “population bottlenecks” in certain breeds.

“Because they are not randomly mating, the genetics in purebred dogs is controlled and simplified,” explained Dr. Matt Huentelman, Professor of Neurogenomics. “So it should be easier to find the genes that are causing disease.”

Deafness – Researchers sequenced the genome of a Doberman Pinscher with a form of deafness known as “dings.” They found that the altered gene that causes “dings” is the exact same gene known to cause deafness in humans. Deafness is also being studied in Dogo Argentino, Australian cattle dogs, border collies, Rhodesian Ridgeback, Dalmatian and Great Pyrenees breeds. A current project studies deafness in white-coated, blue-eyed cats that can provide a model for humans with sensorineural congenital deafness.

“With congenital deafness, it’s usually a single gene alteration,” explained Dr. Isabelle Schrauwen, Assistant Professor of Neurogenomics. “If we find a deafness gene in the dog, but it has not been found in humans yet, then we could sequence the genomes of deaf people and see if we can find it as well. We have demonstrated that we can find a lot of those similarities.”

Epilepsy – Collaborating with the Spokane, Washington-based Paw Print

As breeders select for traits they prefer, such as a soft mouth in golden retrievers, negative traits such as hip dysplasia may also be accidentally enriched in the breed through a concept called “linkage.”

By identifying these disease-causing genes in purebred dogs, TGen researchers can look for similar genes in humans. Among their accomplishments to date:

Necrotizing Meningoencephalitis (NME) – A progressive, inflammatory, often-fatal disease in toy breeds, NME shares some similarities with multiple sclerosis in humans, but it is much more severe. TGen scientists have identified the genes associated with increased risk for NME in Pug, Maltese and Chihuahua dogs. They hope to expand the study to Yorkshire terriers and Pekingese.

Genetics, Dr. Huentelman’s team has identified three candidate genes in the Chinese Crested with a known association of epilepsy in humans. The next step is to determine whether there is a sole cause for epilepsy in the breed.

Dr. Huentelman hopes that breeders would use this genetic information to improve the bloodlines in purebred dogs and “cure” the breed of inherited diseases that are linked to preferred traits.

Through the use of modern genetics, one should be able to help retain all of the beneficial traits for a breed but also remove any elevated risk for particular diseases.

“In the dog, we can do preventative treatments,” Dr. Huentelman explained. “If your dog is at a high risk for a disease that usually doesn’t present until age 5, we’d like to start giving him medicine at age 3 to see if we can prevent it. If this disease has a correlate in humans, and the same medicine has been used but had minimal effect, then we could ask about starting to use it earlier in humans. It works because dogs have an accelerated life span.”

A WAY FORWARD

Whether studying cancer, neurological disorders or infectious disease, TGen scientists agree on the top two needs to advance this critical canine research: More samples and more funding.

To help both goals, retired CEO and Chairman of PetSmart Phil Francis, a TGen Foundation board member, is assembling a National Advisory Council for the Dog and Human Precision Medicine Initiative. His initial gift launched the program in 2009, and now he seeks to leverage the talents of national leaders in veterinary medicine and the pet products industry to raise funds and awareness for TGen’s canine research.

“We talk about proactive care in our practice,” said Dr. Brett “The Vet” Cordes, CEO of Arizona Animal Hospital and a new member of the National Advisory Council. “What’s missing in our industry are those early screening tests, like mammography or colonoscopy or a genetic test for a certain disease. If we had the ability to screen these pets and let owners know that they were at a higher risk, then we could monitor them, which helps us achieve our goal of longevity but also better quality of life.”

Quantity and quality of life are two pillars that support all of TGen’s research – both for people and pets.

As with humans, precision medicine promises to take the guesswork out of veterinary treatment for complex diseases like cancer, neurological disorders and valley fever to create a new standard of care for dogs like Rod, and their owners.
Getting Therapeutic Drugs Across the Blood-Brain Barrier

While the blood-brain barrier protects the brain from many harmful substances, it also keeps out potentially lifesaving ones. Delivering drugs to the brain to treat glioblastoma multiforme (GBM) tumors has been a long-standing challenge in medicine. TGen has identified a drug, propentofylline or PPF, a small-molecule potential therapeutic that can cross the blood-brain barrier.
Brain tumors are among the most difficult cancers to treat, but findings from a recent scientific study led by TGen suggest a drug used in clinical trials for Alzheimer’s disease may also aid cancer patients, offering new hope to brain cancer patients.

Due to the aggressive way in which glioblastoma multiforme (GBM) invades surrounding brain tissue, it is impossible to surgically remove all of the deadly tumors. Because of this inability to remove or destroy every cancerous cell, the disease eventually returns, spreads and claims a life. This insidious cancer invasion also limits the effectiveness of many chemotherapy drugs and radiation therapy.

In a recent study, published in the *Journal of NeuroOncology*, TGen faculty identified an existing drug, propentofylline or PPF, previously used in clinical trials to address Alzheimer’s disease and dementia. A clinical trial using PPF for GBM could begin as early as this summer.

“The fastest way to the clinic is to use repurposed drugs,” explained Dr. Nhan Tran, head of TGen’s Central Nervous System Tumor Research Lab.

Because PPF is a small molecule, it can cross the blood-brain barrier, which is the system of tiny capillaries that buffers the brain from rapid changes in the body’s metabolism and minimizes the brain’s exposure to toxins circulating in the blood.

The TGen study revealed that PPF increases the effectiveness of a standard-of-care chemotherapy drug called temozolomide (TMZ), as well as radiation, in treating glioblastoma. The researchers also found that PPF works to limit the spread of glioblastomas by targeting and knocking down the expression of the TROY protein, which they have linked to the cellular mechanisms that enable glioblastomas to invade normal brain cells, and resist anti-cancer drugs.

TGen has recently tested PPF in the laboratory to better understand its effectiveness and safety, said Dr. Tran. “We are hopeful that by mid-2016 we will potentially have a clinical trial running.”

TGen is exploring possible clinical trial collaborations with the Baylor Research Institute in Dallas, and Abbott Northwestern Hospital in Minneapolis.

**Liquid Biopsies**

To help guide therapies like PPF, TGen is also embarking on a three-year research project that would employ so-called liquid biopsies – the process of identifying strands of DNA circulating in the bloodstream – to monitor patients’ progress.

“This could be the first steps toward continuous monitoring of tumor development during treatment of patients with glioblastoma,” said Dr. Muhammed Murtaza, Co-Director of TGen’s Center for Noninvasive Diagnostics.

“Treatment of glioblastoma often fails because tumors evolve,” said Dr. Murtaza, the study’s principal investigator. From diagnosis throughout treatment, glioblastoma in most patients represents a moving target, limiting therapies guided by the analysis of the initial tumor biopsy. This tumor evolution also stunts the use of any diagnostic test that cannot be practically repeated.

Using a simple blood test, researchers hope to use liquid biopsies to predict and detect the effectiveness of drugs against brain tumors, and to predict and detect the recurrence of cancer during and following surgery, radiation and drug therapies.
Liquid biopsies are less invasive, less costly and less risky than conventional tissue biopsies, which essentially are minor surgeries. Obtaining liquid biopsies could occur more frequently, providing physicians with up-to-date information about how a patient’s GBM might be changing. This, in turn, could help in the selection of the best possible treatments to combat the cancer at any given point in its evolution.

**New Drug Targets**

TGen also recently identified a new drug target, a protein called SGEF, which promotes the survival of glioblastoma, helps this cancer invade brain tissue, and also plays a role in how GBM develops resistance to drug treatment.

Radiation and drug treatment of GBM can lead to DNA damage. This study, published in January in the journal *Molecular Cancer Research*, shows that SGEF promotes cancer cell survival in response to TMZ treatment by allowing tumor cells to rapidly repair the damaged DNA that otherwise would lead to cell death.

“The role of SGEF in promoting chemotherapeutic resistance highlights this previously unappreciated protein,” said Dr. Tran. “Importantly, this also suggests that SGEF could be a new candidate for development of targeted therapeutics.”

All of these studies are funded by the Arizona-based Ben & Catherine Ivy Foundation.

“This research is fundamental to helping patients survive longer and critical to our goal of improving treatments, and eventually finding a cure,” said Catherine (Bracken) Ivy, founder and president of The Ben & Catherine Ivy Foundation.

**Deadly Disease Becomes Cancer Killer**

Malaria protein delivers anti-cancer drugs to tumors

TGen faculty member Dr. Nhan Tran, working as part of an international research team, recently published a paper explaining how a protein derived from malaria could help anti-cancer drugs target tumors.

The study, led by scientists at the University of Copenhagen exploring why pregnant women are particularly susceptible to malaria, found that the mosquito-borne parasite that causes malaria also produces a protein that binds to a sugar molecule in the placenta. They also found that same sugar molecule [oncofetal chondroitin sulfate] is present in many types of cancer.

Scientists at the University of British Columbia, Vancouver Coastal Health and the BC Cancer Agency – working with those from Copenhagen – realized that the sugar molecule could be a target for anti-cancer drugs, and that the malarial protein, called VAR2CSA, could provide the tool for carrying such drugs to tumors.

TGen scientists were called in to help test the theory.

“Based on our clinical data, we helped validate that this could be applied to melanoma and lung cancers,” said Dr. Tran, an Associate Professor in TGen’s Cancer and Cell Biology Division, and a study author. “This specific type of developmental protein [oncofetal chondroitin sulfate] is expressed in the placenta, and is also expressed in lung cancer and in melanoma.”

Malaria uses VAR2CSA to embed itself in the placenta – hiding itself from the immune system – by binding to oncofetal protein.

In laboratory experiments, researchers found that if they used the malarial protein, VAR2CSA, and attached an anti-cancer drug to it, it would bind with the oncofetal protein in the cancer, delivering the drug to the tumor.

The results of study – *Targeting Human Cancer by a Glycosaminoglycan Binding Malaria Protein* – appeared October 12 in the journal *Cancer Cell.*
When his friend and mentor Charley Freericks, former president of DMB Associates, suggested that David Lodwick “get involved” with TGen, Lodwick didn’t know what he was getting into. “I knew the full name – Translational Genomics Research Institute – and I knew it was downtown, but I didn’t know a whole lot about TGen,” Lodwick explained. “When I sat down with the people and started meeting the scientists, and I learned what TGen is doing for patients around the country, and in Arizona in particular, it’s extremely compelling.”

It was so compelling that Lodwick became the first charter member of the TGen Ambassadors.

An invitation-only collection of professionals dedicated to philanthropy, networking and advocacy, TGen Ambassadors has grown to almost 50 members since its launch in December 2015. TGen Foundation board chairman Bennett Dorrance hosted the launch party for charter members of the Ambassadors on February 18 at Club 360 at Hanger One in Scottsdale.

“TGen Ambassadors draw from a diverse group of professionals who share an entrepreneurial spirit, a passion for innovation and a commitment to philanthropy and service,” said Michael Bassoff, TGen Foundation President. “These men and women represent a new generation of leadership, eager to support TGen’s work and share our discoveries with their peers.”

Successful in fields ranging from medicine and marketing to real estate and banking, the Ambassadors leverage their time and expertise to enhance their community. They serve on boards and committees for causes like the Phoenix Art Museum, the National Multiple Sclerosis Society and Southwest Human Development, as well as their collegiate alumni associations, booster clubs and houses of worship. They represent classes of the Phoenix Business Journal’s 40 Under 40, Valley Leadership and more, but all come to the Ambassadors for personal reasons.

“Some may be familiar with the concussion studies or early detection efforts – everyone has a different hook personally,” said Lodwick, the Chief Financial Officer of the southwest division of Alliance Residential. “Many did not know there was an opportunity to get involved. The ability to get a good number of young leaders involved means we can make a difference.”

For Bob Hobbs, Jr., a third-generation Arizonan, the opportunity to honor a family legacy motivated him to join the Ambassadors and to recruit four others, including his brother Tom. Both of their parents are cancer survivors, and their uncle Lee Hanley served on the TGen Foundation Board of Directors before succumbing to pancreatic cancer. “TGen has always been there for us,” said Hobbs Jr., CEO of Bob Hobbs Jr. and Associates. “To have this community in the spotlight due to the world-renowned research at TGen is incredible. This isn’t about just writing a check. It goes beyond that. The more people that can know about TGen, the better.”

As medical director at Cigna Medical Group, Dr. Leslie Barakat has followed the breakthroughs emanating from TGen laboratories for years. A pediatrician, her practice serves as a medical home for families, and TGen’s patient-centered research approach was one reason for joining the Ambassadors.

“Families don’t want cookie cutter care – they want to be treated as a whole individual, and not just an illness,” Dr. Barakat said. “There’s something different in the way TGen uses technology to advance research, and that’s something I’m passionate about. I’m meeting people I haven’t worked with before to gain insight from different parts of the community.”

The TGen Ambassadors have drawn from a broad swath of small business owners, executives, entrepreneurs and more – all united in their desire to increase awareness of TGen’s discoveries and raise funds to support its innovative research.
The DNA of Barrett-Jackson
Passion for TGen, Early Detection Drives CEO

Cleaning out his big brother Brian’s home in the wake of his untimely death, Craig Jackson stumbled across an appointment slip for a colonoscopy in a kitchen drawer. He called the doctor’s office to ask whether anything could have been done to help Brian.

“They said he never showed up,” Jackson remembered. “If he’d have shown up, like he promised, they could have found it a couple years earlier. A couple of years would have made a big difference.”

Colon cancer claimed Jackson’s father Russ in 1993 and Brian two years later. These tragedies forced Craig Jackson into the driver’s seat of the family business, the Barrett-Jackson Auction Company in Scottsdale, but they also transformed him into passionate advocate for early detection.

Jackson took the first step on that journey when he gave Brian’s eulogy.

“I told everybody to go out and get tested,” he recalled. “One of my good friends went and got tested, and they found something. He told me, ‘If you hadn’t said that, I would never have thought to go, and my doctor told me it would have evolved.’”

A handful of people at the funeral thanked Jackson for sounding the alarm, and fans have let him know that his advocacy resulted in their getting screened as well.

Today, as Chairman and CEO of the Barrett-Jackson Auction Company with more than 5 million watching his signature events on Discovery and Velocity networks, and another 500,000-plus in attendance at four events nationwide, Jackson has a megaphone to amplify that message. His commitment extends beyond raising awareness: In 2010 at the suggestion of his friend and TGen supporter Rick Holland, Jackson established the Barrett-Jackson Cancer Research Fund in Memory of Russ and Brian Jackson at TGen. Since then, he has raised more than $2 million to accelerate development of new diagnostic tests and therapies to help those facing colon and prostate cancer.

In January at the Barrett-Jackson auction in Scottsdale, an anonymous individual donate a 2015 Chevrolet Camaro Z/28 for TGen; it raised $75,000. Next up at the Palm Beach, Fla., auction, April 8-10, Clarion USA has donated its first Clarion Builds car, an iconic 1974 BMW 2002 resto-mod, with proceeds benefiting TGen.

“We are very pleased to be able to extend the reach of the lives touched by the Clarion Builds program with the donation of the auction proceeds to the TGen Foundation in support of cancer research,” said Allen H. Gharapetian, Vice President of Marketing and Product Planning for Clarion Corporation of America and Chief of the Clarion Builds Program.

Celebrating its 45th anniversary in 2016, Barrett-Jackson began as a charitable car show – Fiesta de Los Autos Elegantes – benefiting the Scottsdale Public Library and arts organizations back in 1967. Today, Barrett-Jackson has been a platform to raise more than $88 million for children, cancer research and veterans causes.

“We started as a charity fundraiser and we’ve carried that through the DNA of Barrett-Jackson.”

As a man who takes pleasure in proving naysayers wrong, Jackson has been described as being “driven by passion.” No where was that more on display than at his flagship auction in Scottsdale this year: He met country music star Zac Brown backstage at their Phoenix show on October 8, 2015. Three-and-a-half months later, the three-time Grammy winner and multi-platinum artist gave a surprise private concert at the 2016 Barrett-Jackson Opening Night Gala.

“Everyone that I was working with on this shared that same passion,” Jackson recalled. “Wouldn’t it be cool if we could make this happen? In between you had agents, attorneys, logistics, schedules, moving people, but that’s what makes these deals that seem really hard to do, so much fun.”

Continued
Jackson's passion shone through when he sat on the front row to bid on the 1934 Cadillac V12 370D Fleetwood coupe that his mother Nellie had driven from Michigan to the family's new home in Arizona, with 1-year-old Craig in the front seat. A junkyard find, the Cadillac was the first that his father Russ and big brother Brian had ever restored, and it became Nellie Jackson's "daily driver." The family sold "the car that started it all" at one of their very first auctions, and it had only had two owners since.

"I offered to buy it ahead of time," Jackson recalled. "But the owner really wanted to auction it, so I told him, if you don't mind, I want to bid on it, and he goes, 'Do what you want!'" Jackson rarely bids against his own customers, but he went down to the front row and raised his paddle on live television, as his bidders egged him on.

"Some of them took great joy in it. They knew I wanted the car," Jackson said. "The consigner is super happy and the car is back in the family. Now I have to teach my wife how to drive it. That wasn't a logical purchase. That was a passion purchase."

Colon and prostate cancer patients, survivors and caregivers are grateful that his passion extends to raising funds and awareness about TGen's research into early detection and genomic guided therapy.

"We are very blessed to have TGen here in Arizona, and I am proud to help support them," he said. "I believe in what TGen is doing, and their research is the key to the future of beating cancer."

The Barrett-Jackson Collector Car Auction in Palm Beach, Florida, runs April 8-10. This year’s charity car is a 1974 BMW 2002 Restomod (see below). On-line bidding is available by registering at www.barrett-jackson.com/bidder/home.

Own A Piece of Auto and Audio History

Barrett-Jackson Palm Beach Charity Car, April 8-10

A Classic 1974 BMW 2002

The first "Clarion Builds" top-to-bottom restoration project by Clarion Corporation of America. Clarion’s complete restoration of the BMW — a car that spawned the sports sedan revolution and put BMW firmly in charge of this automotive segment for the past four decades — has the lines of the ‘70s, but is now equipped with among the most modern of engines, transmissions, brakes, suspension and — most importantly — sound. This classic 1974 BMW 2002 is set to be auctioned off at Barrett-Jackson Palm Beach, Florida, April 8-10. All proceeds to benefit the Barrett-Jackson Cancer Research Fund at TGen in memory of Russ and Brian Jackson.
A Decade of Success
Helios Scholars at TGen Celebrates 10th Anniversary


In 2016, Helios Scholars at TGen celebrates its 10th anniversary of training the next generation of biomedical researchers. An eight-week, full-time paid internship, Helios Scholars at TGen matches Arizona high school, undergraduate and graduate students with TGen scientists to work on research projects in cancer, neurological disorders, diabetes and infectious disease.

“Helios Scholars program was what definitively proved to me that I wanted to pursue research as a career,” said Kristine Tsantilas, Class of 2013, and now a first-year graduate student in the Biochemistry Ph.D. program at the University of Washington in Seattle.

“It gave me so much confidence in my capabilities and has helped me develop in my professional life with my scientific background,” Lam explained.

Though many have moved on to other careers, the work the Scholars started at TGen continues to resonate for patients. Now an engineer at GE Aviation, Caitlin (Auther) Miller, Class of 2007, was among the first to explore the role of the protein TROY in glioblastoma, explained her mentor, Dr. Nhan Tran. The study eventually led to four publications and two major grants, including the identification of the drug propentofylline or PPF, which could help patients with the deadly brain cancer (see related story on pg. 7).

“She decided that engineering was her passion,” Dr. Tran said, “but the analytical thinking she obtained in research gave her a competitive edge to be hired at GE Aviation and excel at her work.”

Helios Scholars at TGen was funded for 25 years by a $6.5 million grant from the Helios Education Foundation. In addition to hands-on work in the laboratory, Scholars participate in professional development workshops on networking, etiquette, presentation skills and more.

“We look forward to recognizing the 10th anniversary of Helios Scholars at TGen throughout 2016,” said Paul J. Luna, President and CEO, Helios Education Foundation. “The program has become one of the most sought after bioscience internships in Arizona, providing opportunities for intensive, hands-on learning to a diverse student population.”

Angel Lam, Class of 2012, now works as a nurse in the neuro-ortho-stroke trauma unit at HonorHealth in Scottsdale.

Caitlin (Auther) Miller, Class of 2007, now works as an engineer at GE Aviation in Evandale, Ohio.
How do you find a broken heart?

An avid runner, Jean Schultz’s ruptured aneurysm gave her a run for her money. Her stress-induced cardiomyopathy, a rare heart disease also known as “broken heart syndrome” led to multiple seizures, a near death experience and months of recovery.
Brain hemorrhage triggers woman’s ‘broken heart’

Jean Schultz of Scottsdale was a physically fit 52-year-old in April 2010 when one day – out of the blue – she suffered a broken heart. “I’ve been an avid runner and always taken good care of myself. I had no health issues,” said Jean, who at the time had run a marathon and several half-marathons.

As she was exercising in her community gym, a sudden pain shot through the right side of her neck. Schultz didn’t think much of it at first, believing she had just pulled a muscle. She dressed her neck with an ointment and applied a heating pad. But over a few days, the pain didn’t go away. She saw a doctor who ordered an immediate X-ray.

“I was on the table, getting an X-ray of my neck, when I went into a severe seizure,” Schultz said.

After being taken to a nearby hospital where a CT scan revealed a ruptured aneurysm – a weak wall in a tiny artery supplying oxygen to her brain – bleeding into her skull cavity. Doctors informed Schultz’s family that she might die. Rushed by helicopter to Barrow Neurological Institute in downtown Phoenix, surgeons threaded a micro titanium coil through her veins, from her groin up to her head, to seal the hemorrhage.

She continued to have vascular brain spasms and suffered a series of minor strokes that immobilized the right side of her body. Toxic levels of adrenalin surged through her. Four days after her surgery, her heart slowed to a near stop.

“There was too much stress on my body,” Schultz said. “There was no blood being pushed though my body. I was very critical. It was touch and go.”

Surgeons installed a cardiac pump along a major artery in her groin to keep up her oxygen flow. She was in and out of a coma for weeks.

Schultz suffered, her doctors said, from “broken heart syndrome,” a stress-induced cardiomyopathy, a rare heart disease. It can strike without warning, and can be triggered by intense emotional or physiological distress. In her case, the brain hemorrhage made her heart go limp.

Six years ago, after a long rest and time on the cardiac pump, Schultz would undergo weeks of physical therapy. Because of her past training, she gradually built up her weight, her strength and stamina. Within weeks of leaving the hospital she graduated from a wheelchair, to a walker, to the hiking trails.

And today?

“I feel wonderful. I’m doing great. I’m stronger than ever,” said Schultz, now 58, who last year hiked more than 25 miles from the north rim to the south rim of the Grand Canyon – in one day. She plans another rim-to-rim assault this year.

A team of scientists recently discovered the first genes associated with one of medicine’s classic mysteries: What causes a broken heart?

TGen led the study in collaboration with investigators at the Barrow Neurological Institute. Dr. Matt Huentelman, a Professor with TGen’s Neurogenomics division, and colleagues identified genes associated with stress-induced cardiomyopathy (SIC).

This rare and life-threatening type of heart disease displays no early warning signs, and can be triggered by intense emotional or physiological distress.

The passing of a loved one, losing a relationship, or a hemorrhagic stroke – all can cause the heart to shut down for a period of time, or even stop. Which means one can, literally, die of a broken heart.

But who is at most risk?

In a study published in the journal Neurosurgery, researchers identified four genes associated with SIC: MYLK2, DSG2, FKTN, and LDB3. Importantly, previous research identified all of these genes as playing a role in other cardiac diseases, but not in SIC.

TGen-‐led study identifies genes associated with type of heart disease

For the first time, the researchers identified a select group of genes that could indicate whether an otherwise normal heart would fail under extreme stress. Knowing which patients harbor the genes associated with SIC could help guide their care and treatment before, and after, they suffer a life-threatening stressor that induces SIC.

“Identification of patients at risk for SIC, based on genetic predispositions, would allow for tailored treatment upon admission of these patients to the intensive care unit, and perhaps prior to a decline of the heart and brain,” said Dr. Huentelman, the paper’s senior author. “The panel of genes identified by our analysis provides a means of identifying patients who may be at risk for developing this type of heart disorder, and may also be useful in helping those at the highest risk avoid SIC altogether.”

Using ultra-high resolution cameras and supercomputers, the researchers identified the suspect genes by sequencing the genomes of seven women who exhibited SIC following a brain aneurysm.

“It’s an exhilarating time in research,” said Dr. Huentelman. “SIC has intrigued physicians for a very long time and by applying advanced technology, we answered an age old question and explained the phenomena of broken heart syndrome.”
In her five years on earth, Mylee Grace Eaton lived an outsized life – teaching her family, friends and even complete strangers to “Never Give Up,” as she bravely faced a diagnosis of incurable mitochondrial disease.

“If you talk with any family whose child has been diagnosed with a terminal illness, it’s a roller coaster – there’s never a safety net,” Mylee’s mom Sara Eaton said from the family’s home in North Phoenix. “Our family motto is ‘Never Give Up’ and she taught us those words and what it meant to love. Mylee tugged at the heartstrings of a lot of people.”

Inspired by Mylee’s spirit, a generous donor has come forward to continue her fight – donating $100,000 to fund the Mylee Grace Mitochondrial Disease Research Project. And while the donor wishes to remain anonymous, the impact will be felt far and wide.

Housed in TGen’s Center for Rare Childhood Disorders, the Mylee Grace Mitochondrial Disease Research Project will investigate ways to “turn off” genes that may be causing disease as a potential therapy. Scientists are also growing cell lines in the laboratory to identify targeted treatments, offering hope to patients and families.

“There is still so much that’s unknown about mitochondrial disease and there are so many mitochondrial diseases,” Sara explained. “It wasn’t just our fight with Mylee. This isn’t about just finding what was happening with our daughter, but connecting with all of those families that are going through what we went through.”

Mitochondrial diseases result from failures in the mitochondria, which are located within most cells and produce more than 90 percent of the energy the body needs to live and grow. These are chronic, genetic diseases affecting about 1 in 4,000 births in the U.S. Mitochondrial diseases can cause damage to the brain, heart, kidneys, muscular-skeletal, endocrine and respiratory systems, according to the United Mitochondrial Disease Foundation.

Mylee suffered from lung disease and required a gastrostomy tube for nutrition because she was unable to eat or drink. Her body steadily became weaker as the disease progressed until she passed away in 2012. Mylee Grace left behind her mom, dad Dave, little sister Khloe, now age 6, and two adopted siblings under age 18 months. The family learned later about TGen, and the Center for Rare Childhood Disorders was able to piece together the genetic cause of Mylee’s mitochondrial disease posthumously, using her tissue.

The Mylee Grace Mitochondrial Disease Research Project provides the seed funding for these investigations that could lay the groundwork for large-scale research grants. Ultimately, this work will benefit children like Mylee, and their families, inspiring others to “Never Give Up.”

“Mylee left an important impression on many people,” Sara said. “[The donor] is just an angel. There are not enough words to explain or express our love for them.”

TGen’s Center for Rare Childhood Disorders was able to piece together the genetic cause of Mylee’s mitochondrial disease posthumously using her tissue. To support rare disease research in Mylee’s honor, visit www.myleesfund.org.
With the glitz and glamour of a Jay Gatsby speakeasy, Roaring for Research raised friends and funds for TGen’s Center for Rare Childhood Disorders on February 27. Complete with live jazz and casino games, the 1920s-themed soiree graced the historic A.E. England Building, constructed in 1926 for a local automobile dealership. With exposed rafters and brick walls, the setting lent an aura of mystery and authenticity to the inaugural event.

Decked out in a fedora and mini-Zoot suit, 10-year-old Campbell Faulkner ascended the podium and addressed the more than 200 costumed flappers, dames, Daddy-o’s and tough guys.

“TGen brings lots of hope to my family and me,” explained Campbell, who is being treated at the Center for mitochondrial disease and has tubes in his abdomen to help with nutrition and elimination. “I always want to try new things, but my greatest wish is to get a cure. When TGen said they wanted to test my blood, it was the same day I asked Santa Claus for a cure.”

Campbell invited the guests to join Campbell’s Crew and support rare disease research at TGen. VIP guests received a Campbell’s Crew wristband to wear at the blackjack, craps and roulette tables. Patrons participated in a silent auction highlighted by original artwork from patients at the Center; an Arizona Diamondbacks box suite experience; a private bourbon tasting and more.

“What a blast! It’s so much fun getting dressed up in costume and seeing everyone looking so wonderful!” said Kelley Shope of Fountain Hills, Arizona. “This was a great event and I can’t wait to see what they do next year!”

Photos courtesy of Yuliya Blake Photography
By following a DNA trail through the secretive world of heroin use, researchers may have shown the way for public health officials to solve infectious disease problems affecting the wider population.

Led by Dr. Paul Keim, Director of TGen’s Pathogen Genomics Division and Regents’ Professor and Cowden Endowed Chair of Microbiology at Northern Arizona University (NAU), a collaborative team of international scientists has shone new light on an old question about injectional anthrax by demonstrating the latest advances in whole genome sequencing.

Researchers from the US, Germany and England reconstructed a decades-old outbreak of injectional anthrax by DNA analysis of the anthrax conveyed to victims from injecting heroin.

The study results appeared in the journal EBioMedicine. In the article, the research team demonstrated the potential of whole genome sequencing, a data-rich process used to determine an organism’s entire DNA sequence.

“It’s an application of a technology that’s been incrementally improving over the last decade,” said Dr. Keim, who used a similar approach to the 2001 anthrax letter attack at the Hart Senate Office.

Evidence pointed to the idea that heroin had become contaminated by anthrax along the way from Afghanistan to Europe, where some heroin users were becoming infected and dying. Cases were tracked to Germany, France, Denmark, Norway, England, Wales and Scotland.
Building in Washington, DC, a case that garnered widespread attention amidst fears of bioterrorism. But today’s sequencing work is far more expansive, rapid and less expensive – so much so that the insights from this project have added new considerations to some of the foundational principles of epidemiology.

“This work is an example of the paradigm for future investigations,” said Dr. Keim, the study’s lead author.

Evidence pointed to the idea that heroin had become contaminated by anthrax along the way from Afghanistan to Europe, where some heroin users were becoming infected and dying. Cases were tracked to Germany, France, Denmark, Norway, England, Wales and Scotland.

While the new investigation leaves open the question of where the contamination took place, it identified two distinct disease clusters occurring over a period of more than 12 years. The conclusion defied the epidemiological bedrock of space-time correlation that had pointed to only one disease event, Dr. Keim said.

The implications are powerful for public health officials who face obstacles of money and time to accurately identify and track a disease event, such as a food-borne pathogen outbreak.

“That’s the whole purpose of doing molecular epidemiology,” Dr. Keim said. “And this is the biggest, baddest way to do it.”

NAU played a central role in the international effort with its inventory of more than 3,000 anthrax strains and because of its investment in high-capacity computation. Dr. Keim pointed to the exchange of information as an example of how whole genome sequencing effectively crosses international boundaries, which restrict the distribution of live anthrax.

“This type of technology is very amenable to standardization,” Dr. Keim said, noting that this project involved two labs in Germany, two in the United Kingdom, the U.S. Centers for Disease Control, NAU and TGen. “You can easily put genome sequences into a standard language for the exchange of data. It’s like putting a pie back together if you have all the slices.”

Dr. Keim said one of the goals of the research funding from the U.S. Department of Homeland Security was to encourage such global collaboration.

“They wanted international scientists to use this technology to solve a problem and establish ties,” Dr. Keim said. “If there is ever such an event, we have established the international cooperation for an investigation. This is setting the stage for future collaborations.”

Dr. Paul Keim has been named a Fellow of the American Association for the Advancement of Science (AAAS). Election as a Fellow of AAAS is an honor bestowed upon members by their peers for meritorious efforts to advance science or its applications.

Dr. Keim’s peers recognized him for “distinguished contributions to the fields of microbiology, evolution and genetics through the use of genomic analysis for applications in forensics, biology and public health,” according to the AAAS announcement in the Nov. 27, 2015, issue of the AAAS journal Science. Dr. Keim and other Fellows were recognized Feb. 13 during the 2016 AAAS Annual Meeting in Washington, D.C.

Dr. Keim is a world-renowned expert in anthrax and other infectious diseases.

“There is no question that AAAS’s recognition of Dr. Keim is extremely well deserved,” said Dr. Jeffrey Trent, TGen President and Research Director.

“I’m gratified to know this honor also brings recognition to everyone in the lab, including the students who work with us,” said Dr. Keim, a Professor at TGen and Regents Professor of Microbiology at NAU. “Their contributions, achieved through dedication and talent, are meaningful and well deserving of the attention.”

Dr. Keim is a former member and chair of the federal government’s National Science Advisory Board for Biosecurity (NSABB), where he helped draft national research policy guidelines for blunting bioterrorism while elevating ethical standards and improving the quality of scientific research.

The tradition of AAAS Fellows began in 1874.
6th Annual Cycle for the Cure Expands to Five Locations

Registration is now open for the 6th Annual Cycle for the Cure, a two-hour indoor cycling and fitness event on Sunday, May 1, to benefit TGen’s cancer research programs. Led by co-chairs Vicki Vaughn and Robyn DeBell, Cycle for the Cure is expanding to five locations in 2016: The Village Health Clubs at Camelback, D.C. Ranch, Gainey and, new this year, Ocotillo, as well as Studio 360 in Phoenix. With a goal of raising $200,000 to fund early detection efforts for cancer, Cycle for the Cure enlists the hearts and minds of riders to raise funds and awareness, starting with a $200 registration donation. For those who prefer a more meditative pace, Yoga for the Cure classes will be held at DC Ranch and Camelback Village. All rides and yoga classes will culminate in a festive after-party at Camelback Village featuring the Nate Nathan and the MacDaddy-o’s Band. Register today at www.tgenfoundation.org/cycle.

Lowey wins international Customer Project of the Year Award

TGen Chief Information Officer James Lowey recently won the Customer Project of the Year Award at the V3 Technology Awards in London. Lowey worked with Dell and TGen scientists to secure this award, which is given to an exceptional customer project aiming to change the world using innovative technology. According to the V3 Technology Awards nomination, “TGen is the force behind the most ground-breaking research into pediatric cancer.” Last year, Dell renewed its commitment to TGen with $3 million to support, and expand to France and Lebanon, its FDA-approved precision medicine clinical trial in association with the Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC). The extended partnership will optimize critical high-performance computing, allowing TGen to store more data and reach more patients than ever before.

TGen research results in FDA approval of pancreatic cancer treatment

Patients with advanced pancreatic cancer now have access to a new FDA approved drug, Onivyde, which produced significant overall survival rates in an international clinical study conducted in part by researchers at TGen. “As part of the team of medical researchers who studied the effectiveness of MM-398 [Onivyde] plus 5-FU and leucovorin drug combination, we are thrilled that the FDA has approved the drug for use in patients throughout the nation,” said Dr. Daniel D. Von Hoff, TGen Distinguished Professor and Physician-in-Chief, and the global principal investigator of the NAPOLI-1 (NAnoliPOsomal Irrinotecan) study. The large, randomized clinical trial for Onivyde evaluated patients enrolled at more than 100 sites in North America, South America, Europe, Asia and Australia, including patients at HonorHealth Research Institute, TGen’s clinical trials partner in Scottsdale, where Dr. Von Hoff serves as Chief Scientific Officer.
stepNout 5K Run | Walk | Dash Celebrates 10 Years

More than 1,000 runners, joggers, walkers and supporters celebrated the 10th Annual stepNout 5K Run | Walk | Dash on November 1, 2015 under crisp blue skies at the Scottsdale Sports Complex. Honorary Chairman Derrick Hall, the president and CEO of the Arizona Diamondbacks, presided over the event for the second year. The stepNout 5K raised $131,000 in the fight against pancreatic cancer, bringing its total to more than $1 million to battle the third leading cause of cancer death. Patients, survivors, caregivers, friends and families came out to support those who are battling pancreatic cancer and to help fund TGen’s research efforts in early detection. The 11th annual stepNout 5K will be November 6, 2016. Registration will open in August online at www.tgenfoundation.org/step.

Upcoming Events Benefitting TGen:

April 8-10, 2016
Barrett-Jackson Collector Car Auction [Palm Beach, FL]
Clarion Builds is donating its first project car, an iconic 1974 BMW 2002 restomod, to benefit colon and prostate cancer research at TGen. www.barrett-jackson.com

April 9, 2016
2nd Annual Casey’s Cup for ACC [Anaheim, CA]
A fun 3-on-3 ice hockey tournament for all age levels and abilities. It raises funds for Adrenocortical Cancer (ACC) Research at TGen. www.tgenfoundation.org/events

May 1, 2016
6th Annual Cycle for the Cure [Phoenix, Chandler, Scottsdale, AZ]
Enjoy a heart-pumping, high-energy indoor spin event that supports cancer research at TGen. www.tgenfoundation.org/cycle

June 7-8, 2016
16th Annual Bernice E. Holland Golf Tournament [Colorado Springs, CO]
Golf, VIP reception and silent auction to benefit colon cancer research. www.hollandfoundation.org

June 16, 2016
Focus on Lyme Golf Tournament [Flagstaff, AZ]
Tee it up to raise funds in the fight against tick-borne illnesses and bring a new diagnostic test for Lyme disease to clinical trials. www.focusonlyme.org

August 28-29, 2016
14th Annual Seena Magowitz Golf Classic [Boston, MA]
David Dombrowski, Boston Red Sox President of Baseball Operations, will serve as the events honorary chair, which supports TGen’s pancreatic cancer research initiative. www.seenamagowitzfoundation.org

September 3, 2016
Sarod for C4RCD [Tempe, AZ]
Ustad Amjad Ali Khan, the world’s foremost virtuoso of the Sarod, a lute-like stringed instrument of India, gives a concert benefitting TGen’s Center for Rare Childhood Disorders. www.helpTgen.org/sarod

To learn more about these events, please call the TGen Foundation at 602-343-8411 or visit: tgenfoundation.org/events
Wendy’s® Jr. Frosty® Promotion Benefits TGen’s Cancer Research

This spring, a frosty treat provides a cool benefit for cancer research at TGen! Starting in March, select Wendy’s restaurants are selling five Jr. Frosty coupons for a $1 donation while supplies last. All proceeds will be donated to TGen for their efforts to provide earlier diagnostics and smarter treatments for cancer patients. This promotion is being hosted by the Wendy’s restaurants in Arizona in partnership with the Bernice E. Holland Foundation.

The Arizona Wendy’s family has faced their own battles with cancer including Rick Holland, who established the Bernice E. Holland Foundation in 1999 in memory of his mother after losing her to cancer. Wendy’s has decided to continue supporting TGen because in Rick Holland’s words “although awareness is on the rise, we must make greater strides in funding the research that will lead to a cure”.

Jr. Frosty coupons will be sold at 139 participating Wendy’s locations in Arizona, Southern and Western Colorado, Rapid City, S.D. and select locations in Michigan, Ohio and Indiana. For a full list of participating restaurants, please visit www.helpTgen.org/Wendys.

“We couldn’t be more pleased with the results of our partnership with Wendy’s. This latest promotion supports our cancer research efforts and provides Wendy’s with the opportunity to showcase their focus on giving back to the communities they serve,” said TGen Foundation President Michael Bassoff.

In the past decade, Wendy’s has contributed more than $1 million to cancer research. In 2016, Wendy’s franchisees have set a goal to raise $150,000 to further benefit TGen through this promotion. In addition, the annual Bernice E. Holland Golf Tournament and Auction, on June 12-13 at the Country Club of Colorado in Colorado Springs has a goal of raising $100,000 for this research. Help them reach that goal by visiting a participating Wendy’s today to get your Jr. Frosty coupons!

If your company would like to create a Community Partnership with TGen, please call the Foundation at 602-343-8411.