Dear Friends,

Without you, there is no us. This statement, shared by Dr. Michael Berens at our recent Founders Dinner, set the tone for a special evening and the start of TGen’s 20th Anniversary year. This edition of TGen Today continues and amplifies our 20th year in multiple ways. The pages contain stories of hope, collaboration and advocacy, as we pay tribute to two decades of advances, both scientifically and economically, promises made, and promises kept. We highlight achievements and milestones, and recognize those whose belief in our work makes a difference in the lives of many and those whose lives we have bettured through our work. This is told through stories of precision aging, life-extending clinical trials, and by Wonder Woman herself, Lynda Carter Altman. Much has changed over 20 years. Technology now allows our faculty to move at speeds only imagined when the institute first began. They sequence patient genomes in hours and the information that genome reveals arrives in the hands of treating physicians within days. The bench-to-bedside paradigm envisioned at our inception is now reality, as precision medicine — a construct few spoke about in 2002 — replaces the one-size-fits-all approach toward treating disease.

Our scientists and doctors innovate daily. Their dedication to help patients, to push the boundaries of potential, constantly amazes. We live in a time where nearly anything is possible and scientific intellect fuses fact and knowledge to envision and develop the latest diagnostic or life-extending therapy. I know, too, much of this would not be possible without the support of our donors. The commitment and passion they share to inspire and drive our work remains vital. It is, in no small way, what enables us to succeed and reminds us that past achievements are the foundation for future successes.

A musical chord is a harmonic melding of pitches and notes that when heard, sound as if the collective were occurring simultaneously. You, our donors and supporters, are the chords that work in concert to lift up our research and support our faculty in untold ways. Every gift — whether large or small — brings hope and answers through TGen’s work to those who need it most. I hope you feel a sense of great pride for the role you play in our success.

Without you, there is no us.

With gratitude,

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

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

2  Build It and They Will Come
TGen celebrates 20 years of economic growth and advances in precision medicine

5  Milestones
Twenty years of innovation and precision medicine

12  20 Years of Translational Research
The approach to treating and preventing disease based on an individual’s genomic makeup — which would later come to be known as precision medicine.

15  Q&A with Dr. Jeffrey Trent
TGen’s President and Research Director Dr. Jeffrey Trent answers five questions about TGen’s past, present, and future

16  Odds are...Better All the Time
How TGen renewed the hope of Elizabeth O’Conner

18  Rewriting the Playbook on Aging
The future of medicine may not be determined by those who are sick, but those who are well

21  In-Brief
News and notables

The John S. McCain Leadership Award
The John S. McCain Leadership Award was presented to Linda Carter Altman at the 2022 TGen’s Annual Founders Dinner
After a tumultuous, yet incredibly impactful 2020, TGen accelerated its role as an important economic engine for the Phoenix region and the State of Arizona. TGen operations, commercialization of research and spin-off activity generated $657.7 million in economic impact. It has been a busy year for TGen. From a fully integrated COVID response, developing the first FDA-approved diagnostic COVID test in Arizona, nearly doubling the staffing at TGen North to deploy public health testing efforts, ramping up testing activities and completing two large commercial transactions, it is not surprising that the economic impact of TGen’s operations and spin-off activity has increased significantly.

— Tripp Umbach, October 2021

In June 2002, Arizona Governor Jane Hull sent Dr. Jeffrey Trent a letter where she urged him to consider a change of address for he and his family. Would he like to once again call Arizona home? She went on to say that the State Legislature had approved and she had signed a measure that designated more than $30 million in taxpayer funds, in addition to more than $70 million in commitments from the broader Arizona community, to help build the infrastructure needed to secure Arizona’s place in bioscience and biomedicine and seed the founding of the Translational Genomics Research Institute, or TGen.

Dr. Trent, founding scientific director of the National Human Genome Research Institute at the National Institutes of Health (NIH) in Bethesda, Maryland — the NIH Institute that led the public effort to sequence the first-ever human genome — had a vision for an institute that would use that completed human blueprint to translate research into medical advances for patients in need and do so in far less time than ever before. Arizona was one of five states vying to call TGen home. Following a meeting in the Capital Hill office of the late Sen. John S. McCain, Trent accepted Arizona’s offer. At the time, the Governor and leaders across the State believed that having TGen based in Arizona would help drive economic development in the burgeoning knowledge-based economy of biomedical science and medicine. These investment dollars would also augment the historical 5 C’s of Arizona — copper, cattle, cotton, citrus and climate — and provide stability amid the ups and downs of a construction-dependent economy. And, over time, generate jobs, spin-out companies, and allow graduates in the biosciences from the state’s universities and colleges the choice of staying in Arizona.

Four Governors and twenty years later, all this and more has come to pass, but no one could have predicted the economic return TGen would provide year-over-year on those state supported dollars.

Full Measure

To understand fully the economic return of those dollars on the Arizona economy, TGen leadership turned to another science — economic impact analysis — to generate a baseline and track TGen’s steady fiscal growth over the past 20 years. The first report came in 2006, with subsequent reports in ’09, ’11, ’15, ’18 and the most recent in ’21 entitled Promises Realized: The Economic and Social Impact of TGen on the State of Arizona.

TGen retained Tripp Umbach, a national consultant with expertise in economic impact studies, who based their findings on point-in-time economic snapshots of TGen’s impact on the Arizona economy, versus the traditional studies that included a multiplier effect.

Of this latest report in 2021, Tripp Umbach president Paul Umbach said, “TGen has seen extraordinary growth in recent years, leading to the betterment and diversity of the Arizona economy, which was one of the original goals TGen set out to achieve.”

He went on to state that, “Given TGen’s consistent and accelerating trajectory upward, we see no reason why TGen wouldn’t continue to improve going forward.”

It’s a vision shared by William J. Post, Chairman of the TGen Board of Directors, who sees a unique scientific research organization with a powerful spirit about to fly even higher, in great part because TGen became part of City of Hope in late 2016 and City of Hope’s recent acquisition of Cancer Treatment Centers of America (CTCA).

Not only will TGen have access to clinical trial studies at City of Hope’s Duarte, California, hospital — which is a National Cancer Institute-Designated Cancer Center — but through City of Hope, TGen also will have access to patient studies at CTCA hospitals in Chicago, Atlanta and Phoenix.

“it’s very significant,” Post said. “As a part of City of Hope, TGen has a step up in opportunities for grants and contracts. It opens up a whole new horizon because it allows TGen to explore more areas of research into a broader array of diseases and medical conditions.”

And, TGen’s continued commercialization of its scientific discoveries, he said, are creating a more robust revenue stream to help fund more high-caliber scientists and expand TGen’s scope of scientific investigations.

One of the keys to TGen’s continued success is keeping the culture of creativity, independence, professional freedom and personal satisfaction,” Post said. “Those are characteristics that TGen has had from the beginning.”
Today, one of the most rewarding parts of TGen so far, adds Trent, has been the ability to witness the growth of the 30-acre biomedical campus in downtown Phoenix and the expansion throughout the State. What began with TGen in 2002 on the downtown campus has grown to include over a dozen biomedical-focused institutions and companies, including ASU, UA, NAU, Exact Sciences, and OncoMyx Therapeutics. Statewide more than 1,500 biomedical, biotech and life sciences entities now call Arizona home.

And while TGen’s operational research activities today provide a total annual economic impact on Arizona of $426 million (A 300% increase from 2017) and its business spinoffs and commercialization of its research technologies brings that total to $658 million, for Dr. Trent, it remains about more than the dollars.

“TGen plays an important role in the local and state economy, for certain, but our progress is more importantly reflected in the precision-medicine-driven research that benefits patients, especially those in Arizona.”

This success has helped Arizona become known as a desirable location for biomedical investment.

“TGen has indeed held to its promise, providing Arizona not only with a tremendous return on investment and high-value employment opportunities, but also positioning the state with a healthcare asset that is the envy of others,” said Rep. Joanne Osborne, chairman of the House Health and Human Services Committee. “It’s no wonder that hospitals the world over partner with TGen.”

TGen’s Chief Operating Officer and President of TGen Accelerators, which is responsible for commercializing TGen’s technologies, believes TGen’s prospects look bright.

“TGen’s impact helps create jobs, support local and state-wide businesses, and drive growth across the research and medical space, most recently in the areas of epidemiology and precision medicine. Developing our discoveries into clinical workflows for the benefit of patients is a top-of-mind consideration for setting priorities.”

Additional findings from TGen’s most recent economic analysis include:

- Full-time, highly-compensated, knowledge-based jobs generated directly and indirectly by TGen totaled 2,179 in 2020, more than twice the 816 in 2017, and nearly 10 times the 220 in 2006.
- Total annual tax revenue paid to the state’s general fund, including spin-off companies and research commercialization, was $33.1 million in 2020, more than tripling the $10 million in 2017, and more than 17 times the $1.9 million in 2006.

These are important metrics for the Arizona Legislature, numbers that reflect the promises delivered by TGen and Arizona’s growing biotech economy.

“Over the past two decades, TGen has become an economic powerhouse, generating high-tech medical innovations, while also providing Arizonan patient’s with the first opportunity to take advantage of those discoveries to advance better health and a higher quality of life,” said Sen. Nancy Barto, chairman of the Senate Health and Human Services Committee. “TGen is at the forefront of Arizona’s strong modern economy.”

IN EARLY 2001, THE LEADING SCIENTIFIC JOURNALS Nature and Science published rival accountings of the first-ever human genome sequence. Nature detailed the public and collaborative Human Genome Project version while Science shared the corporate version from Celera Genomics. Their respective efforts produced a blueprint for understanding human biology at a depth far greater than ever imagined, ushered in the genomic era in biomedical research, and the approach of treating and preventing disease based upon an individual’s genomic makeup — what came to be known as precision medicine.

While the race between the public and private effort received a great deal of attention — particularly around anointing a winner — the real work, mining the genome to accelerate research and discovery, lay ahead. Jeffrey Trent, Ph.D., the founding scientific director of the NIH Institute leading the public effort, understood the potential to improve human lives as research shifted from discovery to developing methods to diagnose, treat or prevent disease.

He began to outline his vision of an institute that would leverage — or translate — the blueprint to advance the diagnosis and treatment of various cancers, neurologic and metabolic diseases such as Alzheimer’s and diabetes. In June, 2002, that vision became a reality when TGen launched in Phoenix.

On the following pages, we highlight 20 milestones from TGen’s history as we look back on the evolution of translational research and precision medicine.
On June 26, 2002, Arizona Governor Jane Hull announces that Arizona has lured Dr. Jeffrey Trent back to his home state to establish the Translational Genomics Research Institute — more commonly known as TGen — and set up its headquarters in downtown Phoenix.

On June 13, 2003, Arizona Governor Janet Napolitano, city officials, TGen leadership, bioscience experts and more than 350 guests took part in a ceremonial groundbreaking for TGen headquarters building. On March 22, 2005, officials from TGen and the City of Phoenix joined U.S. Senators John McCain and Jon Kyl, Governor Janet Napolitano and more than 500 guests for TGen’s building dedication.

The ceremony officially consolidated the majority of TGen’s research and administrative teams and served as a major step forward in a process begun in June 2002 by state and local governments, the state universities and community colleges, Native American communities, foundations, health systems, businesses and private supporters who joined together to form TGen.

TGen President and Scientific Director, Jeffrey Trent, Ph.D., expressed his pride and enthusiasm to the nearly 1,000 people who had gathered to mark this important milestone in the Institute’s young history. “This is a catalyst, a stimulus that will move the biomedical sciences forward,” he said.

On December 8, 2004, TGen announced the co-founding of the Molecular Profiling Institute with the International Genomics Consortium and Scottsdale Healthcare (now HonorHealth). A precursor to whole genome sequencing, molecular profiling allowed scientists to look for abnormal gene changes inside cancer cells.

On June 29, 2005, a ribbon cutting ceremony for the Mayo Clinic Collaborative Research Building marked a major milestone in the advancement of cancer research for residents of Arizona and beyond. The building, a collaborative effort between TGen and Mayo Clinic, housed TGen’s Cancer Drug Development Laboratory and TGen Drug Development (TD2). The facility was funded by Scottsdale developer Tom Hornaday of Hornaday Development.

Hornaday and his wife, Ruth Ann, lost their daughter to melanoma and Hornaday’s mother died of breast cancer. At the grand opening, he said, “My hope, my prayer and my belief is that the research conducted in this building will result in cures so others will not experience these kinds of untimely losses.”

TGen scientists in collaboration with the Clinic for Special Children, Strasburg, Pennsylvania, identified the genetic basis for one form of sudden infant death syndrome (SIDS). The researchers named the newly described form as sudden infant death with dysgenesis of testes, or SIDDT. The researchers identified patients with SIDDT in a small Old Order Amish community in central Pennsylvania. Over two generations, nine families from this community had lost twenty-one infants to this sudden death syndrome. This familial clustering suggested a genetic basis for the syndrome. The findings appeared July 2004 in the journal Proceedings of the National Academy of Sciences.

In December of that year, TGen interns Albert Shieh and Anne Lee received $100,000 for First Place in the team category at the 2005-06 Siemens Westinghouse Competition in math, science and technology. Lee, a senior at Phoenix Country Day School in Paradise Valley, and Shieh, a junior at Chaparral High School in Scottsdale, won the team category prize for developing software that more accurately analyzes genetic data — software that helped lead to the SIDDT discovery. In addition to the prize, the winners rang the closing bell at the New York Stock Exchange following the awards ceremony in New York City.

GENETIC BASIS FOR SIDS

CO-FOUNDERING OF MOLECULAR PROFILING INSTITUTE

TD2 COLLABORATION CELEBRATION

“This is a catalyst, a stimulus that will move the biomedical sciences forward.”

— DR. JEFFREY TRENT
DISCOVERY OF KIBRA GENE
TGen researchers, along with colleagues in Switzerland and Arizona, announced the discovery of a gene — coined Kibra — that plays a significant role in memory performance in humans. The findings, appeared in the October 20, 2006, issue of Science. The researchers linked Kibra to memory performance in over 1,000 individuals — both young and old — from Switzerland and Arizona. This study was the first to describe scanning the human genome at over 500,000 positions to identify cognitive differences between the volunteers.

FIRST GENOME-WIDE LINKAGE TO PROSTATE CANCER IN AFRICAN AMERICANS
TGen announces the results of the first genome-wide linkage study of prostate cancer in African Americans. Using genetic markers, researchers identified several regions of the human genome that likely contain genes that, when altered, increase the risk of developing prostate cancer.

HELIOS EDUCATION FOUNDATION SUPPORTS TGEN INTERNSHIPS
In May, 2007, TGen received a $380,000 grant from the Helios Education Foundation to pilot a paid summer internship program that brought 50 students into laboratories to gain hands-on research experience under the mentorship of TGen faculty. The eight-week program supported students from all backgrounds in their efforts to develop foundational skills as they pursued careers in science or medical-related fields. Following the success of the pilot program, a $6.5 million endowment from the Helios Education Foundation in January, 2008, officially established the Helios Scholars Program at TGen. Designed for incoming and continuing undergraduate, graduate, and medical school students, the program offers a one-of-a-kind summer experience in biomedical research under the mentorship of TGen faculty and staff. At the time, the announcement prompted Arizona Governor Janet Napolitano to state, “These types of public-private partnerships hold the key to what must be the central goal of an Arizona education: giving our students the skills they need to succeed in the high-tech, high-knowledge world of the 21st century.” Since its inception, over 650 students have participated with nearly 90% entering STEM-related careers.

NATURE GENETICS REPORT ON MELANOMA RISK
TGen researchers and colleagues in Australia report in Nature Genetics identifying a region on chromosome 20 (20q11.22) that influences a person’s risk of developing melanoma. The discovery helps move science closer to discovering a new gene that could help explain variation in melanoma risk. The researchers narrowed the gene location through a genome-wide association study — a first in melanoma research. Genome-wide studies involve rapidly scanning DNA of many people to find genetic variations associated with a particular disease. After identifying new genetic associations, researchers can use the information to develop better strategies to detect, treat and prevent the disease.
10 | TGen Today - May 2022

12 PANCREATIC CANCER DREAM TEAMS
TGen and the University of Pennsylvania receive $18 million from Stand Up to Cancer (SU2C) to create a pancreatic cancer research “Dream Team.” The award marked the first of three Dream Team awards presented to TGen. In 2015, TGen received a third SU2C award totaling $12 million sought to double the survival rate of patients with pancreatic cancer. Joining TGen were the Salk Institute for Biological Studies in La Jolla, California and the University of Cambridge, U.K.

13 MELANOMA DREAM TEAM
TGen mapped the genome of a Mayo Clinic patient with pancreatic cancer. A male patient with pancreatic cancer was the first whole genome sequencing was performed on both his tumor and non-cancerous cells as part of a clinical research project. In 2011, SU2C and the Melanoma Research Alliance funded a $6 million national and international study of a deadly type of skin cancer led by TGen and the Barbara Ann Karmanos Cancer Institute. The unique clinical study would pursue new therapies for a type of melanoma known as BRAF wild-type, for which there are few treatment options. The project aimed to accelerate the application of new therapeutic agents, quickly moving new scientific discoveries to clinics where they can immediately benefit patients.

14 TGEN LICENSES FIRST DRUG
In May, 2011, TGen licensed its first drug, a unique compound that targets cancer tumors by modifying the actions of proteins. This demonstrates TGen’s ability to turn laboratory discoveries into therapeutics that patients can use to improve their quality of life. The drug, ONCO-101, licensed to OnchoHoldings Inc., a Syracuse, NY-based pharmaceutical company focused on the acquisition and development of innovative anti-cancer compounds. At the time, TGen President and Research Director, Dr. Jeffrey Trent said, “This milestone is a significant accomplishment that validates the potential of TGen’s drug discovery efforts to deliver new drugs to patients battling life-threatening illnesses.”

15 DELL PARTNERSHIP DRIVES PRECISION MEDICINE TRIAL IN MEDULLOBLASTOMA
Dell through TGen, announces a major commitment of funding, employee engagement and cloud computing technology to support pediatric cancer research programs globally, including the world’s first personalized medicine trial for pediatric cancer conducted by the Neuroblastoma and Medulloblastoma Translational Research Consortium (NMTRC). Through the scientific experience of TGen’s genomic researchers and the technological hardware and software prowess of DELL Computers, the premier computational “black box” by which to rapidly, accurately, and rigorously process the information content from the human genome sequence to help turn weeks into hours, giving months and years back to children with cancer.

16 RARE MUTATION LINKED TO HIGHER-RISK OF PROSTATE CANCER
Faculty at TGen, Johns Hopkins University and the University of Michigan publish a study in the New England Journal of Medicine that details the identification of a rare, inherited mutation linked to a significantly higher risk of prostate cancer. Men who inherit this mutation have a 10-20 fold higher risk of developing the potentially deadly disease.

17 SEQUENCING ENDS A DIAGNOSTIC ODYSSEY
Resolving the plight of a 12-year-old Phoenix girl named Shelby helped pave the way for the launch of TGen’s Center for Rare Childhood Disorders. Wheelchair-bound for nearly a decade, Shelby had difficulty walking, talking, holding her head up, swallowing and breathing. An endless stream of medical exams failed to reveal a diagnosis — that is until TGen sequenced her genome. That one act revealed Shelby’s body had a problem making dopamine, a key brain chemical that helps regulate movement, muscle control and balance. Within a few months of receiving a medication to address this deficiency, Shelby began walking, dining out, shopping, and attending school with friends. Today, having sequenced over 700 children worldwide and more than 1,600 family members in search of answers for these youngest of patients, TGen’s Center for Rare Childhood Disorders is one of the premier centers in this specialized field of research and clinical care.

18 TRIPLE NEGATIVE BREAST CANCER STUDY MOST CITED FOR THE YEAR
TGen faculty and collaborators publish the results from an ongoing clinical trial designed to examine the utility of whole-genome sequencing to identify therapeutic drug targets for the difficult-to-treat, metastatic triple-negative breast cancer (TNBC) specific to each patient’s genetic profile. Published in Molecular Cancer Therapeutics (MCT), the findings revealed significant recurring mutations and other changes in more than a dozen genes and identified mutations previously unseen in metastatic TNBC. In 2015, the journal’s publisher, the American Association for Cancer Research, announced that the paper was the most cited in MCT for all of 2013. This day, the study stands as a great example of precision medicine in practice. The results have provided novel and interesting clues into breast cancer biology, and highlighted the promise and challenges associated with this ground-breaking area of biomedical research.

19 TGEN JOINS CITY OF HOPE
In a move designed to accelerate genomic discoveries into clinical trials, advance standards of care, and improve patient outcomes and quality of life, TGen joined the City of Hope system by becoming a subsidiary of the City of Hope parent organization. The move enabled both institutes to complement each other in their common areas of research and patient care, with City of Hope providing a significant clinical setting to advance scientific discoveries made by TGen. The deal accelerates the speed with which scientists and medical staff convert research discoveries into cures for patients as City of Hope and TGen focused on leveraging their respective strengths in patient care and genomics to develop a comprehensive program to detect disease sooner, and improve patient quality of life and survival.

20 TAKING ON COVID-19
Within days of the first reports of a potentially deadly new coronavirus coming out of China, TGen North scientists, led by David Ergulitcher, Ph.D., began developing a genomic-based clinical test to determine if a person has contracted the virus. Five weeks later — one day before the first reported death — they had developed and received FDA authorization for a PCR-based test for the COVID-19 virus, while simultaneously receiving state certification for its new CLIA laboratory, a step necessary to return testing results to patients and their physicians. TGen quickly applied the tools, technologies and approaches that drove its many successes in cancer and infectious disease research full force to the genome of the virus. The results included the development of a serology test (a blood plasma test for individuals exposed to the virus), a saliva-based test, methods for tracking how the disease moves and mutates, and work toward COVID-19 treatments.
Diving into New Frontiers

“TGen is not helping people, why are we doing this work?” asked Dr. Trent over the din of party chatter in a packed Phoenix living room. It was 2001, TGen was more vision than reality, and the question was one he often asked in those days. The cocktail party drew out civic leaders and socialites from around the state. At the time, Trent served as the founding Scientific Director of the NIH Institute overseeing the world’s largest collaborative biological undertaking — the Human Genome Project — a 13-year effort to determine the complete sequence of DNA bases in the human genome.

The result was a mosaic of the central ingredients that make up human beings. For the first time, all the estimated 20,000-25,000 human genes were accessible for further biological study.

This was important work, no question, but Trent felt an urgent need to apply this knowledge. “We need to do something with these findings,” he found himself saying. This party was a step toward that something. To build an institute that would translate the blueprint for understanding human biology to advance the diagnosis and treatment of various cancers, neurologic, and metabolic diseases, such as Alzheimer’s and diabetes.

Trent envisioned a partnership between public and private sectors aligning industry, academia, and government. “University research is focused on educating and informing,” he says, elaborating on his perspective. Government knows population and scale, they foster great work, but they are conservative in their approach. They swim in their own lane. Confined. Industry provides the opportunity to scale. Realistic applications. They know how to do that. Bringing these approaches together could focus efforts on the individual patient. Even if the science wasn’t completely understood that evening, its significance was almost palpable to some of the guests. History was being made. The kind of history that comes along maybe once in a lifetime — an epoch-altering event — ushering in the genomic era of biomedical research. An approach to treating and preventing disease based on an individual’s genomic makeup — which would later come to be known as precision medicine.

Bennett Dorrance, Managing Director and co-founder of DMB Associates, a Phoenix-based real estate firm, was among the guests that night. He sensed the possibilities.

“I didn’t know a lot about the science, but I was convinced that TGen was onto something,” he explains.

Initially, for Dorrance, it was about jobs. Bringing opportunity to the state. He and his wife, Jacquie, had attended the University of Arizona. After graduation, they settled in Phoenix. They started a family, built a business, made a life. Arizona was their home.

The economic downturn in the early aughts hit the state hard. Bringing TGen here could mean establishing the epicenter of an emerging industry. Phoenix could be a real hub for biomedical research.

“TGen represented more than new terminology. It meant a paradigm shift in genomic research. The Institute facilitated a move from discovery to diagnosis, treatment, and prevention of disease. It represented the transition from expanding our knowledge and understanding of human biology to applying it directly. That was the promise and possibility just over the horizon—all it required was a leap of faith.
Moving from Promise to Practice

Imagine building a boardwalk backward across a shifting dune in the dark. You are twice blind. The terrain is unknown and constantly changing. Ground that was stable moments ago is unknown and constantly changing. This circles back to Trent’s original metaphor. Overseeing the Brain Tumor Unit at TGen, he has helped build a lot of boardwalks. “This is explosive, exciting work,” he says. “We are learning how to help patients’ own immune system go after their cancer. Brain cancer is such a devastating disease. It is aggressive and moves quickly. In the last 13 years, there hasn’t been a new drug developed for treatment in this area. The blood-brain barrier is frightening,” he says, referring to the unique properties possessed by blood vessels that vascularize the central nervous system (CNS). “Most try to avoid it because we don’t want to run the risk of side effects happening in the brain. My lab races into that fire. It is something we try to use to our advantage.”

Dr. Daniel Von Hoff, TGen Distinguished Professor and Executive Vice President of the Molecular Medicine Division, focuses on equally exciting work in oncology—specifically pancreatic cancer. His ceaseless efforts to create drugs and treatments that extend quality of life often aim to keep his patients alive until the next breakthrough. His cases are some of the toughest and most persistent. After conventional treatments have failed, targeted medicine has become a last resort.

“The CNS is a major contributor in this area. Of the five drugs approved by the FDA for advanced pancreatic cancer, TGen has done pre-clinical trials in three of them. This is on Stage 4 patients.” Von Hoff’s clinical trial work has led to the approval of three of the four drugs approved by the FDA for the treatment of patients. This remarkable work would not have been possible if not for the personal level. I wanted to do something for the patient sitting in front of us today. That was important. That was what was missing from this work.

Lessons from COVID

When the COVID virus first emerged more than two years ago, TGen went into action. In 2007, TGen North opened to focus on detecting and preventing biological threats and viral outbreaks. Now, they joined a growing number of facilities concentrating on the virus. As the pandemic spread, TGen pivoted to combat COVID head-on.

TGen applied the tools, technologies, and approaches that drove so many successes in cancer research and infectious disease research full force to the genome of the virus. The results: a blood plasma test that looked for antibodies in those individuals exposed to the virus, a saliva-based test, methods for tracking how the disease moves and mutates, and contributions toward the development of treatments.

Dr. Michael Berens, Director of the Cancer and Cell Biology Division at TGen, who focuses primarily on melanoma risk in 2008, co-developed a unique compound that targets cancer patients in 2009, and licensed it were just a cold. More than 40% of COVID survivors are estimated to have developed “Long COVID,” with complications outlasting the virus. We see the variance in how the disease is expressed from person-to-person that answers to larger, often unspoken, questions in the medical community.

TGen researchers contributed to the discovery of Kibra, a gene that plays a significant role in memory performance in humans. In 2006, TGen announced findings from the first genome-wide linkage study of prostate cancer in African Americans. They contributed to the discovery of the genes that contribute to melanoma risk in 2008, co-developed individualized therapies for pancreatic cancer patients in 2009, and licensed a unique compound that targets cancer tumors by modifying the actions of proteins.

Over the last two decades, the terminology that once seemed so foreign has experienced an uptake. Nearly every research university in the country now has a genomics department. Genomics is no longer a strange concept but is now routinely applied. Precision medicine as a concept is better understood and more well known. “I see this more as a gift to our advantage.”

What was some of the early challenges you encountered? Our focus as a nonprofit medical institution was to combine cutting-edge genomics with drug treatments. We wanted to not just talk about the work but really align it. The science required a lot of educating the public and private sectors. Aligning industry, government, and government. Making knowledge actionable if we are not helping, what is the point?

How did you decide on Arizona? I am from here originally. I grew up in Phoenix. To come home was a big draw, but we were looking. PricewaterhouseCoopers helped create a business plan. We shopped it to five or six states, and Arizona came home was a big draw, but we were looking. I am from here originally. I grew up in Phoenix. To this day, I see the flow of promise to practice.
Elizabeth O’Connor couldn’t have been happier.

Life was good for the 31-year-old school teacher, enjoying her second trimester of pregnancy and eagerly awaiting the birth of her second child — a boy. Fear soon replaced her happiness when she inexplicably began losing weight and developed digestive problems.

Her doctors struggled to pinpoint the cause. When her son, Andrew, arrived 7 weeks premature by cesarean section, they realized something was terribly amiss with her ovaries. Because ovaries.

The odds were slim. At the time of Elizabeth’s diagnosis, less than 5% of pancreatic cancer patients survived five years.

Odds are... Better All The Time

The Search Begins

Randy initially searched in and around Atlanta for the best oncologists, a journey that eventually led him to Phoenix and TGen’s Daniel D. Von Hoff, M.D., considered one of the nation’s leading authorities on pancreatic cancer.

Elizabeth still had a strong immune system and was put on what, in 2010, was the FDA standard-of-care for pancreatic cancer, gemcitabine, plus oxaliplatin. The goal was to eliminate as much tumor as possible to pave the way for surgeons to remove the cancer in her pancreas. If the drug failed, surgery wasn’t an option. However, because no progress was being made against the cancer in 2011, Dr. Von Hoff put Elizabeth on a new drug combination of gemcitabine and nab-paclitaxel, also known as Abraxane, a combination that in 2013 would eventually become an FDA-approved national standard-of-care for pancreatic cancer. That combination was developed in the TGen laboratory with TGen Professor Dr. Haiyong Han.

“From Day One, I can tell you how good Dr. Von Hoff was, making Elizabeth feel that eventually led him to Phoenix and TGen’s Daniel D. Von Hoff, M.D., considered one of the nation’s leading authorities on pancreatic cancer.

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“From Day One, I can tell you how good Dr. Von Hoff was, making Elizabeth feel that soon replaced her happiness when she inexplicably began losing weight and developed digestive problems. Because ovaries.

The joy of childbirth soon gave way to the unknown and the possibility that she may not live to see her children grow up. Her doctors believed it was too late. Elizabeth and her family heard the news that no one should ever hear: go home, enjoy the moments you have but prepare yourself for the inevitable. Her doctors promised to make her as comfortable as possible, but indicated she likely did not have long to live.

Elizabeth’s father, Randy Dobbs — a highly successful CEO and board member of multiple companies — simply could not accept Elizabeth’s fate as offered by her doctors. Surrender ran counter to his natural instincts. He had spent a lifetime solving problems in business and wasn’t about to sit idly by and let cancer control his daughter’s life.

That instinct would prove prophetic. Initially, however, the news delivered a gut punch.

“My initial thought,” said Randy, “was oh, my God. What are we going to do?” He had learned that a diagnosis of advanced pancreatic cancer amounted to a death sentence for most patients. “She’s only 31. We can’t lose her.”

By early 2012, the tumor had shrunk enough to begin radiation treatment. These steps further reduced the size of the tumor, which allowed surgeons to remove the remaining cancer located on the difficult-to-reach tail of her pancreas. The day-long procedure involved removing one of her adrenal glands and rerouting her intestines and a number of blood vessels. After she recovered from surgery, Dr. Von Hoff added another agent, F-5-FU (fluorouracil).

By 2014, the cancer reappeared, requiring the surgical removal of a portion of Elizabeth’s left lung. Later that year, she began having seizures as a result of the cancer having reappeared in her brain. Neurosurgeons removed as much of the cancer as possible, but the procedure left her unable to use her right leg and foot, requiring extensive physical therapy. Follow-on radiation treatments to battle recurrences claimed the use of her right arm.

In 2015, Elizabeth began a triple-drug regimen of gemcitabine, nab-paclitaxel and cisplatin, another combination designed by Dr. Von Hoff and his colleagues, which clinical trials showed improved survival for 7 out of every 10 pancreatic cancer patients. That regimen worked for some time. When it stopped working, a newly developed agent was added that targeted a specific genomic signature in Elizabeth’s tumor, making it susceptible to a PARP inhibitor.

Immunotherapies: A Godsend

In March 2017, under the care of Erik Borazanci, M.D. and Gayle Jameson, N.P., TGen adjunct faculty members, at HonorHealth Research and Innovation Institute, Elizabeth began an innovative immunotherapy regimen, using drugs that re-ignite her body’s own immune system to fight the cancer by targeting her specific DNA mutations.

“After progressing through every treatment regimen possible,” said Randy, “her immunotherapy has been a godsend.”

His encouragement stems from Elizabeth’s ability to drive again, eliminate pain medication, overcome depression, and return to performing routine tasks. These past holidays, for the first time in years, Elizabeth wanted to decorate a Christmas tree.

As much as anything, Randy is grateful for the effect Elizabeth’s improvement is having on her children: Andrew, now 11, as her first child, Abigail, 16, who just started driving and is looking forward to college.

“The good news for both of them is that they’re getting to be teenagers, and getting to live their lives, instead of everything being, ‘What’s going to happen to mom next?’ The fact that she’s a mom, and happy and engaged with her children, is really good,” Randy said.

“None of us knows what’s ahead, but I’ve been so blessed to still have my daughter and for her to be with her family,” he added. “I’ll do whatever is necessary to support her and everything I can to support the medical personnel who are supporting her.”

For Elizabeth, the moment is what’s most important.

She is grateful for having joined Dr. Von Hoff and his associates in the past decade’s journey toward ever-better cancer treatments. “I can’t put it into words how much it means to me; to spend more time with my family; to not have that fear that I wouldn’t be around for them,” she said.

The Road Ahead

Never one to rest, Dr. Von Hoff continues to push the boundaries of what is possible. And while the past decade has seen innovations in treating pancreatic cancer, he knows patients need more.

“The improvements we have made in pancreatic cancer treatments would simply not be possible without the pioneering bravery of patients like Elizabeth, who have traveled with us in this journey toward increased survival and a higher quality of life.”

Today, Randy is helping fund a clinical trial for yet another new pancreatic cancer treatment designed by Dr. Von Hoff, along with new technology developed by an Irish academic team that targets a genetic mutation present in up to 90 percent of all pancreatic cancer patients.

“There can never be enough for me to do to honor Dr. Von Hoff, his colleagues and team, and all they have done for me and my family,” Randy said.

And while Elizabeth continues to defy the odds, Dr. Von Hoff and his colleagues continue their pursuit of the next best thing.

Elizabeth O’Connor’s family photo for a family shoot in November 2021.

Photo courtesy of Kajal Furlan Photography
Wants to rewrite the playbook on aging

This Scientist

One might think that a biomedical researcher, a lawyer and a banker have little in common. Science, after all, is a profession that applies analysis to determine the rules, while the legal field and banking are professions that apply the rules to follow the law.

For Desirae Outcalt, a vice president at Bell Bank, and T.J. Mitchell, an attorney with Jennings Haug Keleher McLeod LLP, a study on aging and age-related diseases forms a unique connection to TGen professor Matthew Huentelman, Ph.D.

Dr. Huentelman’s research requires studying a multitude of populations on a genomic level to fully understand aging and how it effects all walks of life and all aspects of society, from urban to rural and everywhere in between.

But he believes outmoded methods hamper his attempts to recruit study participants.

Traditional recruitment of study volunteers involves asking participants to visit a lab or by collaborating with a clinician who interacts with patients, which means your sample population contains individuals who already have an illness or disease.

For over a decade now, the work Dr. Huentelman’s laboratory at TGen has focused on exploring and demonstrating ways this can change.

In 2013, Dr. Huentelman and colleagues at the University of Arizona launched MindCrowd, one of the first — if not the first — study to not only recruit subjects, but to conduct the study itself, via the Internet. MindCrowd would inform how the healthy brain works and provide a stronger baseline of understanding for when it doesn’t.

To date, more than 300,000 people from all over the world have taken part in the study.

A Deeper Understanding

Today, with promotional help from the TGen Ambassadors — an invitation-only network of working professionals and emerging leaders — including Outcalt and Mitchell, Dr. Huentelman will soon roll out MindCrowd 2.0, an expanded version resulting, in part, from a recent $60 million federal grant.

For Mitchell, the desire to help involves a personal connection.

“Two of my grandparents suffered from severe memory loss before they passed, so this initiative hits close to home for me,” he said. “As a TGen Ambassador, I feel an obligation to reach out to the community to help recruit the diverse population of volunteers TGen will need for this study.

Together, our group of Ambassadors are making MindCrowd 2.0 the focus of our efforts for 2022.”

The original MindCrowd.org website included two brain games — one to gauge memory, and another to measure reaction time — which researchers use to analyze brain performance. MindCrowd 2.0 includes 8 additional brain games, with data from these games helping researchers understand how different parts of the brain work. As with the original version, participants will be able to see how they fare on each game and how they compare to others who’ve participated.

“You use different parts of your brain when you play these games and that allows us to capture information about several different regions of the brain,” said Dr. Huentelman. “It’s a data-rich measurement of how human brains work at various ages and under a variety of demographic, health, medical and lifestyle factors.”

The additional games will allow Dr. Huentelman and his colleagues to assemble a more complete picture of each person’s brain, and better understand the process of brain aging.

“Our objective,” he said, “is to have a person’s cognitive healthspan match their physical lifespan.”

Beyond the online games, participants who wish to help further will have opportunities to submit a blood sample for sequencing, take part in a face-to-face assessment, or undergo brain imaging. Current plans include centers for these assessments in Baltimore, Atlanta, Miami and Tucson.

“I joined the Ambassadors program to get a better understanding of TGen and the many fronts on which they’re using precision medicine to patient benefit,” said Outcalt, “and now, by helping promote MindCrowd, I am able to share this extraordinary work with others by encouraging them to come alongside the Ambassadors in support of TGen’s groundbreaking discoveries.”

Eventually, the researchers want to use this information to help individuals prioritize how to cope with stress, sleep better, control blood-sugar, and other strategies to maintain both a healthy body and a healthy mind. They envision new therapeutic approaches that target and enhance different parts of the brain in a fully personalized fashion.

Precision Aging and Improved Outcomes for All

“Cancer researchers already use genomic information to develop specific drug regimens tailored to each individual patient, a process known as Precision Medicine. We are taking a tested formula and directing it toward a new discipline that we call Precision Aging,” said Dr. Huentelman.

If all goes according to plan, MindCrowd 2.0 will create an enormous amount of data. Pulling together and helping
TGen Today - May 2022

It is important to remember that race and ethnic differences matter for disease risk and disease treatment,” said Huentelman. “Geographical location matters. ZIP codes matter. We have to do a better job of understanding the why and how for the multitude of diseases and disorders that exist, and the associated risk factors.”

Huentelman believes the web-based aspect of MindCrowd provides a great advantage to his study, knowing that so many track their daily workouts and other activities on mobile apps, celebrate their progress and question their declines. MindCrowd taps into that curiosity by harnessing the collective power of these like-minded individuals all asking similar questions.

“Imagine if you had the ability to share this information with a scientist,” said Huentelman. “Imagine if you felt this sense of community so deep that you were interested in sharing your data to better understand your health, the community’s health, what happens when you age, and how things change across time.”

That is MindCrowd 2.0.

A $1.05 million gift from Atlanta-based charity Fundora founded Purple Pansies in 2007 and has contributed more than $3.4 million in support of TGen research and clinical trials. Fundora’s dedication toward supporting the development of improved treatments for pancreatic cancer patients is tireless and serves as an inspiration for us all,” said Erin Massey, Chief Development Officer for the TGen Foundation. “What began as a tribute to her mother has become something much larger and with far reaching hope.”

If successful, the study will lead to a clinical trial for patients with pancreatic ductal adenocarcinoma whose cancer has metastasized, or spread, to other parts of the body.

In late February, the American Society for Clinical Investigation (ASCI) recognized Floris Barthel, M.D., an assistant professor at TGen and City of Hope, with its Young Physician-Scientist Award, which recognizes physician-scientists who are early in their first faculty appointment and have made notable achievements in their research.

Barthel oversees a cancer genomics laboratory focused on utilizing state-of-the-art genomic approaches to study the development and evolution of glioblastoma multiforme. The lab has a particular interest in the fundamental role of telomere dysfunction in glioma development, but is generally interested in all aspects of evolution including but not limited to longitudinal studies of tumor tissue and liquid biopsies. ASCI comprises more than 3,000 physician-scientists from all medical specialties representing the rich diversity of backgrounds inherent to those they serve.

In early March, the Phoenix Business Journal recognized TGen’s Kandall Van Keuren-Jensen, Ph.D., as a recipient of their annual Outstanding Women in Business award for her community leadership, professional accomplishments, and personal achievements. Jensen was among the 25 honorees the Business Journal’s panel of judges selected from over 220 nominations.

Dr. Van Keuren-Jensen joined the TGen faculty in 2003. She became Deputy Director in 2019. At TGen, her research focuses on extracellular vesicles — or EVs — and why so many in the field refer to them as the “next frontier of genomic medicine.”

True to her leadership style, Dr. Van Keuren-Jensen supports and fosters cultural understanding across the Institute, and is a strong promoter of organizational goals, diversity and inclusivity at all levels.

In honor of her many notable achievements in their research.

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The well-known actress, singer-songwriter and advocate Lynda Carter Altman received the 2022 John S. McCain Leadership Award at the annual TGen Founders Dinner, held April 7.

Carter Altman, who portrayed Wonder Woman in the original television series, received TGen’s John S. McCain Leadership Award in recognition of her advocacy for TGen’s and City of Hope’s research and clinical advances in precision medicine. Named after the late U.S. Sen. John McCain of Arizona, the annual award recognizes individuals or organizations whose leadership and dedication have made a significant impact in the fight against disease and improving the quality of life for patients worldwide.

“I am so grateful to have received this award. The ceremony reminded me of everything John McCain stood for: leadership, strength, and bravery, all in service to the great state of Arizona,” said Carter Altman.

“We present the leadership award, named after the late Sen. McCain, to someone with that maverick spirit, that willingness to be fearless in what they believe and advocate for the causes they support. Lynda Carter fits that bill perfectly including, her groundbreaking support for breast cancer and several social issues,” said TGen President and Research Director Dr. Jeffrey Trent, who also welcomed her as the newest member of the TGen Foundation Board of Directors.

In terms of her board appointment, Carter Altman remarked, “My greatest hope in working with TGen is that we can work together to lessen the suffering that comes with a terminal diagnosis.”