

# TGen Today

DECEMBER | 2017

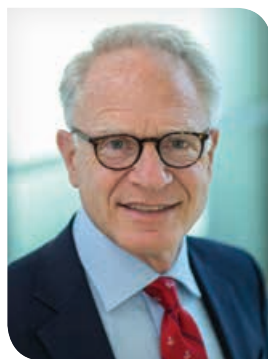
A PUBLICATION OF THE TGEN RESEARCH INSTITUTE

## Dr. Sunil Sharma

USES HIGH-PERFORMANCE COMPUTING TO  
DEVELOP AND TEST NEW CANCER THERAPIES

**tgen**<sup>®</sup>  
AN AFFILIATE OF City of Hope.

A Non-Profit Biomedical Research Institute



## A Look Inside...

Dear Friends,

Collaboration is a hallmark of TGen's success: Our willingness to seek out and work with the brightest minds — whether in academia, healthcare or private industry — has led to our biggest breakthroughs. Together, we can do more to help patients battling cancer, neurological disorders, metabolic diseases and infectious outbreaks.

In this issue of *TGen Today*, you'll learn how our collaborations within the institute and outside are going to transform the practice of medicine here at home and around the world. Through its affiliation with City of Hope, TGen has been able to attract two new, innovative and influential faculty members:

An expert in drug development and a respected oncologist, Dr. Sunil Sharma joined TGen this fall as Deputy Director of Clinical Sciences, where he will serve alongside TGen Physician-in-Chief Dr. Daniel D. Von Hoff, in the clinic at HonorHealth. A Professor in the Division of Molecular Pharmacology at City of Hope, Dr. Andrea Bild works on the reversal of drug resistance in cancer and she has built a reputation for her lab's unique ability to tear tumors apart. These additions to the TGen team will provide new hope to patients facing colorectal, breast, ovarian and pancreatic cancers.

Through a grant from the Bill and Melinda Gates Foundation, scientists at TGen's Pathogen and Microbiome Division, or TGen North, have taken on a challenge that affects one in three people worldwide: Tuberculosis. Closer to home, the TGen North team is collaborating with Dr. Von Hoff's Stand Up to Cancer Pancreatic Cancer Dream Team to investigate how the microbiome impacts the pancreas.

From surprising new therapies for glioblastoma to the development of clinical trials for ovarian cancer, TGen owes a great debt of gratitude to our donors: You are the philanthropic collaborators who see the promise in our work and invest in its success through your gifts.

We hope you will consider accelerating this research through a charitable gift to the TGen Foundation. This simple and profound act can affect change that will impact patients around the world for years to come.

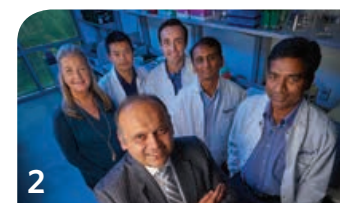
Thank you for your ongoing support of TGen. Wishing you a peaceful and prosperous new year.

With gratitude,

Michael Bassoff  
President, TGen Foundation

# TGen Today

A Publication of The Translational Genomics Research Institute



## 2 Cover Story

### Rising to Unmet Challenges: Dr. Sunil Sharma

The Sharma Lab uses high-performance computing to develop and test new cancer therapies.



## 4 When it Comes to Tuberculosis, Seconds Matter

TGen North stands guard against this worldwide threat.



## 6 Lighting up Genomic Research

TGen-USC team develops LumosVar, a new tool in the field of precision medicine.



## 8 Bild-ing Collaboration

Director of new Women's Health Program at TGen believes teamwork is key to defeating cancer.



## 10 A Little Arsenic, A Lot of Potential

Findings show that, for some patients, arsenic could be a powerful therapy.



## 12 TGen Briefs and Upcoming Fundraising Events

News and notables

### Back Cover

## Trinidad and Tobago: Island Nation Joins Worldwide Fight against Pancreas Cancer

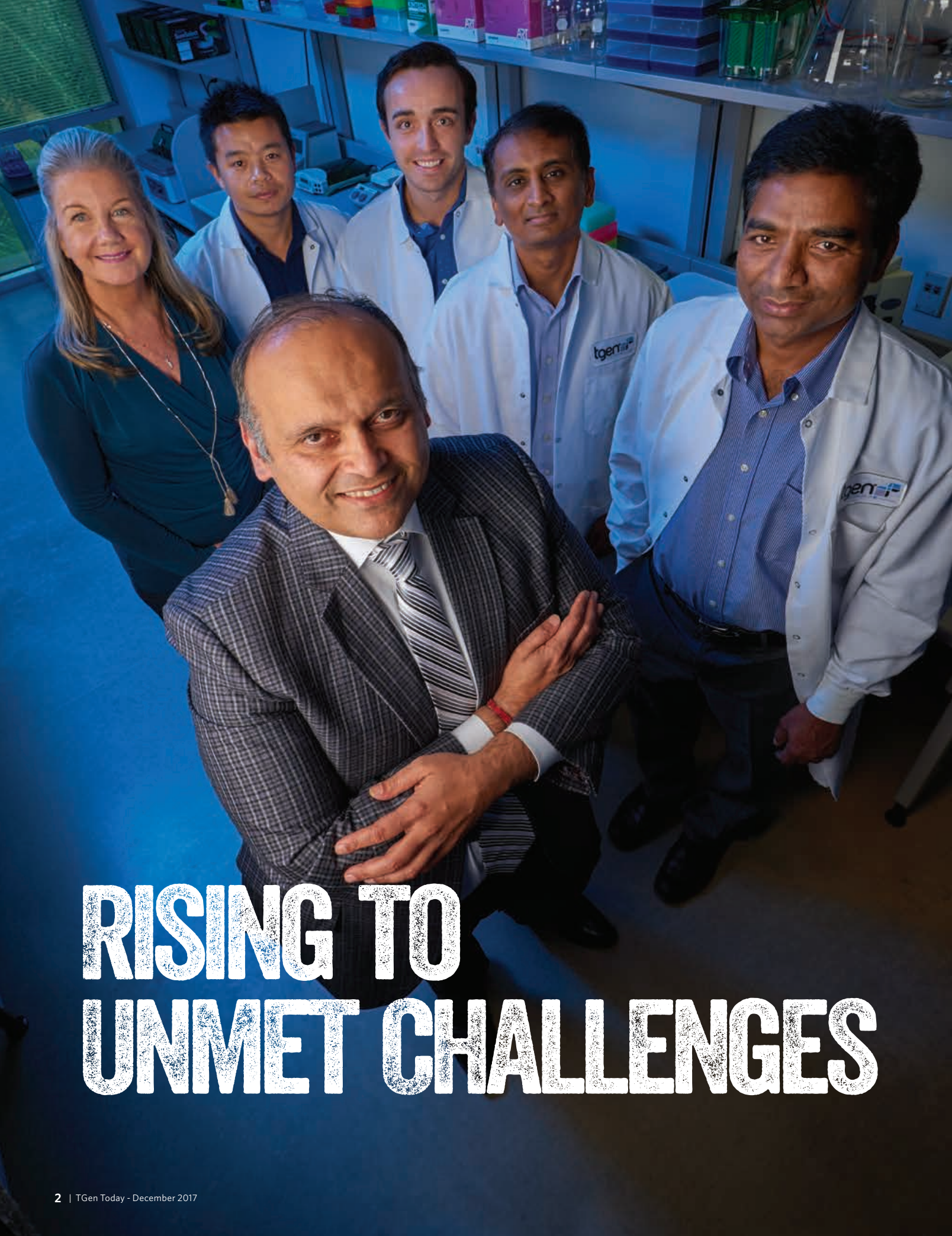
Enlisting Trinidad and Tobago in a \$1 million effort to support the John E. Sabga Clinical Trial for Pancreatic Cancer

TGen, the Translational Genomics Research Institute, is an affiliate of City of Hope. We are an Arizona-based, nonprofit medical research institute dedicated to conducting groundbreaking research with life-changing results. We work to unravel the genetic components of common and complex diseases, including cancer, neurological disorders, infectious disease, and rare childhood disorders. By identifying treatment options in this manner, we believe medicine becomes more rational, more precise and, well, more personal. For more information, visit: [www.tgen.org](http://www.tgen.org). Follow TGen on Facebook, LinkedIn and Twitter @TGen.



## Listen Now: TGen Launches Monthly Podcast

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



# RISING TO UNMET CHALLENGES

## USING HIGH-PERFORMANCE COMPUTING TO DEVELOP AND TEST NEW CANCER THERAPIES

A mother and a mentor inspired Dr. Sunil Sharma to become an oncologist, but it is the challenge of cancer that continues to push him onward.

“When I was looking at my specialization, oncology was very attractive because there was a lot of science being done, but the therapeutic challenge hadn’t been met yet,” he recalled. “There was a whole unmet challenge in medicine that I wanted to be part of.”

Today, Dr. Sharma faces these challenges head-on at TGen as the newly appointed Deputy Director of TGen Clinical Sciences, Professor and Division Director of Applied Cancer Research and Drug Discovery. He is also Professor of Medicine at City of Hope and Chief of Translational Oncology and Drug Development at HonorHealth Research Institute in Scottsdale.

In his new roles, he stands on the shoulders of two giants: His mother, Dr. Urmil Sharma, and his mentor, Dr. Daniel D. Von Hoff, TGen Distinguished Professor and Physician-in-Chief.

A true pioneer, Dr. Urmil Sharma was the first woman from India to receive a fellowship at the Royal College of Radiologists in England. Following her training, she returned to India and ultimately retired as a dean at the All India Institute of Medical Sciences — what many consider to be the Harvard of India.

“She was my hero and the person that inspired me to go into medicine,” Dr. Sharma explained. “She was a mold-breaker as a woman — to be educated abroad in the 1960s and then come back and basically set up oncology in India. There are hundreds of thousands of people that she had a hand in training.”

When he was applying for fellowships of his own in the 1990s, Dr. Sharma turned down a prestigious opportunity at M.D. Anderson Cancer Center to go to the University of Texas-San Antonio and work with Dr. Von Hoff on Phase 1 clinical trials and drug development.

“I have had the gratifying responsibility of helping train more than 2,200 budding cancer doctors,” said Dr. Von Hoff, who also serves as Chief Scientific Officer and the Virginia G. Piper Distinguished Chair for Innovative Cancer Research at HonorHealth. “I couldn’t be more excited to have one of my top students, and now an esteemed colleague, Dr. Sharma, join me in pursuing the use of genomic science to help bring precision medicine solutions to our patients.”

The Sharma lab will collaborate with Dr. Von Hoff in the clinic and also on new approaches to colon and pancreas cancer.

Dr. Sharma is also focused on cancers that lack effective therapies: adrenocortical carcinoma (ACC) and small cell carcinoma of the ovary, hypercalcemic type (SCCOHT). Both are rare and deadly cancers where TGen scientists have made recent discoveries. The next step is translating those discoveries into patient benefit.

For ACC, Dr. Sharma is working closely with patient advocacy groups and TGen Foundation to launch new clinical trials with our partners at HonorHealth and Baylor Research Institute in Dallas.

“We don’t like to work on things that have an obvious solution already. If there are existing drugs that are good, they can use those drugs,” explained Dr. Sharma, who came to TGen after nine years at the Huntsman Cancer Institute in Utah. “There are a large number of druggable proteins that haven’t been worked on,

“There are a large number of druggable proteins that haven’t been worked on, and we want to contribute in a way that is going to add to the repertoire for cancer therapy.”

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With Research Associate Professor Dr. Hariprasad Vankayalapati and Research Assistant Professor Dr. Mohan Kaadige, the Sharma Lab uses high-performance computing to design and test virtual drugs on targeted proteins. They then synthesize the compounds “in real life” and test the computer hypothesis in the lab, going back and forth between the real and virtual worlds to determine their effectiveness on the challenge at hand.

Their innovative process works: Dr. Sharma helped launch two drug development firms, Beta Cat Pharmaceuticals and Salius Pharmaceuticals. While working for Swiss-based Novartis, he helped develop anti-lung cancer drugs and immunotherapies that activate the body’s own immune system against cancer cells.

One challenge Dr. Sharma would like to investigate is also very personal: In the last two years, his mother was diagnosed with Alzheimer’s disease. He has started discussions with Dr. Matt Huentelman, TGen Professor of Neurogenomics,

about his research into the sixth-leading cause of death in the United States.

“This is personal to me, but it’s also a problem that TGen is working on,” Dr. Sharma said. “We feel like we’re experts in building drugs, but on the other hand, we can’t be domain experts on the biology and the things to go after. We can make drugs for Alzheimer’s, but we can’t be the experts on Alzheimer’s. The urgency that TGen has to get these advances into the clinic is attractive, and TGen has the ecosystem to develop these ideas.”

PHOTO: Dr. Sunil Sharma (front) with the Sharma Lab (left to right) Teri Richards, Executive Assistant; Dr. Zhaoliang Li, Post-Doctoral Fellow; Trason Thode, Research Associate; Dr. Mohan Kaadige, Research Assistant Professor, and Dr. Hariprasad Vankayalapati, Research Associate Professor

TGen North Research Associate Michael Valentine works with infectious diseases like tuberculosis to protect public health.

## WHEN IT COMES TO TUBERCULOSIS, SECONDS MATTER

TGen North stands guard against this worldwide threat

Each year across the globe, nearly 2 million people die of tuberculosis (TB) — that's one death every 17 seconds.

"TB is still one of the great health threats in the world," said Dr. David Engelthaler, Co-Director of TGen's Pathogen and Microbiome Division, or TGen North, in Flagstaff, Arizona.

TB is an infectious disease caused by *Mycobacterium tuberculosis* (*Mtb*) bacteria, which attacks the lungs and is spread through tiny droplets released into the air from coughs and sneezes.

The leading infectious disease worldwide, TB infects nearly 1 in 3 people on the planet, more than 2.5 billion human beings. And while most develop no symptoms, more than 10 million cases occur annually, more than the second- and third-leading infectious health threats — HIV and malaria — combined.

Through the advent of modern medicine, TB infections are

rare in the U.S. and other developed nations. But for those living in underdeveloped regions in countries such as India and South Africa and the eastern part of Europe, TB afflicts greater than half of the population. With an increasingly mobile world population, the need to protect the health of Americans is ever more dependent on protecting the health of all humanity.

"TB is a chronic condition that is part of the daily life of much of the world's population," Dr. Engelthaler said. "Here in the U.S., hardly anyone is infected with TB. In other parts of the world, almost everyone knows someone who is infected with TB. That's really tragic."

And researchers are working against the clock. TB is continually mutating, creating drug-resistant varieties as fast as science's ability to create effective new antibiotic counteragents.

### The Power of Partnership

In May, Tucson's Critical Path Institute (C-Path) forged a partnership with TGen North as part of their \$1.1 million grant from the Bill & Melinda Gates Foundation to significantly enrich its TB data platform developed to better understand the genetic basis of drug resistance in *Mycobacterium tuberculosis*. Over the next three years, TGen North will sequence more than 12,000 TB samples, or isolates, from more than 35 countries around the world.

This project will help track and map the ever-changing genomic signatures of this disease, as it continues to mutate and evolve. By exactly mapping different types of TB isolates, TGen North will help guide a global precision-medicine response to this elusive health threat.

"This effort will provide us with a complete view of the DNA of TB from across the globe," said Dr. Engelthaler, adding that the primary goal of the effort is to make all the sequencing information publicly available. "By bringing all of this data together, it will essentially benefit the world's researchers and clinicians working on TB. It's about building a global resource. The abilities of all these researchers will be brought to bear."

### Creating a Precise Genetic Test for TB

TGen North is also working to develop a Rapid Drug Sensitivity Test (RDST), a diagnostic kit that is both compact and economical for use in the world's most remote locations, providing physicians with an exact identification of each patient's strain of TB. Such a test would help ensure that doctors get the right drugs to treat each patient's specific type of TB.

"We believe that new targeted sequencing technologies can help physicians care for patients with drug-resistant TB," Dr. Engelthaler said. "Drug-resistance occurs when the wrong antibiotics are prescribed at the wrong time. This new approach is designed to not only help doctors better treat patients, but to help slow or stop the global threat of multi-drug resistant TB."

Collaborating with researchers in California — University of California, San Francisco and University of San Diego — Cape Town, South Africa, and the eastern European country of Moldova, TGen North faculty proved the potential of such a test using Single Molecule-Overlapping Reads (SMOR) technology developed at TGen, which precisely identifies variants of TB, even in cases where other technologies found no drug-resistant mutations.

### 'It's not quite the tricorder, but it could be'

Known as an amplicon sequencing tool, an RDST diagnostic includes molecules and compounds that quickly extract DNA from a sample of saliva and mucus and feed it into a desktop sequencer, where the billions of bits of data can be automatically analyzed and the type of TB quickly identified.

Currently, most samples must be grown in a petri dish before testing to identify which drugs might work. Because *Mtb* grows

so slowly, this process often takes two to six weeks and leaves physicians guessing how to treat patients, which often leads to the wrong medication for a specific infection.

If successful, the TGen test would provide an exact analysis in as little as 24 hours. And on the horizon is an even newer generation of "nanopore" sequencers, which would be capable of delivering results in less than two hours.

Think of how fictional *Star Trek* physicians analyze patients by using a hand-held "tricorder" scanner to produce an instant diagnosis.

"We can see a day in the not-too-distant future when, with this kind of test, you could get results back in a couple of hours," Dr. Engelthaler said. "You could get the results while the patient is still in the clinic. It's not quite the tricorder, but it could be someday."

### TGen North strives to protect public health

Such exciting technological advances could someday put such devices in the hands of physicians everywhere, Dr. Engelthaler said.

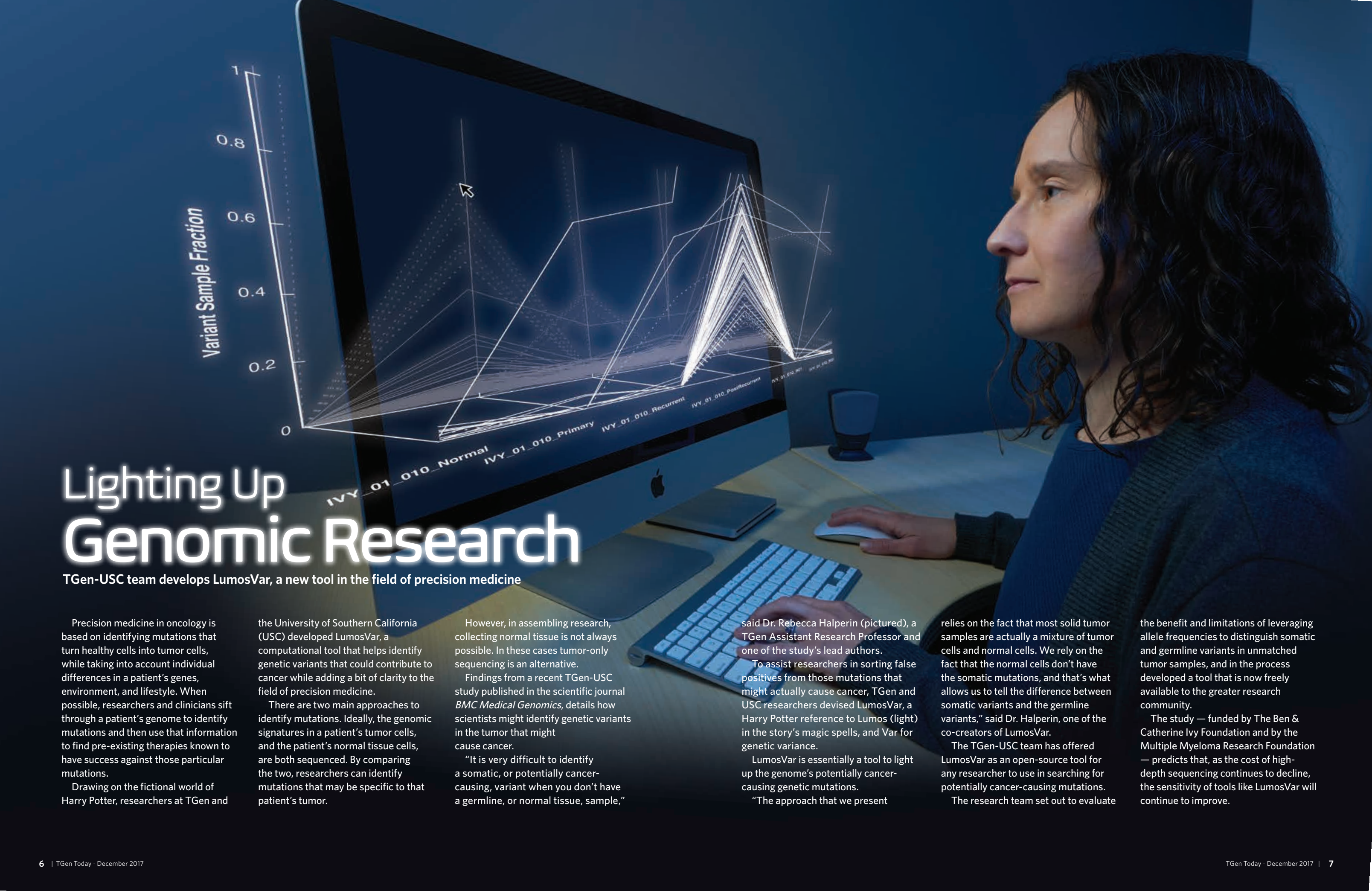
"These tools give us so much more precision and accuracy so that, at the very beginning of an infection," he said. "We could detect the very first resistant bacteria, and give doctors time to provide the precise drug treatment, and hopefully, allow their patients to be cured of TB."

This effort is yet another example of how the translational efforts of TGen North are helping protect public health, working with local, state, national and international health agencies, non-governmental organizations and private industry.

"We're able to use these next generation tools to advance the state of public health," Dr. Engelthaler said, "to improve our ability to do disease tracking and surveillance; to identify outbreaks, and to chase down some of these long-time problems, like antibiotic resistance."



Watch Dr. David Engelthaler's TEDx presentation: [www.youtube.com/watch?v=XjODyyB1knc](http://www.youtube.com/watch?v=XjODyyB1knc)



# Lighting Up Genomic Research

TGen-USC team develops LumosVar, a new tool in the field of precision medicine

Precision medicine in oncology is based on identifying mutations that turn healthy cells into tumor cells, while taking into account individual differences in a patient's genes, environment, and lifestyle. When possible, researchers and clinicians sift through a patient's genome to identify mutations and then use that information to find pre-existing therapies known to have success against those particular mutations.

Drawing on the fictional world of Harry Potter, researchers at TGen and

the University of Southern California (USC) developed LumosVar, a computational tool that helps identify genetic variants that could contribute to cancer while adding a bit of clarity to the field of precision medicine.

There are two main approaches to identify mutations. Ideally, the genomic signatures in a patient's tumor cells, and the patient's normal tissue cells, are both sequenced. By comparing the two, researchers can identify mutations that may be specific to that patient's tumor.

However, in assembling research, collecting normal tissue is not always possible. In these cases tumor-only sequencing is an alternative.

Findings from a recent TGen-USC study published in the scientific journal *BMC Medical Genomics*, details how scientists might identify genetic variants in the tumor that might cause cancer.

"It is very difficult to identify a somatic, or potentially cancer-causing, variant when you don't have a germline, or normal tissue, sample,"

said Dr. Rebecca Halperin (pictured), a TGen Assistant Research Professor and one of the study's lead authors.

To assist researchers in sorting false positives from those mutations that might actually cause cancer, TGen and USC researchers devised LumosVar, a Harry Potter reference to Lumos (light) in the story's magic spells, and Var for genetic variance.

LumosVar is essentially a tool to light up the genome's potentially cancer-causing genetic mutations.

"The approach that we present

relies on the fact that most solid tumor samples are actually a mixture of tumor cells and normal cells. We rely on the fact that the normal cells don't have the somatic mutations, and that's what allows us to tell the difference between somatic variants and the germline variants," said Dr. Halperin, one of the co-creators of LumosVar.

The TGen-USC team has offered LumosVar as an open-source tool for any researcher to use in searching for potentially cancer-causing mutations.

The research team set out to evaluate

the benefit and limitations of leveraging allele frequencies to distinguish somatic and germline variants in unmatched tumor samples, and in the process developed a tool that is now freely available to the greater research community.

The study — funded by The Ben & Catherine Ivy Foundation and by the Multiple Myeloma Research Foundation — predicts that, as the cost of high-depth sequencing continues to decline, the sensitivity of tools like LumosVar will continue to improve.

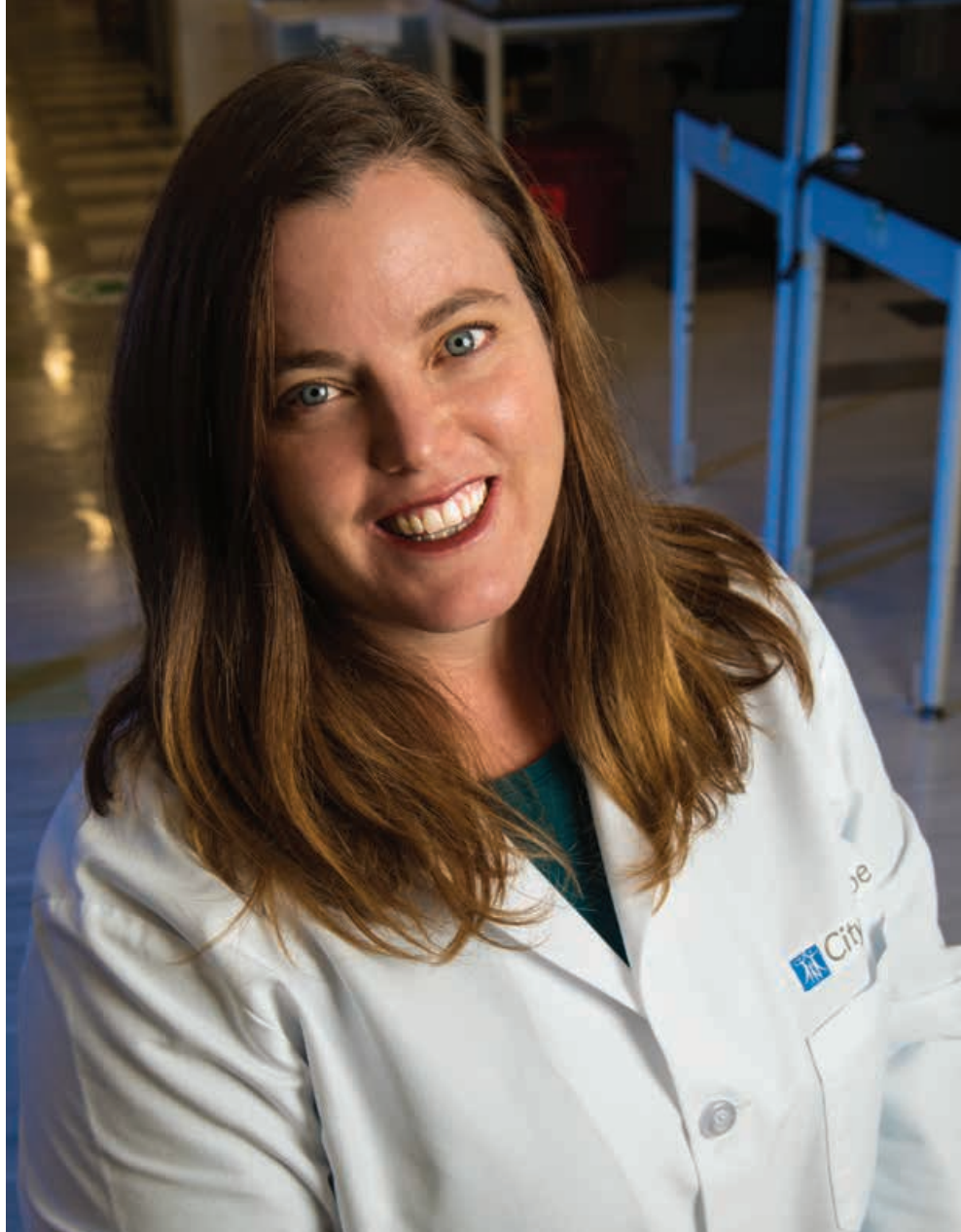


Photo courtesy of Craig Takahashi, City of Hope

# Bild-ing Collaboration

**Director of new Women's Health Program at TGen believes teamwork is key to defeating cancer**

DR. ANDREA BILD, WHO RECENTLY BECAME THE FIRST MAJOR JOINT RECRUIT OF THE YEAR-OLD AFFILIATION BETWEEN TGEN AND CALIFORNIA'S CITY OF HOPE, AIMS TO COMBAT CANCER USING MULTIDISCIPLINARY TEAMS THAT TARGET A CANCER'S COMMON VULNERABILITIES.

Key to Dr. Bild's research program is the realization that when patients no longer respond to initial treatments —when their cancer becomes resistant to certain drugs— there may remain a way to target the evolving cancer. Identifying characteristics (phenotypes) along the biological signaling pathways within cells, and studying the patterns of these potentially cancer-related phenotypes, might lead to new therapeutics.

"As a postdoc, and then later leading my own research team, I realized that we had to move beyond identifying mutations in tumors alone and that we should be using the more common phenotypes as information that can help treat patient tumors in an individualized manner," she said.

From an initial *Nature* paper in 2006 (*Oncogenic pathway signatures in human cancers as a guide to targeted therapies*), which was the foundation for the phenotype analysis of tumors, up to a current *Nature Communications* paper published last month (*Combating subclonal evolution of resistant cancer phenotypes*), Dr. Bild is combating tumor phenotypes in the lab and in the clinic.

At TGen, Dr. Bild holds the titles of Professor, Integrated Cancer Genomics and Director of TGen's new Women's Health Program. At City of Hope, she is a Professor in the Department of Medical Oncology and Therapeutics Research.

Through her undergraduate training at the University of Florida and doctoral work at the University of Colorado, her academic focus is trans-disciplinary as a pharmacologist and systems biologist. Her inclination has always been the translational effort of moving laboratory discoveries as soon as possible to patients.

She understands the need — in complicated inquiries — to assemble a band of experts in a variety of fields: from physicians to clinicians, pathologists, biologists and bioinformaticians.

And did we mention fun? "When there's opportunities on complex problems like this, the way you bring people together is finding those who share your interests, and have the skillsets needed," she said, "and then making it fun for everyone to work together."

Dr. Bild's number one priority is helping the patient.

*"The way you bring people together is by finding those who share your interests, have the skillsets needed, and then making it fun for everyone to work together."*

"For me, what that means is figuring out therapeutic strategies that either prevent (drug) resistance from developing, or combat a resistance state," she said. "That's my long-term objective."

## Center of HOPE

Dr. Bild brings with her a \$9 million, 5-year grant that started in April from the National Cancer Institute (NCI) — a grant called the *Center of HOPE* (Heterogeneity Of Phenotypic Evolution). She could not have guessed when she named the grant that she would soon be working for a healthcare enterprise that also had "hope" in its name.

When she submitted her *Center of HOPE* grant application, she was still an Associate Professor of Pharmacology and Toxicology, and Director of the Genome Sciences Program at the University of Utah. It was there that she met Dr. Sunil Sharma (see cover story) an oncologist who specializes in

gastrointestinal cancers, such as pancreatic cancer, but who also consults on a variety of cancers, including the type of breast and ovarian cancers that is the main focus of Dr. Bild.

Much of Dr. Bild's work is tied to her membership in NCI's Cancer Systems Biology Consortium, where she is a Principal Investigator of multi-institutional grants. Her team focuses on the development and application of genomic-based tools for cancer prevention and treatment. One defining method of her inquiries is to keep her

research directly linked to the patients she is trying to help through the use of actual patient tumor samples, rather than cell lines.

"The foundation of our program is based on what happens in patient tumors so that we can ensure our research is relevant," she said, "and so we're able to use systems biology to track the complexity of evolving resistance states over the course of treatment. You can only get data that tells you exactly what is happening with the patient if you use tumor cells from the patient."

## The Mathematics of Precision Medicine

Dr. Bild also experiments with mathematical formulas as a way of probing new ways to attack cancer. It was a talk by Dr. Frederick Adler, a Harvard-Cornell-UC Davis-trained Professor of Mathematics and Biology at the University of Utah, which enticed Dr. Bild to study how the evolution of plants might help explain how cancer evolves

and evades treatment.

In the analogy with plant ecology, subclones correspond to plant species, cells to individual plants (which have both a species and a phenotype), and the tumor to the entire community.

"How do populations of different plants interact with each other? How do plant populations survive when there's other invasive species?" she said. "We now characterize single-cell phenotypes in patient tumors as they are emerging under the stress of therapeutics — chemotherapies — and use that

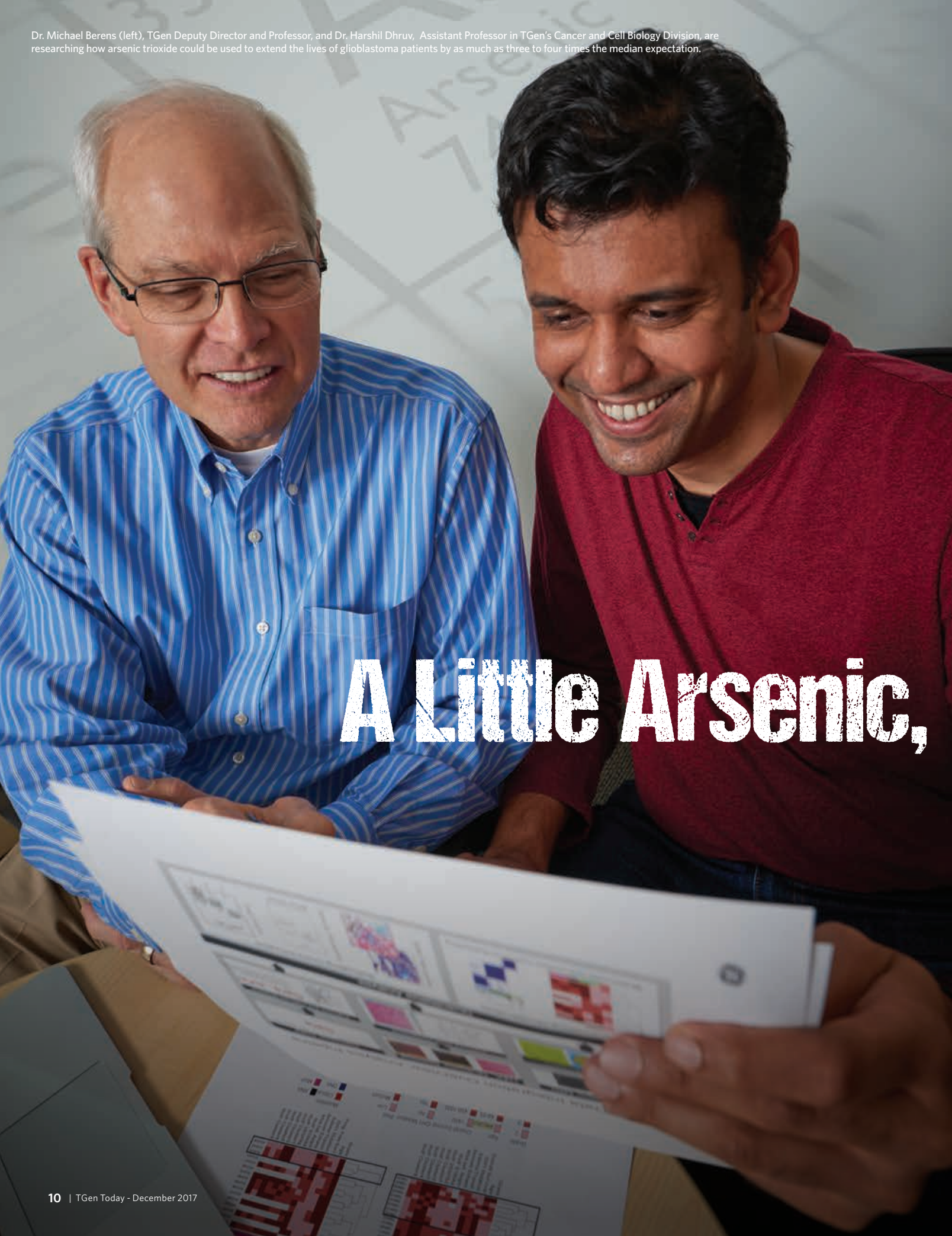
data in models that, initially, were derived from plant biology.

"We're using really innovative mathematical models taken from plant evolution to profile our patient tumor cells and identify vulnerable points at which we could use novel therapeutic strategies."

It holds promise of breakthroughs by looking at cancer in ways no one else has tried before, though Dr. Bild says there are no guarantees: "We're taking a completely new mathematical approach to problems. That could yield different ways of looking at these complex systems that haven't been tried before. We hope it yields something meaningful."

More than anything, she is excited to be working at TGen and City of Hope where she can apply her discoveries to patients.

"Given City of Hope's strength in medical oncology, and TGen's computational expertise," Dr. Bild said, "we can lead the way in incorporating complex genomic information in drug treatment decisions."



## A Little Arsenic,

Arsenic is one of nature's basic elements — number 33 on the periodic table — and is used in everything from car batteries to semiconductors. But it is perhaps best known for its sinister use as a poison, especially in mystery-novel whodunits.

Now, a team of researchers at TGen and Northwestern University are shaking off the cobwebs of Sherlock Holmes and Agatha Christie to show how extremely low dosages of a particular form of this element — arsenic trioxide — may have a remarkably positive effect on patients with the most common and deadly of brain tumors, glioblastoma multiforme, or GBM.

GBM rocketed into public consciousness this summer when Arizona's U.S. Sen. John McCain, Chairman of the TGen Foundation's National Advisory Council, was diagnosed with this aggressive disease.

For years, arsenic trioxide has been used to fend off a rare subtype of blood cancer known as acute promyelocytic leukemia (APL). Its potential use against

The origin of this new study had all the serendipitous turns of a mystery novel.

TGen had recently identified arsenic trioxide among a library of 650 compounds screened for potential use against different subtypes of glioblastoma. While Dr. Dhruv was presenting these findings at a scientific conference, he met Dr. Jonathan Bell, who at the time was a graduate student in the Medical Scientist Training Program at Northwestern University. He described his work, showing resistance of a specific subtype of GBM against arsenic trioxide. In two clinical studies they examined, the therapeutic effects of arsenic trioxide were initially dismissed. But as Drs. Dhruv and Bell drilled down into the studies, they discovered that a specific subtype of GBM cells were more responsive to the arsenic trioxide treatment.

Northwestern was involved in one of the clinical trials that tested the efficacy of arsenic trioxide in combination with temozolomide (TMZ) and radiation in the treatment of GBM. Researchers at Northwestern were able to share

would receive TMZ, which is the current standard-of-care drug for GBM patients.

"This is an amazing convergence of complimentary thinking," Dr. Berens said. "We tripped over a clinical partner who said, 'Oh, we've already done the (preliminary) clinical trial.'"

Researchers reassessed the earlier clinical trials and zeroed in on mesenchymal (MES) and proneural (PN) glioma subtypes, whose genomic signatures differ according to distinct underlying misbehaving genes.

An advantage of arsenic trioxide is that it is a small molecule, able to penetrate the network of ultra-small capillaries — the blood-brain barrier — that surrounds the brain and spinal fluid and protects the central nervous system from most toxins and spikes in hormones. It is this barrier that prevents most other anti-cancer drugs from attacking brain tumors.

"Rather than treat all patients, we want to design a prospective clinical trial that we can enrich for those patients whose genomic signatures indicate they would be the best candidates for success," Dr.

## A Lot of Potential



GBM was documented in a recent study published in *Molecular Cancer Research*.

"Our findings show that, for some patients, arsenic trioxide could be a powerful therapy that could extend the lives of certain glioblastoma patients by as much as three to four times the median expectation," said Dr. Harshil Dhruv, an Assistant Professor in TGen's Cancer and Cell Biology Division and one of the study's authors.

Median survival of glioblastoma patients is only 15 months, and survival statistics have improved only minimally over the past three decades. An estimated 17,000 Americans will die this year of brain and other nervous system cancers.

biospecimens from their clinical trial with TGen.

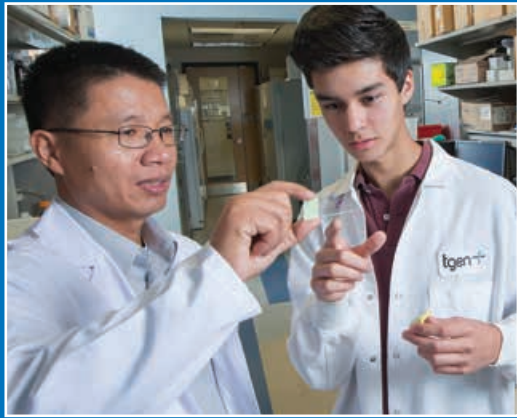
"We were then able to identify these particular patients as having the same genomic signatures as those we had tentatively identified in our computer and laboratory screenings of potential therapies," Dr. Dhruv said.

The next step will be to validate the findings published in *Molecular Cancer Research* by initiating a new clinical trial specifically designed to match arsenic trioxide with glioblastoma patients that have a specific genomic signature, according to Dr. Michael Berens, a TGen Deputy Director and Professor in TGen's Cancer and Cell Biology Division, and one of the study's authors. These patients also

Dhruv said. "This would be a biomarker-driven, precision-medicine clinical trial for glioblastoma — a way to match the right drug to the right patient."

Funding for this study — *Differential Response of Glioma Stem Cells to Arsenic Trioxide Therapy is Regulated by MNK1 and mrna Translation* — was provided by grants from the National Institutes of Health, the Department of Veterans Affairs, and The Ben & Catherine Ivy Foundation.

**LEARN MORE |** To learn more about this arsenic discovery and about our latest glioblastoma research, listen to TGen Talks our podcasts with Dr. Berens and Dr. Dhruv. Find TGen Talks at [tgen.org](http://tgen.org) or iTunes or SoundCloud.



20 Arizona high school students will have the opportunity to spend two weeks with TGen's world-class scientists, learning advanced scientific and professional skills.

### TGen Unveils Bioscience Leadership Academy for summer 2018

TGen and Helios Education Foundation have created a new biomedical studies program designed specifically for high school students. ■ TGen Bioscience Leadership Academy will launch in summer 2018, offering 20 Arizona high school students the opportunity to spend two weeks with TGen's world-class scientists, learning advanced scientific and professional skills. Each graduate of the program will receive a \$1,000 scholarship. ■ The inaugural class runs from June 18-29, 2018. Applications open Jan. 3, and close Feb. 9. Applicants must be 16 by the time the program starts, and about to enter their junior or senior year at a school in Arizona. Only one student will be selected each summer from any one high school. ■ For more information, visit [tgen.org/academy](http://tgen.org/academy)

### Key to the Cure Features Fashion by ETRO

Against a backdrop of rich color and intricate designs by ETRO, the 19th Annual Key to the Cure brought more than 150 influential women and men together to fight cancer with fashion at Saks Fifth Avenue in Phoenix. ■ Chaired by Carole Moreno, Jacquie Dorrance and Katie Mueller, the runway show and gourmet breakfast raised more than \$80,000 for cancer research at TGen. ■ Dr. Ingrid Hedenfalk, an associate Professor in Oncology at Lund University Cancer Center in Sweden, talked about TGen's worldwide reputation as a collaborator and leader in cancer research. Dr. Muhammed Murtaza, TGen Assistant Professor, shared new directions the institute is taking in breast cancer research.



Dr. Muhammed Murtaza, TGen Assistant Professor, shared new directions the institute is taking in breast cancer research during the 19th Annual Key to the Cure.

### TGen secures Chan Zuckerberg grant for 'single-cell' sequencing

TGen has received a grant from the Chan Zuckerberg Initiative, which will help revolutionize how researchers identify the genetic source of diseases and how best to treat each patient. ■ Sequencing — or spelling out — the billions of data bits of an individual's genetic code has relied, until recently, on sequencing multiple cells and using averages to get results. This new project, part of the international Human Cell Atlas project, will help enable researchers to get results by sequencing individual cells. ■ Single-cell RNA sequencing promises to enable researchers to more quickly and precisely identify the cellular processes underlying disease states and to predict if a diseased tissue will be susceptible, or resistant, to drug therapies and eventually lead to better patient care

### Colleen's Dream donates \$100,000 for ovarian cancer research

Colleen's Dream Foundation recently donated \$100,000 to TGen in support of clinical trials that could lead to better treatments for a rare type of ovarian cancer that mostly afflicts girls and young women. The donation follows a successful series of fundraising events organized by Colleen's Dream during September for National Ovarian Cancer Awareness Month. ■ TGen led a team that discovered a mutation in a gene known as SMARCA4. SMARCA4 drives a specific type of extremely aggressive ovarian cancer known as Small Cell Carcinoma of the Ovary, Hypercalcemic Type (SCCOHT). This type of ovarian cancer usually does not respond to standard chemotherapy, and 65 percent of patients die within 2 years. TGen research already has resulted in a simple new test to diagnose SCCOHT.



Chloe Cundiff held a lemonade stand in the lobby of TGen's headquarters in Phoenix, one of the successful series of fundraising events organized by Colleen's Dream.

### STEP-N-OUT Supports Patients in Arizona, Around the Globe

More than 1,000 walkers, runners, patients, survivors and supporters kicked off Pancreatic Cancer Awareness Month at the 12th annual STEP-N-OUT 5K FUNdraiser on November 5 at Scottsdale Sports Complex. ■ Led by Team Lee, STEP-N-OUT raised more than \$137,000 to support TGen's pancreas cancer clinical trials at HonorHealth in Scottsdale. Three survivors — Sandra Forrest, Stan Vitikas and Andy Kent — credited those trials as the reason they were able to participate in the opening ceremonies. ■ "Almost three years later, I stand here with no active cancer, able to thank you for your wonderful generosity and my friends and brilliant doctors and nurses that saved my life," said Sandra, from Peoria, Ariz. "I feel that a cure is just around the corner. I have hope for not only myself, but for many like me." ■ STEP-N-OUT was sponsored by the Arizona Diamondbacks, Phoenix NAP LLC, Vestar and Wells Fargo. ■ Save the date for Sunday, November 4, 2018 for the 13th annual STEP-N-OUT FUNdraiser.



Runners get ready at the 12th annual STEP-N-OUT 5K FUNdraiser to support TGen's pancreas cancer clinical trials.

### WelderUp "Cancer Car" Raises Funds for Childhood Cancer

Featured on the hit Discovery Channel show *Vegas Rat Rods*, the Cancer Car was inspired by a 2-year-old boy's triumph over kidney cancer. ■ Forged by Steve Darnell and his team at WelderUp, the Cancer Car sold for \$60,000 to an anonymous donor at the Barrett-Jackson Collector Car Auction in October in Las Vegas. ■ "My vision for this car was to make it look like it's hitting cancer head on," Darnell explained. ■ Starting with its debut at Barrett-Jackson in Scottsdale last January, the Cancer Car drew crowds in Florida and Connecticut. ■ All proceeds from the Cancer Car benefited TGen's childhood cancer research. Barrett-Jackson returns January 13-21 in Scottsdale.



Forged by Steve Darnell and his team at WelderUp, the Cancer Car sold for \$60,000 to an anonymous donor at the Barrett-Jackson Collector Car Auction.

## Upcoming Events Benefitting TGen



#### Barrett-Jackson Collector Car Auction [Scottsdale, AZ]

January 13-21, 2018

World's greatest collector car auction benefits TGen colorectal cancer research [www.barrett-jackson.com](http://www.barrett-jackson.com)

#### Chip in for Kids [Scottsdale, AZ]

February 22, 2018

Join us at Top Golf for an evening of fun contests and prizes to raise funds for TGen's Center for Rare Childhood Disorders [www.tgen.org/events](http://www.tgen.org/events)

#### Kidz 4 Causes Run for Rare Disease Research [Phoenix, AZ]

February 25, 2018

Annual 5K and 1-mile run/walk benefits TGen's Center for Rare Childhood Disorders. [www.tgen.org/events](http://www.tgen.org/events)

#### 8th Annual Fitness for the Cure [Phoenix, AZ]

April 29, 2018

Spin to win the fight against cancer. Get ready to ride, run and sweat to support TGen's cancer research at this annual fitness event. [www.tgen.org/events](http://www.tgen.org/events)



Kidz 4 Causes annual 5K and 1-mile run/walk benefits TGen's Center for Rare Childhood Disorders.



## Island Nation Joins Worldwide Fight against Pancreas Cancer



TGen Foundation President Michael Bassoff (center) with the children of John and Natalie Sabga. Amanda Sabga (left) and Matthew Sabga (right) at the November kickoff event.

When John Sabga was diagnosed with pancreas cancer in April 2016, he and his wife Natalie joined a close-knit community they never knew existed.

"You create a special bond among pancreatic cancer patients because the statistics are so grim," Mrs. Sabga said from her home in Trinidad and Tobago. "It's like a secret you're all fighting together. Everyone shared the same passion and the same compassion."

The disease would take John's life in nine short months and inspire in Natalie a passion to heal their nation.

Mrs. Sabga enlisted business and community leaders throughout Trinidad and Tobago in a \$1 million effort to support the John E. Sabga Clinical Trial for Pancreatic Cancer, led by TGen and HonorHealth. She hopes the trials will have an immediate impact on the health of her nation.

A tiny two-island nation, Trinidad and Tobago has seen a five-fold increase in pancreatic cancer deaths since 1990. On November 16, World Pancreatic Cancer Day, TGen Foundation President Michael Bassoff visited Trinidad and Tobago for the kickoff of the effort and met with Trinidad and Tobago President Anthony Carmona and the Honorable Terrence Deyalsingh, the nation's minister of health.

"After journeying with John during his battle with this horrible disease," Mrs. Sabga said, "I was convinced that something had to be done to ensure better treatment options for pancreatic cancer."