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TGen Today

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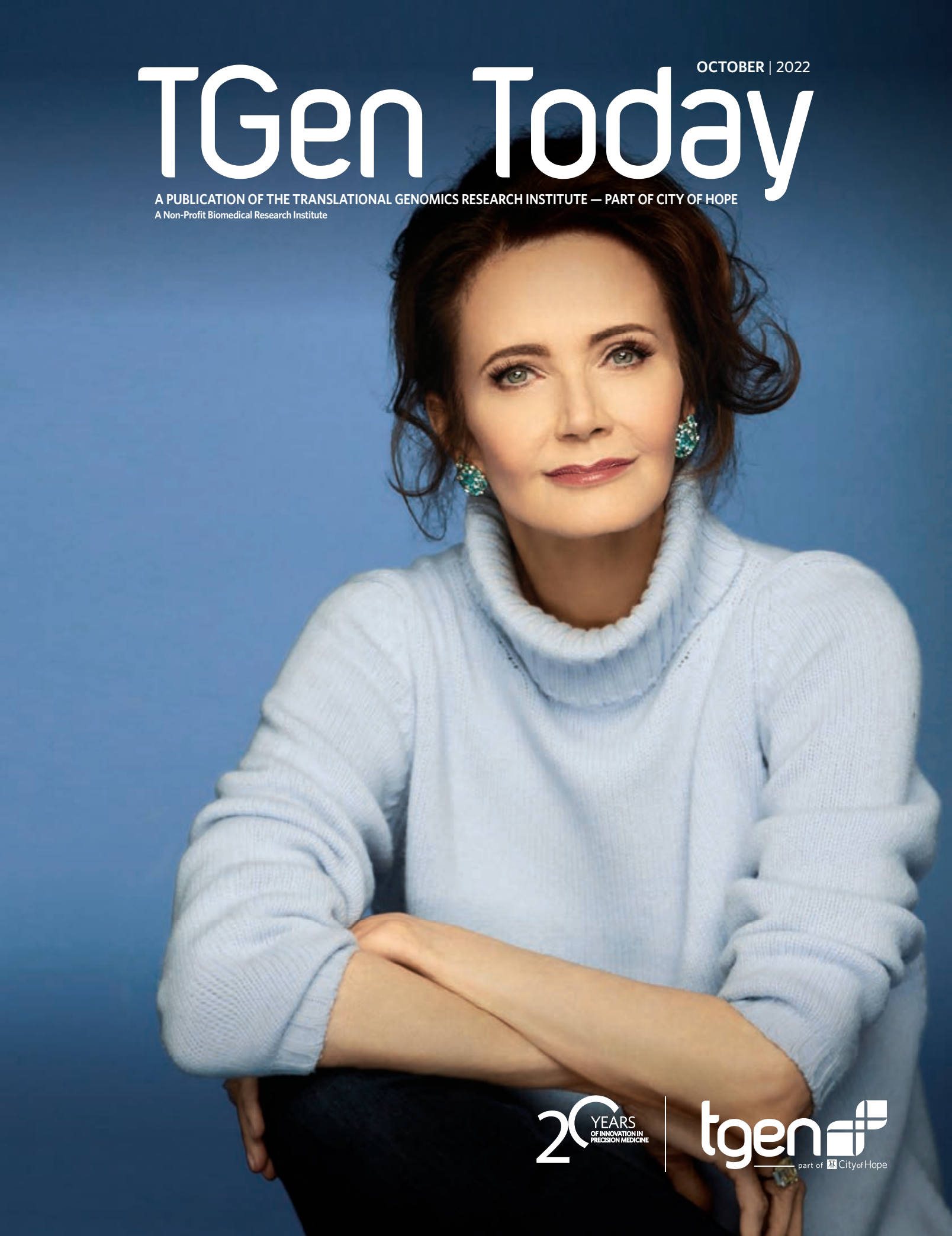

20 YEARS OF INNOVATION IN PRECISION MEDICINE

tgen part of City of Hope

A Look Inside...

Dear Friends,

If asked to define the theme this edition of *TGen Today* conveys, I would say the art of humanity.

The individuals profiled, the research, interactions, and purpose behind each story illustrates this through a mix of loss, determination, and driving one's destiny. The stories—their stories—define not only where the Institute is today, but also where we are going, carried forward by the momentum created through past achievements and medical advances.

If you follow the celebrity featured on our cover, you will know that not even Lynda Carter Altman (a.k.a. Wonder Woman) could save her husband, Robert, from his fateful diagnosis. Lynda's is a story about honoring a beloved spouse and partner, of making a difference for future generations faced with similar health challenges, and a deep belief that TGen and City of Hope can help accomplish both.

You'll also read about Rick Stanton's cancer journey which personifies how research and patient care are changing constantly. The shifts, some subtle, a few seismological, redefine with each advancement, the impact of precision medicine and how patients benefit. An advanced prostate cancer patient, Rick's story finds him at the center of a TGen-led study designed to help aggregate his personal cancer data and perform subsequent analyses that could lead to a treatment that will save his life.

For Rick and TGen, the future is now.

You need look no further than the work of Drs. Cristian Tomasetti and Kamal Lahouel to believe greater advances are on the horizon.

Newly recruited to TGen and City of Hope, the pair bring a passion for merging mathematical modeling, statistical methods and machine learning to transform genomic data into new advances toward disease detection and a deeper understanding of a patient's response to treatment. These highly sought mathematicians are making a name for themselves in the field of applied science, as their skills provide solutions in many areas of biomedical research.

Our feature on Dr. Vinodh Narayanan takes you inside the man's heart and reveals a personal perspective on how the power of genomics can change lives for the better, and how he and his colleagues help those in search of much-needed answers when they visit TGen's Center for Rare Childhood Disorders.

These are but a few of the stories that frame TGen's current efforts as we explore new avenues of research and treatment breakthroughs.

In closing, I will say that I have never felt more optimistic that our work as part of the City of Hope enterprise will expand the boundaries of what's possible in research and treatment. Beyond that, however, lies a far simpler truth: we could not have done it without your continued belief in TGen and your support of our work in precision medicine.

I hope you enjoy the read.

Best,

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

TGen Today

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PODCAST

TGen Talks is a monthly podcast that explores our latest science and discoveries. Find *TGen Talks* on the tgen.org homepage, through iTunes or on SoundCloud.

TGen's Nicholas Schork, Ph.D., (left) meets with Rick Stanton (center) and his daughter, Christy, to discuss the PEOPLES protocol, which allows Stanton to access his cancer data and request new analyses with the help of TGen researchers.

Power to the "PEOPLES"

TGen study offers path for late-stage cancer patients to leverage their own health data to guide their care

RICK STANTON THINKS IT MIGHT BE THE LITTLE things that count.

At a June virtual meeting of the cancer hackathon he's participating in, he's asking about a very little thing called an organoid. A lab-grown ball of his own prostate tumor cells, about as wide across as a strand or two of hair.

At the meeting, Payel Satterjee, Ph.D., explains how she and her team craft organoids from tumor cells, pitting them against a carefully curated list of drugs to find promising "hits" against a patient's unique cancer.

Maybe, Stanton thinks, an organoid could start bearing the brunt of what he's had to endure for four years and counting. He's an advanced prostate cancer patient, yes, but he's also a surfer and a guitar player. His latest bout of chemotherapy, however, has left his fingers tingling too badly to play.

And now one of his doctors is talking about the possibilities of yet another new drug.

"But I'd rather have you test it," he says, his lively face taking up center square in the Zoom discussion, "then, you know, then have me test it—"

"—then you go through the whole thing, yes, I understand that," Satterjee, chief scientist at SEngine Precision Medicine, finishes Stanton's sentence from her own square.

They laugh together. "Yeah," Stanton says. "So it's not just, 'oh wow, it didn't work. Sorry, bud.'"

IN MANY WAYS, STANTON IS LIKE A LOT OF CANCER patients. The endless blood draws, biopsies, scans, genetic testing, clinical trials, all of it creating a tidal wave of data that describes his unique cancer journey. He is nearing the end of the national guidelines for prostate cancer care, without a lasting response for his stage IV cancer.

But in another way Stanton is unique: he is the sole patient participant in TGen's PEOPLES Protocol, a new study that shows how patients can direct their own tidal waves of data to guide their future treatment.

The protocol (PEOPLES stands for Patient Engagements, Operational Practices, and Laboratory Environment Standardization) allows Stanton to access his cancer data and request new analyses with the help of TGen researchers.

Stanton meets weekly to talk through how best to organize and present his data that have been collected so far. The group, led by TGen's Nicholas Schork, Ph.D., also discusses new tests and analyses that could expand the range of treatment possibilities for Stanton.

The PEOPLES protocol was inspired in part by a growing "right to try" movement among patients, who advocate for access to experimental medicines or procedures for conditions not treatable by currently available drugs. Under the rubric of "compassionate care," for instance, the U.S. Food and Drug Administration now offers an Expanded Access Program for patients and their doctors to apply for some of these treatments.

If these programs exist for drugs, thought Schork, why not for data?

"For many people who are in the later stages of their cancer, the treatment guidelines no longer apply," he says. "If we're OK with people trying drugs at end of life, we should at the very least be OK with them trying to explore their data for information that may help lead to a drug."

Schork, along with his TGen colleagues Laura Goetz, M.D.

and Edward Kalpas, M.D., hope the protocol offers a way for Stanton and future patients to use their data safely and perhaps even creatively. The prostate cancer hackathon that Stanton participates in, organized by CancerHacker Lab founder Brad Power, is one of the pathways that the TGen researchers had in mind when they began the protocol.

"What Rick and the hackathons have been opening up for advanced cancer patients in general is more testing to guide personalized treatment decisions," Power says.

"Our motivation for this study was thinking about what data we could bring to the table to help the patients and interested physicians make decisions about the next steps," says Schork, "to make it less guesswork and more scientifically backed."

Stanton's motivation for participating?

"In a nutshell, it was the hope of a best chance to extend my life."

THERE'S ANOTHER WAY IN WHICH Stanton isn't a typical cancer patient, or a typical healthcare data consumer. He's an engineer, specifically one with 20-plus years of experience in bioinformatics and biological signaling. A family-run company, Stanton Biosciences, performs some of the same kinds of tumor testing that he's using to search for his next treatment.

So his discussions with Schork and colleagues about how to handle and sort through his data can take on a top-level technical tone. But even he is looking for new ways to understand what his data mean.

The engineer in him likes to visualize problems, he says, so he is creating a "battle map" of sorts. The battlefield consists of some of the complex concepts in cancer treatment—immunotherapy, the cell environment around the tumor, and the specific molecular signaling pathways that researchers know are related to certain cancers.

A patient's data are sort of like the battalions that have been mustered so far, placed on the battlefield to show "where and how it makes the most sense to intervene," he says.

Stanton thinks visualizations like the battle map can help people like his companion Brian McCloskey in the ongoing hackathon. McCloskey feels comfortable with data from his work as an e-commerce and tech marketing executive. But at this point in his advanced prostate cancer treatment, the father of three is facing a bewildering array of 17 possible treatment options.

"He was saying that I'm trying to understand my cancer and fight it, and it seems like I'm supposed to learn Ph.D. material in a few weeks just to know what this stuff means," Stanton says of McCloskey.

There's no real precedent for how best to share research data with a patient, which is another reason why the PEOPLES protocol is so important, says Schork.

Genetic sequencing of tumors, for example, has become more frequent for patients. "The companies that do the sequencing tend to focus on the presence of mutations that have been shown already to match the effects of certain drugs," Schork explains. "There is a lot information that is generated from sequencing that might all be filtered down to one or two recommendations consistent with the guidelines. But then the question is what about all that other stuff?"

> Schork is quick to point out that the idea that patients should have access to and control over their health data is nothing new. The PEOPLES protocol, he says, shows that it's possible for a patient to gain access to their own data in a safe and ethical way.

Finding ways to share the "research-only" data that are generated during these tests, in a format that is intuitive and understandable to a patient, "is something we've been grappling with," says Schork.

Under the protocol, the TGen team has provided Stanton with new analyses that could expand his treatment possibilities. Stanton received neoantigen profiling, for instance, which looks for tumor proteins that activate the immune system. Stanton and his doctors can now consider new cell-based therapies based on these data.

Neoantigens, organoids, whole genome sequencing—Stanton is eager to have all these data to move forward. "Each is a stone unturned, and possibly an important one," he says. "But is the key under there? You won't know until you look."

SCHORK IS QUICK TO POINT OUT THAT the idea that patients should have access to and control over their health data is nothing new. The accompanying concerns that these patients will seek out inappropriate, dangerous or costly treatments have also been around for a long time.

The PEOPLES protocol, he says, shows that it's possible for a patient to gain access to their own data in a safe and ethical way.

For Stanton, the protocol has given him a path forward just as he reaches the end of standard care.

"What the PEOPLES protocol and TGen have enabled is a suite of analyses and multiple shots on goal that could save my life," he says.

Not all patients will want to take Stanton's route of sharing his data in hackathons or drawing up battle maps. But the TGen team hopes that their protocol will help empower patients as they discuss their options with their healthcare team.

"Physicians may feel threatened when patients want to explore experimental testing strategies, because they [the physicians] often don't know how to order, let alone interpret, such tests. Dr Kalpas and I want to encourage our colleagues to embrace such efforts and see the PEOPLES protocol as a first step in normalizing this process for medical professionals," Goetz said.

"We don't doubt that there are patients out there who are perfectly willing to put this decision-making into their physicians' hands and trust them completely," Schork says "But in an era of big data and the right to try, why not make an effort and say it's OK to cater to the interests of patients that would like to go a little bit deeper?"

True to its Western roots, TGen has spent the better part of 20 years mining the human genome for insights and inspiration to advance the diagnoses and treatment of disease. For Nicholas Schork, Ph.D., these explorations sift through—and make sense of—vast sums of genomic data to help others lead healthier, happier lives through what he and colleagues refer to as precision aging.

He's a modern day prospector. Armed with supercomputers instead of sieves, he blurs the lines between statistical analysis and population health in search of a nugget that sparks discovery, pushes the boundaries of what's possible, and delivers actionable information that holds the potential to change our lives for the better.

The following Q and A has been edited for length and clarity.

A Modern Day Prospector

5 Questions for Nicholas Schork, Ph.D.

How do you define precision aging and why is it important?
The concept of precision aging centers around a framework of healthy aging enabled by tailoring interventions and strategies to the individual. It is a way of maintaining health throughout the aging process, motivated by each person's unique profile — their behaviors, their genetics, their biochemistry, etc. Today, there are over 500 clinical trials underway focused on slowing aging, and there's even a new class of drug called geroprotectors that look to slow the aging rate and potentially prevent one from developing different age-related diseases.

You collaborate with Dr. Matt Huentelman: tell us about that.
Matt's focus is primarily on brain health or cognitive health, while my work focuses more on physical health and physical decline. The question we ask each other is how independent are the two? Evidence suggests that perhaps they are somewhat independent. Many people develop Alzheimer's disease, for example, who are physically fine. The opposite happens as well, in that there are those individuals whose mental acuity is fine but their bodies fail them. Matt and I trade notes often and currently our labs are collaborating on several projects due to our mutual interest in determining what common elements might exist that control resilience to cognitive decline and physical disease as one ages.

What should people know about longevity and healthy aging?
Like any new endeavor, there's hype (live longer, better, faster), but there are also a number of serious efforts, such as the ones that Matt [Dr. Huentelman] and I and others are taking that are more science-based. Google has an initiative called Calico that they've invested $2.5 billion in and Amazon's Jeff Bezos recently invested $3 billion to set up Altos Labs to develop geroprotectors that can halt or reverse the human aging process. In terms of hype, you might read a newspaper article touting huge advances in aging science and suggesting that within a decade we'll all live to the age of 500, but you should take these stories with a grain of salt. There are, however, serious efforts to better understand the aging process and one day perhaps that science might enable us to slow the aging rate and allow people to live longer and healthier lives.

What do you do for yourself regularly to promote longevity and healthy aging?
It's pretty simple right now: I exercise, I watch my diet, and I make sure that I'm eating clean foods to the greatest degree possible. I also take a C15 supplement, which is an essential fatty acid. There are certain nutrients that are essential to the body, since the body doesn't make them internally. When you deprive the body of these essential nutrients, the body sort of falls apart. So one simple thing everyone can do is to make sure their body receives enough of these essential nutrients, whether through food or a supplement. In my case, I don't eat fatty food to a great extent so the C15 provides my body with what it needs without the worry or negative consequences that accompany eating a lot of fatty foods.

What excites and inspires you about the future?
I'm indeed excited about the future. With respect to precision aging research, I think near-term, we'll see a paradigm shift in how to treat and prevent diseases. I see biomedical research moving toward a more interdisciplinary 'pan disease' approach that focuses less on any one disease, but rather on strategies to avoid all diseases. Of course, at the end of day, much will still fall on the individual in terms of making smart health choices and adjusting any unhealthy behaviors. At some point there may be medications that help one remain healthy, but I believe even pills will never be complete substitutes for leading a healthy life.

The Luckiest Pediatrician in the World

Vinodh Narayanan, M.D., balances his clinician-scientist role with equal doses of curiosity and compassion. Dr. N, as he's known to his patients, poses for a recent photo sans the typical clinican's smock, explaining that he never wears a white coat as it frighten's his young patients.

Picture your child suffering from a disease so rare it doesn't have a name. The heartache of seeing their pain, coupled with the agony of not knowing its cause, creates a sense of deep despair. Even this hypothetical can feel unbearable.

One parent, Aseem, described years of searching for a diagnosis for his son as moving through a dark cave, feeling the way forward inch-by-inch, child on his hip.

Parents often refer to this as the "diagnostic odyssey," a process of fumbling in the dark through misdiagnosis and confusion for years on end. The advocacy group Global Genes estimates that rare disease patients spend, on average, seven years searching for answers: visiting eight or more specialists and receiving at least three misdiagnoses.

That is a long time to be underground in the dark.

"At the Center, we're able to diagnose about 40 percent of our patients," explains Vinodh Narayanan, M.D., Medical Director for TGen's Center for Rare Childhood Disorders, who has spent much of his professional career guiding parents through such darkness. The Center uses the latest in genomic technologies to diagnose and manage children with rare (neurological) disorders.

"Even though it might not lead immediately to treatment, there's a lot of power in attaching a name to a child's disorder. Many families spend years in search of an answer, going from specialist to specialist without ever gaining an understanding of what is happening to their child," he says. Following diagnosis, the focus shifts to understanding the biology behind the disorder and searching for specific treatments.

Narayanan began a clinical research partnership with TGen in 2005. At the time, he worked at St. Joseph's Hospital in Phoenix, where his Neurogenetics Clinic was based.

"I wanted to create a neurogenetics collaboration to probe the real nature of the pediatric neurological disorders at the genetic level, and it eventually morphed into TGen's Center for Rare Childhood Disorders," he says, which TGen launched in 2012 with Narayanan as its founding medical director.

Narayanan moved his research lab to TGen in the summer of 2014.

There's a lot of power in attaching a name to a child's disorder. Many families spend years in search of an answer, going from specialist to specialist without ever gaining an understanding of what is happening to their child.

Since its inception, the center has enrolled more than 2000 participants and analyzed the genetics or genomics of more than 700 families.

"To be the first one to describe a disease is very, very hard, but after the first one is discovered, the second and the third are easier," he says. "There are tools available now that facilitate connection with clinicians and scientists around the world, sharing information, to allow us to recognize these new diagnoses".

That moves a lot of patients, parents, and families out of the darkness.

Pioneering Work in the Genomics Revolution

While identifying a disease can provide peace of mind for parents and empower patients and their families, the longer-term benefits lie in the possibilities for treatment. As many as 30 percent of children with rare disorders do not live to age 5.

Using gene editing technologies or identifying so-called orphan drugs—drugs intended to treat diseases so rare that sponsors are reluctant to develop them—may help provide interventions that represent frontiers beyond gene identification.

"Genomic sequencing revolutionized our approach to disease diagnosis," Narayanan says, "but being able not only to identify but repair pieces of the genome creates untold possibilities. The technology and progress made is truly amazing. When I started my career, the idea that we could repair genes to treat disease was not even on our horizon."

Gene therapy involves targeting a disease-causing gene by delivering a healthy copy to replace the damaged one, or editing the existing copy to treat or stop the disease.

When Narayanan started his career, he was interested in neither neurology nor genetics. "Life is convoluted," he says with a smile. "The path we take to get somewhere. My father was a developmental neuroscientist and my mother was a classical geneticist, and they encouraged us to pursue medicine as a career. I used to help in my father's lab when asked—mainly counting wing or beak movements in developing chick embryos—but this was not my focus in college. I started in engineering but was soon completely engrossed with mathematics and modern physics. That changed gradually as I developed a strong interest in neuroscience. The transition from that point to pursuing training in clinical child neurology was easy – guided by great teachers and mentors."

Years later, as a resident trainee in pediatric neurology, a mentor suggested he read a recently published paper on Rett syndrome. "He was guiding me about a patient I was seeing, but the real message was that I should constantly be studying the literature and applying this knowledge to my patients," Narayanan explains. The paper was the first written manuscript in English to describe Rett syndrome.

Rett syndrome is a rare genetic neurological disorder that affects brain development, causing a progressive loss of motor skills and language—primarily in women. While driven by a mutation in the gene, Rett is rarely inherited, which made it a particularly challenging genetic mystery to solve.

Reading the paper lit a fire that inspired Narayanan and became a driving force in his career.

"I want to understand down to the level of the molecular pathway. What is the genetic problem? If it is a genetic problem, and even if it is not, what is the pathway that leads to the disease process, and how can we intervene?" he surmises.

Library of the Future

"Imagine a library of gene therapies," he says, "where you can take solutions off a shelf to fix a broken gene. We know the exact disease or disorder down to the cellular level, we can pinpoint the exact location we need to change, and—in the future, I am imagining now, we can intervene without drugs or surgery. The future pharmacy may include thousands of gene therapy vectors, each one targeting a specific group of mutations in a specific gene."

This, Narayanan believes, is the future of research, where these treatments are not just possible but readily available.

At TGen, Narayanan now works with an entire "army of scientists" to make this vision possible: including genomic researchers, drug developers, bioinformaticians and genetic counselors. They are able to take a team approach to tackle the same issue from different angles. "That is the true gift of these collaborative partnerships within TGen. To have so many experts in so many disciplines working together."

Narayanan balances a clinician-scientist role with equal doses of curiosity and compassion. While the complicated puzzle work of science motivates him, he never loses sight of the families at the center of these mysteries and their real struggles. The photographs of patient families he has worked with over the years that cover his walls serve as daily reminders.

"I am the luckiest pediatrician in the world," he announces. "I learn something new every day."

Families Can't Wait

Lynda Carter Altman helping fund and advocate for blood cancer research

On television, Lynda Carter Altman played *Wonder Woman*, a resilient, resourceful superhero. Through the iconic role, her likeness became synonymous with strength. Throughout the years, her representation has endured as a celebrated symbol of these characteristics.

In real life, she isn't all that different from her legendary on-screen persona.

When Robert, her husband of 37 years, became ill with myelofibrosis—a malfunction of cells in the bone marrow—Carter Altman was every bit as resilient, resourceful, and strong. She threw herself into understanding the disorder, what treatment options were available, and what lay ahead.

TGen and City of Hope were there to help.

Tragically, Altman passed away last year when his myelofibrosis transformed into secondary acute myeloid leukemia (sAML), a rare blood cancer with limited treatment options. As his caregiver, Carter Altman experienced first-hand the unique challenges associated with treating and managing a rare cancer and the need for improved timely diagnosis and treatment.

In September, she provided a philanthropic gift to accelerate critical research at TGen and City of Hope (COH) aimed at helping patients and families experiencing diagnosis and treatment challenges of this blood disorder.

A Book with Two Pages

Because people often show no symptoms in the early stages of myelofibrosis, doctors initially monitor the disease. Essentially, you wait. Watch to see what happens. Test again in a few months. And so on.

When the disease eventually advances to sAML, it's often a case of too little, too late, given existing treatment options and the medical field's relatively limited knowledge of the mechanisms that lead to disease transformation.

"It just doesn't make any sense to me that you watch it until it's going to kill you," Carter Altman says bluntly. "Then you hurry up and do something. It doesn't make any sense to me to approach a disease, this kind of potential cancer, and then you're just going to watch it until it turns deadly."

To complicate matters further, Robert got sick during the COVID lockdowns. "Not being able visit the doctor in person was very frustrating," Carter Altman elaborates. "So, I'm calling Dr. Trent to get answers."

Photo courtesy of Nathan Congleton

Jeffrey Trent, Ph.D., President and Research Director at TGen, and Carter Altman are lifelong friends, having known each other since grade school. He's an internationally-renowned scientist in the field of genomics, particularly the field of translational genetics that applies genomic information for physician treatment decision support.

"I called him about Robert. And he was so patient, explaining so much of it to me; and that's what I needed. Information. Understanding. You know, an answer to 'what is going on here?'"

Early detection of disease progression—identifying the critical transition point when myelofibrosis has advanced to the deadly secondary acute myeloid leukemia (sAML)—is critical to finding effective treatments.

Now, Carter Altman's quest for answers has transitioned to helping other families in the same situation.

"It's basically a book with two pages," Trent says, displaying a gift for explaining complex science in accessible terms, "The first page, it's all focused on early detection, early detection, early detection."

Despite advances in medical research, patients and their families still lack information and options to identify the problem early, detect critical transition points of the disease, and target these transition points for a cure. Early detection of disease progression—identifying the critical transition point when myelofibrosis has advanced to the deadly sAML—is critical to finding effective treatments.

Using ultra-rapid, whole genome sequencing, TGen researchers hope to reduce the window for returning results to clinical teams from two weeks to two days.

That two-day turnaround can provide much-needed answers much faster for a patient and their loved ones, regardless of what comes next. As Carter Altman put it, "I just want the truth, and I want it in real-time. We want a cure, of course, but in the meantime, we want to improve the quality of life and keep it from moving on to the next stage." For the medical teams treating patients, early detection provides a larger window for intervention.

"The second page is on therapy to prevent and eventually cure sAML," Trent continues.

The overarching goal of this program is to develop new genetic tests and initiate clinical trials with new drugs designed based on the novel discoveries from these new genetic tests. The physician-scientists at COH are leaders in developing next-generation cancer therapies and rapidly deploying them for patient benefit.

Beyond a Needle-in-a-Haystack

Early detection is often described as a "needle-in-a-haystack" problem. You are trying to pinpoint when myelofibrosis transforms into sAML—or, rather, when the blood disorder becomes deadly—and COH physicians and scientists have shown that by measuring when cells have begun losing a specific gene (miR-142) the disease may be accelerating. Having an "early detection" signal can help patients like Robert who are told to just "wait" and "monitor." Currently doctors send blood from the patient with myelofibrosis off to the lab to test every couple of months, sometimes over years, to see when the disorder becomes a cause for concern—but by the time it does, they are in a desperate race against time without life-saving solutions for the onset of sAML.

If you can observe these cells at the earliest possible moment when they are very rare, you have a much less complicated disease and a wider window to intervene. Earliest detection comes down to identifying such cells when they are 1:100,000 to 1:1,000,000.

"Needle-in-a-haystack doesn't quite cut it," Trent observes. "Remember, if we look at somebody's genome, we're looking at billions of data points, sequenced hundreds of times, so it's easily hundreds of billions of data points ... and that's a lot of information."

Instead, Trent says, better to imagine the Webb Telescope peering from galaxy to galaxy in search of a single star at a single point in time. Lots of data to sort through to find the gene mutation or mutations that cause this disorder.

"It turns out physics equations can be adapted and can provide a very effective tool to predict when cells in the body evolve from good to bad," says Guido Marcucci, M.D., a physician-scientist of COH with world expertise in AML. "We can utilize mathematical modeling to look at the evolution of the disease and predict how and when it is going to transform into sAML."

Marcucci was born in Rome, Italy, but moved to the U.S. in 1990. He trained at Roswell Park Cancer Institute in Dr. Caligiuri's laboratory and then joined him in a move to The Ohio State University (OSU) Comprehensive Cancer Center to work as a physician-scientist in 1997. In 2015, he became Director of the Gehr Family Center for Leukemia Research and as Chief of the Division of Hematopoietic Stem Cell and Leukemia Research at City of Hope. Dr. Caligiuri is the former Director of OSU's Cancer Center and CEO of OSU's James Cancer Hospital. He rejoined Dr. Marcucci at COH in 2018 when he became President of City of Hope's National Medical Center. "Our lives have been intertwined around AML for 30 years," says Caligiuri, "and I've gone from mentor to student".

New methods of analyzing individual cells allow scientists to measure molecules like miR-142 and other gene changes even when the events are very rare. This enhances the ability to identify the disease early. Using a series of samples collected over time from the same patients spanning the period they transitioned from myelofibrosis to sAML can begin to document this evolution.

"We generate incredible amounts of information," Marcucci continues, "Collaborating with mathematicians as a part of our diagnostic team to create mathematical modeling increases our accuracy on knowing when and how the disease will evolve."

This is the bench to bedside back to the bench in action.

"It's actually these mathematicians that do an extraordinary job of refining our search. While there's an incredibly important laboratory component—you get to generate all the data— I give real credit to the fact that we can do some things now with mathematics applied to the wealth of genomic data that are extraordinary," Trent adds.

Left to right, Robert A. Altman, Jessica Altman, Lynda Carter Altman and James Altman arrive at the premiere of Warner Bros. Pictures' "*Wonder Woman*" at the Pantages Theatre on May 25, 2017 in Hollywood, California.

Therapy – Finding A Silver Bullet

Caligiuri always wanted to be a physician. His specialization at the intersection of immunology and cancer resulted from a chance occurrence with a patient.

"I had an experience in medical school," he explains. "A patient was rejecting his transplanted kidney. He couldn't make urine. It was serious. I was allowed to give him an experimental drug that reversed the rejection and allowed the kidney to make urine. It was amazing."

For Caligiuri, the right drug at the right time for the right patient was inspiring.

"At that moment, I said I want to be in transplant immunology," he reflects. "I went into a lab to focus on curing leukemia with immune therapy. This was a perfect intersection."

Today, he is recognized as a leading researcher in immunology, lymphoma, and leukemia. At City of Hope, he dedicates himself to developing the next generation of cancer therapies.

While TGen, led by Trent, develops the ultra-rapid genome sequencing, COH focuses on therapeutic avenues targeted to the cells that drive the transition to sAML. Most promising is a systematic, pre-clinical battery of tests necessary to advance the miR-142 drug, CpG-M-142, that could replace the action of a missing signal in defective cancer cells. The human clinical trial that is planned could add years to a patient's life.

"Myelofibrosis is basically the result of one cell misbehaving because of one or a few mutated genes that in turn wreak havoc on neighboring cells causing more genes to mutate until the disease evolves to fatal sAML," Caligiuri explains, "We want to keep that from happening—basically returning normal gene function to the cells before the process gets out of control—allowing the patient to stay alive and not develop sAML."

"We are looking for a silver bullet. CpG-M-142 is able to correct the lack of miR-142 and to prevent transformation or in some cases successfully treat disease that has already transformed. We have seen outstanding results in the preclinical testing of the drug with very little toxicity" Marcucci enthuses.

"Without Lynda's generous donation, our progress would remain incremental and take many years to move into the clinic. Her support allows us to move toward human trials in a very short amount of time—not ten years, not five years—but within the next 3 years. It accelerates what we can accomplish."

And that acceleration potentially translates to lives saved and families spared.

Looking to the Future

"The cure for cancer is going to come by preventing it," Caligiuri states, "utilizing genomic sequencing in normal individuals will someday soon identify those likely to develop cancer and precision therapeutics will prevent it from happening altogether."

It is a wild concept to imagine: being able to know what cancers you will likely develop and begin prevention therapy before it emerges.

Marcucci's distinguished career has been based on the belief that AML is the "prototype of cancer and how cancer develops," which means this research may ultimately extend beyond the trials and treatments developed now.

As the financial cost of genomic technology falls, deployment of data-intensive, whole genome testing will inevitably become the standard of care. As this approach enters the mainstream, the companion challenge will be to deploy the tests early and rapidly. This will require increased efficiencies at every step of the process.

This work supported by Lynda Carter Altman will provide a comprehensive demonstration of how to achieve the genomics-based care for all cancer patients in the future.

"Rapid genome testing is really something remarkable," Carter Altman says, "If we can get those tests down to 2 days and do it in a way that is more cost-effective and more accessible, well, you can have an earlier diagnosis. The earlier the diagnosis, the earlier you can treat it. The earlier you can treat it, the better your chances of survival."

That is a remarkable legacy for any family to leave.

Math as Medicine

Using mathematical modeling, machine learning and more to detect cancer at its earliest stages

DR. CRISTIAN TOMASETTI'S FAVORITE uncle—the one his son is named after—died very quickly from his cancer.

"I took the train to Switzerland to visit him because they told me he was about to die," Tomasetti (above left) recalls. "And I couldn't believe it because I had talked to him just two months before and he looked absolutely fine."

At the hospital, his aunt pointed him to his uncle's room. There, he found four people in beds.

"I looked at each one of them and I came out and said to her, 'look, this is the wrong room, he's not here.' And my aunt told me, no, no, he is in there. I went back in and she told me which bed, and looking at him I then recognized him. He was a man in his 60's yet he looked 90, and completely changed by the cancer."

He pauses. "I will never forget for the rest of my life his expression which was—the very first instance I think was joy to see me—but that lasted a fraction of a second and then he was upset, upset that my aunt allowed me to see him like that."

Almost every cancer researcher has a personal story like this, Tomasetti acknowledges, one that provides powerful motivation for the work that they do. But Tomasetti almost wasn't a cancer researcher.

BEFORE VESALIUS CONDUCTED THE dissections that led to his groundbreaking Renaissance volume of human anatomy, our understanding of the human body was based on animal dissections – mainly of dogs and pigs – made by Galen, a second-century Greek physician. For example, most physicians used bloodletting on their patients based on the wrong understanding of the cardiovascular system, while others believed the uterus was made up of many small compartments rather than a single cavity. Before Robert Hooke glimpsed under a microscope the peculiar square compartments within a slice of cork, the notion of a "cell" was murky. And before the genomics revolution took hold in the early 2000s, scientists were blind to much of a cell's contents and their impacts on human health.

It's these great leaps forward that Tomasetti considers as he and his colleagues embark on what they believe is another revolution in medicine. But instead of a scalpel or a microscope, his unique team at Translational Genomics Research Institute (TGen), part of City of Hope, is wielding the tools of mathematics.

"The era of genomic medicine gives clinicians the ability to look at the human body in a more powerful, precise way. But what it brought with that are three billion letters per copy of DNA per cell," he adds, "which looks like a big mess," says Tomasetti, who leads TGen's Division of Integrated Cancer Genomics and serves as the new Director of both the Center for Cancer Prevention and Early Detection and the Division of Mathematics for Cancer Evolution and Early Detection at City of Hope.

Given those daunting numbers compounded with millions of patients, math as medicine makes sense. The division brings together experts in mathematical modeling, statistics, artificial intelligence and machine learning, bioinformatics and genomic data. Working with their wet lab colleagues and physicians, Tomasetti's team is tracing the path of cells from healthy to malignant, while looking for ways to detect cancer at its earliest stages and monitor its progression so that the best treatments can be delivered at the best moments.

As applied mathematicians, Tomasetti and colleagues like TGen's research assistant professor Kamel Lahouel, Ph.D., (at right in the photo) are some of the first generation of researchers to use probabilistic tools to model the evolution of cancer and to predict cancer's response to treatment.

This work is changing our "model of reality" of how cancer evolves, Tomasetti says. "Twenty years ago, we didn't have the data to build these models, or not to the degree that we can build them today. But now that we have information on the behavior of cells and their DNA, this model has become much more precise," Lahouel adds.

Their findings are already having a significant impact, as a recent study led by Lahouel and Tomasetti demonstrates. The scientists showed that pieces of tumor DNA, circulating in the bloodstream, could help physicians decide whether follow-up chemotherapy would be right for their patients who have undergone surgery for stage II colon cancer.

The analysis helped identify patients who could benefit from further treatment, but it also helped certain patients avoid unnecessary chemotherapy--without affecting their survival. "So here is an example where sequencing data from a blood sample plus mathematics really made a big difference in physical and financial terms for the lives of these people, as half of the patients were spared chemotherapy" Tomasetti says.

The team hopes to uncover similar ways to monitor and personalize cancer treatment, but they are also gearing up for a major project to improve the early detection of cancer with a simple blood test.

"If there is a challenge that I want to succeed among our main goals ... it's really early detection, simply because it has a huge impact on society," says Lahouel. "From the public health point of view, clearly it has the highest impact."

When a cell sheds fragments of DNA into the bloodstream, the fragment can look different depending on whether it came from a cancer cell or a healthy cell, he explains.

Their findings are already having a significant impact, as a recent study led by Lahouel and Tomasetti demonstrates. The scientists showed that pieces of tumor DNA, circulating in the bloodstream, could help physicians decide whether follow-up chemotherapy would be right for their patients who have undergone surgery for stage II colon cancer.

The researchers are now developing algorithms to detect and understand these differences, which could include the length of the fragments and the pattern of genetic "letters" at the end of each fragment, among other features.

In the next nine months, Tomasetti says, the team plans to screen 100,000 healthy people via a simple blood test to look for these cancer fragments that might show up long before a cancer diagnosis.

"The reason why cancer is such a terrible disease today is usually because it's discovered late and then your options are not very good," he explains. "But if we can have something like a blood test once a year that can find cancer at an early stage, it will drastically reduce cancer mortality."

TGen and City of Hope's outreach in southern California and Arizona make it a particularly attractive place to launch such a large project, Tomasetti notes. With a diverse pool of possible study participants that includes people from Black, Hispanic, Asian-American and Native communities in the region, the study's findings will be more widely applicable.

The researchers are also working on ways to optimize the technology behind the test so that it will be less expensive than other genetic screening tools. "We are really at the forefront in this space, with a potential to disrupt the market, if we do this study," Tomasetti says.

SO WHAT'S A MATHEMATICIAN LIKE Tomasetti—or one like Lahouel—doing in a place like a cancer research institute?

Tomasetti, who came to the United States from Italy, had always thought he might do something with math. "It's kind of in my blood, in my family," he explained. "But in Italy it can be hard to do something with it beyond teaching high school."

He thought he might go into financial or economics mathematics, and he began his Ph.D. studying probabilistic tools applied to chaos theory. But with two children and concerns about finding a job in "pure math," he looked for applications and found cancer research.

"When I saw that I fell in love with it," he recalls, "because I thought this is something where I can use the tools I like to work with and may be able one day to have a real impact on the health of people."

Lahouel grew up being 100 percent sure he was going to be an astronomer working only on theoretical problems. By the time he met Tomasetti, he was working on the theoretical side of statistical learning but the cancer applications proved too intriguing to pass up.

"A lot of time you have great mathematicians who build sophisticated shiny models, and then find a real-life problem that fits their model. Here it's completely different," Lahouel says. "Most of the time we start building a model, think it's great, and then find it rarely works the first time. You learn to adapt."

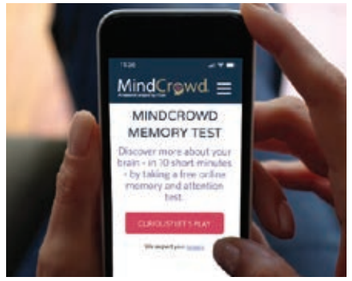
Meanwhile, the field of cancer research is in the midst of its own adaptation, still adjusting to the idea of mathematicians like Tomasetti and Lahouel leading a transformation in how studies are conceived and carried out.

"For a long time, mathematicians were brought in as statisticians, usually not involved in the design of a study," Tomasetti says. "But suddenly mathematicians start having a power and the ability to see things that many traditionally trained M.D.s might not."

But he stresses that he and his colleagues "would be nowhere" without their collaborations with the clinicians and lab scientists. And Lahouel says working at TGen has given him "a lot of flexibility from the lab side."

"We can participate in optimizing the experiments, and people are very open to including mathematical ideas in their lab work," he says.

"I don't know of another cancer center today that has a group of mathematicians of this size essentially all focused on working on cancer evolution and early detection," Tomasetti adds. "I think we have built a little bit of a powerhouse at TGen and City of Hope. That's unique, and I think this will pay back in terms of the difference we will make."



MINDCROWD GETS SMART

Smartphone access and a collection of new tests are taking MindCrowd, a unique online research project aimed at finding the factors that affect the brain's functioning as we age, to a whole new level ... and audience, with more than 6 billion smartphone users in the world today.

To help drive participation, an anonymous donor has pledged $1 to TGen for each test taken. The goal is 500,000 additional participants by year's end.

MindCrowd 2.0 includes eight new "brain game" tests and the ability to participate on the main site using a smartphone, said TGen's Matt Huentelman, Ph.D., a Professor of Neurogenomics and leader of the MindCrowd project. 2.0 should help researchers reach previously understudied groups of people and explore the effects of aging on more aspects of the brain, he noted.

"Not many studies examine the entire adult aging spectrum in one study like we do," said Huentelman, "but part of our motivation is to improve the diversity, equity and the inclusivity."

According to Huentelman, smartphone access will help reach people often underrepresented in cognition studies.

This includes people of color and people living in rural areas too distant from urban research hospitals or academic centers. People living in rural areas, in particular, "should be a big focus of diversity efforts because it's a much-understudied population," he said.

Huentelman and colleagues are also taking the project in new directions by following participants over time, to see how their performance on the games changes over months and years.

The updates to MindCrowd were made possible by a 5-year, $60 million NIH grant from the National Institutes of Health.

Take the test at mindcrowd.org

ENGELTHALER RECEIVES FLINN-BROWN FELLOWSHIP

The Arizona Center for Civic Leadership at the Flinn Foundation selected David Engelthaler, Ph.D., Director and Associate Professor at TGen North, as one of 27 Flinn-Brown Fellows for 2022.

The Fellowship brings membership in the distinguished Flinn-Brown Network and participation in the Flinn-Brown Academy, a 12-session policy institute that offers unparalleled rigorous learning about Arizona policy and politics—and connections with top state leaders and policy experts.

The Academy began in August and concludes with the Flinn-Brown Convention in November, a day-long professional-development gathering for the entire Flinn-Brown Network.

"Flinn-Brown is a chance for these professionals to learn from our state's top experts. They'll also build friendships and networks that will advance their understanding of policy and the political landscape—and provide the support they need to become impactful civic leaders throughout Arizona," said Dawn Wallace, Flinn Foundation vice president for civic leadership.

Flinn-Brown Fellows represent emerging and experienced civic leaders from tribal, rural, and urban communities across Arizona as well as all sectors of Arizona's economy. All recognized experts in their fields, they possess diverse perspectives, political positions, and policy experience.

A core aspect of the Flinn-Brown Fellowship involves the exchange of diverse perspectives and direct engagement with complex public-policy issues.

"I am excited and honored to have been chosen for the Flinn-Brown Fellowship," said Engelthaler. "I look forward to exchanging ideas and viewpoints with the 2022 cohort and extending the program's rich legacy built by over 400 previous Fellows."

CAMPBELL NAMED CIO

TGen recently appointed industry veteran Kevin Campbell as the Institute's Chief Information Officer.

Campbell will oversee the design, development, and implementation of infrastructure systems, software applications, and IT support. He'll also work to identify emerging technologies to be adopted by TGen that support the research and business objectives of the institute.

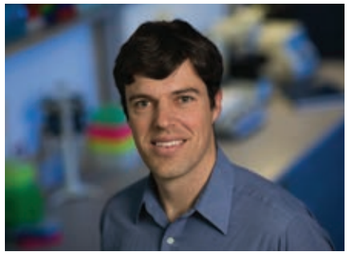
"I am pleased to welcome Kevin as our next CIO," said Jeffrey Trent, Ph.D., TGen President and Research Director. "His knowledge of TGen and his extensive experience working with our faculty provides a seamless transition in the area of information technology and the application of high-performance computing to our life-sciences and precision medicine objectives."

Campbell joined TGen in 2003, where he worked closely with TGen faculty and the scientific community. He was a key driver of the team that designed and built two supercomputer systems that at the time placed in the top 100 most powerful supercomputers in the world.

"I'm honored to be named CIO and look forward to leading TGen's digital efforts by identifying and implementing the latest tools and applications as we continue to push the boundaries of precision medicine," said Campbell.

An industry veteran with over 30 years' experience, Campbell has held numerous IT and technology related positions in metropolitan Phoenix designing, deploying and managing large-scale systems to solve complex problems.

Campbell succeeds James Lowey, who now leads the TGen spin-out Kaligent, which provides software products and services designed to help healthcare and life science customers derive data-driven insights that impact patient care and outcomes.



A UNIVERSAL CORONAVIRUS VACCINE?

Could the SARS-CoV-2 vaccine reawaken previous antibody responses and point the way to a universal coronavirus vaccine? The findings of a study published earlier in *Cell Reports* suggests it's possible.

A new analysis of the antibody response to a COVID-19 vaccine suggests the immune system's history with other coronaviruses, including those behind the common cold, shapes a patient's response.

What's more, the antibody response to these different coronaviruses appears to follow different paths. Over the course of 140 days following vaccination, the response to common cold coronaviruses started early but diminished over time. The response to SARS-CoV-2 continued to get stronger and stronger over time.

"The findings could help fine-tune the design of future vaccines, perhaps leading to a universal coronavirus vaccine," said TGen's John Altin, Ph.D., the study's senior author.

Altin and colleagues are now looking more closely at the antibodies that target the two conserved regions they identified in their study to determine whether these are broadly-neutralizing antibodies that generate immunity extending to new variants of the virus.

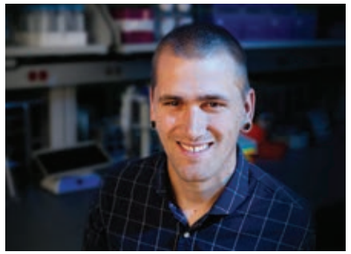
"Our theory is that memory from previous common cold coronavirus encounters exist, and when you get the vaccine for SARS-CoV-2, the vaccine reawakens some of those memories ... then you see this early response which is basically just a rapid memory response to what you've already seen," said Altin.

EXPRESSIONS OF INTEREST

Nonalcoholic fatty liver disease (NAFLD) is both increasingly common and potentially deadly; yet its causes remain poorly understood. Now, a collaborative team of researchers at TGen and Temple University has uncovered a link between decreases in an enzyme that makes choline in the liver—an essential nutrient for humans—and severity of NAFLD.

The study results, published this week in the *International Journal of Molecular Sciences*, suggest that regulation of choline, which is an essential nutrient we usually obtain through our diets, is absolutely critical for the normal, healthy functioning of our livers. The sole source of choline made in the liver is through the activity of an enzyme called PEMT. Without sufficient choline, fat is unable to be transported out of the liver.

"This collaboration has provided insights that implicate choline deficiency, as a result of decreased PEMT in the liver, as a potential cause of both NAFLD and worsened fibrosis in patients who have progressed to nonalcoholic steatohepatitis (NASH). Low PEMT expression in the liver may predispose some individuals to rapid hepatic fat accumulation because they are not able to get fat out of the liver efficiently," said Johanna DiStefano, Ph.D., a Professor in TGen's Metabolic and Fibrotic Disease Program and the study's senior author. "Complicating that further, the modern diet of heavily processed food may not provide as much choline as our bodies need," DiStefano added.



SPATIAL MULTIOMICS ADDS CONTEXT

Genomic sequencing identifies the makeup of DNA, RNA, genes and other elements of the human genome that might be driving disease. To do so, researchers must break down tissue samples, prepare them, and then run them through state-of-the-art sequencers to derive the genetic code of whatever they seek.

TGen recently became one of only a handful of institutes to gain access to new technology that enables researchers to obtain genomic data from cells while leaving them intact within a tissue sample. The technology from Vizgen — called Merscope — combines single-cell and spatial genomics on a single platform.

"Proximity is power with these new technologies," said Nicholas Banovich, Ph.D., Associate Professor in TGen's Integrated Cancer Genomics Division, and Director of TGen's new Center for Single Cell and Spatial Multiomics. "The Vizgen technology brings all the genomic identification power of single-cell sequencing to a study, with the added benefit of maintaining the structure and integrity of the tissue. Proximity definitely counts."

The genomic properties of a cell can evolve, depending for example on how close or far an immune cell might be from a cancer cell. Or how close or far a brain cell might be from a diseased cell in cases of Alzheimer's disease.

"You can start to understand how cells, when they are close to a diseased cell, look compared to cells that are further away," Banovich said.

Kristen Kaus (far left) poses with several Helios Scholars at the year-end symposium.

A SUMMER OF SCIENCE

On July 29, the 16th class of Helios Scholars at TGen, the flagship internship program at TGen, celebrated a summer of science by showcasing their work at a day-long scientific symposium.

The symposium is the capstone event for the eight-week program that supports students from all backgrounds in their efforts to develop foundational skills by placing them alongside faculty and staff.

"Mentorship is an integral part of the scientific experience, especially when you are in the formative stages of a career or, in the case of many Helios Scholars, gaining hands-on experience to validate a career choice," said Kristen Kaus, Manager of Education and Outreach at TGen. "The symposium serves as a nod to their individual accomplishments and recognition of a significant step in their educational and career pursuits."

Since its inception, Helios Scholars at TGen has trained more than 650 students, many who have gone on to careers in Arizona's biomedical research, healthcare, and life science sector.

"Becoming a Helios Scholar helped me solidify the vision for my future," said Freya Abraham, of Maricopa, Arizona, who attends the University of Arizona as a neuroscience and cognitive science major. "It allowed me to join a lab focused on a field I'm drawn to, apply and strengthen my lab skills, and learn more about a topic I hope to continue researching as my educational and professional career unfolds."

BREAKING DOWN THE RESEARCH FOR A LAY AUDIENCE

Ramon Velazquez, Ph.D., (left) and Patrick Pirrotte, Ph.D., (second from left) join *Arizona Horizon* host Ted Simons to discuss a recent finding that suggests that glyphosate, the active ingredient in the majority of herbicides, can cross the blood brain barrier. The collaborative work between ASU's Velazquez and TGen's Pirrotte (and their colleagues), show for the first time that glyphosate infiltrates the brain and elevates the level of certain molecules involved in inflammation. Their work suggests that exposure to this herbicide may be involved in neuroinflammation, a hallmark of many neurodegenerative disorders, including Alzheimer's Disease.

THAT'S A WRAP

June 24 marked the closing day of the 5th annual TGen Bioscience Leadership Academy (TBLA). The two-week program allows 20 qualified Arizona high school students the chance to explore a variety of careers within biomedical research.

TGen faculty and administrative experts share career advice and provide hands-on opportunities that enable students to gain a more in-depth understanding of translational research and the impact it has on clinical trials and precision medicine.

"TBLA participants leave with a foundational understanding of the biomedical research process," said Kristen Kaus, Manager of Education and Outreach at TGen, "and we hope that serves as the spark to ignite their passion to pursue a career in science or medicine."

To learn more or become a sponsor of TBLA, please contact Kristen Kaus at kkaus@tgen.org.

DNA IN BLOODSTREAM HELPS GUIDE TREATMENT OPTIONS

A recent study by an international team including TGen and City of Hope investigators Kamel Lahouel, Ph.D., and Cristian Tomasetti, Ph.D., provided real-world evidence that ctDNA in the bloodstream can help clinicians decide whether chemotherapy is needed for their patients after surgery for stage II colon cancer.

Their findings, published in the *New England Journal of Medicine,* suggest it is possible to tell by using small fragments of genetic material shed into the bloodstream (called circulating tumor DNA or ctDNA) from the patient's tumor.

"The study's findings suggest a way to identify which patients can avoid unnecessary chemotherapy, with its potentially serious side effects and its expense. And for those who have undergone chemotherapy or know someone who has, and know what it means, I think this is really great news," says Dr. Tomasetti.

(See related story on pg. 12)

BACHMAN NAMED SVP OF HUMAN RESOURCES, CHIEF PEOPLE OFFICER

The Translational Genomics Research Institute (TGen), part of City of Hope, today announced the appointment of Page Bachman, JD, as the Institute's Senior Vice President of Human Resources and Chief People Officer. Bachman will lead the development and execution of TGen's overall talent strategy.

"We are thrilled to have such a highly experienced and compassionate person lead TGen's Human Resources team," said Tess Burleson, MBA, CPA, TGen's Chief Operating Officer and President of TGen Accelerators. "Page is an important addition to TGen's future in attracting and retaining the highest quality talent in this increasingly competitive environment."

Bachman brings more than 25 years of strategic and tactical HR experience to his role at TGen, including a strong background in employment law with decades of experience in life sciences and healthcare as well as in strategy, compensation, and operations.

His prior roles include serving as in-house attorney for BankBoston, where he handled employment law matters across the U.S., Latin America, Europe and Asia. He has also held Chief and senior human resource leadership positions for multiple healthcare institutions, including Memorial Hermann Healthcare in Houston, Texas, Ascension Health in Oklahoma and Kansas and, most recently, Phoenix Children's Hospital.

"I am extremely excited to join the team at TGen, and look forward to helping this great organization meet the challenges that lie ahead. It is a privilege to have the opportunity to work alongside people who are doing such important and transformative work," said Bachman.

Bachman's experience includes service as a Peace Corps volunteer in the Dominican Republic and in Uruguay, working alongside community leaders to develop clean water delivery systems and to advance locally owned microbusinesses. He has also held multiple non-profit board positions, including serving as Chairman for Goodwill Industries of Tulsa.

He earned his BA in economics from Syracuse University in New York and his JD from the New England School of Law in Boston, Massachusetts.

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445 North Fifth Street, Suite 600
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TGEN'S
STEP-N-OUT
5K FUNDRAISER

Step-N-Out is a family-friendly event that unites our communities both locally and across the country in the fight against pancreatic cancer.

If you live in Arizona or want to travel, join us as we turn the Valley purple this November and create a world where patients with pancreatic cancer thrive. If you live out of state, you can join us virtually and step out in your community in your own way whether that's hiking a trail, hitting a gym or walking your city.

If you choose to participate, consider creating a team with your friends, coworkers or family.

The in-person activities consist of a 5K run/walk, a 1-mile Fun Run, and an exciting Kids' Dash.

Register at tgen.org/step

RACE FOR A CAUSE

Supporting Pancreatic Cancer Research at TGen

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Presented by:
The Michael Francis Family

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