

Translational Genomics Research Institute

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Please contact Denise A. McClintic, J.D., LL.M., Associate Vice-President, to learn more about giving opportunities that also provide various tax benefits for you and your estate. You may reach her at 602-343-8611 or at dmclintic@tgen.org.

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About TGen

The Translational Genomics Research Institute (TGen) is a non-profit organization dedicated to conducting groundbreaking research with life changing results. Research at TGen is focused on helping patients with diseases such as cancer, neurological disorders and diabetes. TGen is on the cutting edge of translational research where investigators are able to unravel the genetic components of common and complex diseases. Working with collaborators in the scientific and medical communities, TGen believes it can make a substantial contribution to the efficiency and effectiveness of the translational process. TGen is affiliated with the Van Andel Research Institute in Grand Rapids, Michigan. For more information, visit: www.tgen.org



The Magowitz Factor

Connections Drive TGen's
Pancreatic Cancer Fundraising

Roger Magowitz grew up in a broken home, in a one-bedroom apartment in Brooklyn — humble beginnings for someone who would become a highly successful businessman.

But he had an advantage: He learned at an early age how to turn small connections into big opportunities.

His mother had gone to Lafayette High School with Hall of Fame pitcher Sandy Koufax and New York Mets owner Fred Wilpon. Through family and friends — connections — Magowitz often made it to Fire Island, N.Y., a summer playground for the rich and famous. It was there he discovered possibilities and set his sights high.

In 1983, following a three-year stint in the Marines, Magowitz, still in his early 20s, took a part time sales job for Mattress Discounters, a bedding chain with stores in Maryland, D.C., and Virginia. Four years later, by then a Vice President, he had an opportunity to buy the Virginia Beach outlets. Seizing the opportunity, the young entrepreneur leveraged his credit cards, obtained family loans and received favorable terms on inventory from the founders in order to close the deal.

As Magowitz recalled recently, it was touch and go in the early years, but his persistence and belief in his abilities ultimately paid off. In the ensuing years, Magowitz built his business into a multi-million dollar enterprise that spawned 34 stores under the Mattress Discounters and Metropolitan Mattress brands.

Today, having sold most of the stores to national chains, Magowitz maintains the Virginia Beach Mattress Discounters locations, stores that allow him to leverage a life's worth of connections in an effort to conquer pancreatic cancer.

The Accidental Fundraiser

Magowitz never thought about pancreatic cancer until the day doctors diagnosed his mother, Seena, with the disease. Following her death in 2001, he established the Seena Magowitz Foundation, and in 2003, launched the Seena Magowitz Celebrity Golf Classic, an annual affair that supports pancreatic cancer research.

In 2009, the event raised more than \$400,000 for TGen's pancreatic cancer research initiatives led by Physician-In-Chief Dr. Daniel Von Hoff.

"If someone is going to break the code, to come up with the cure, I have to believe that Dr. Von Hoff

WE'RE ATTRACTING A HIGH-LEVEL GROUP OF INDIVIDUALS THAT OTHERWISE WOULD NOT HAVE PUT ANY THOUGHT INTO PANCREATIC CANCER RESEARCH.

will be right there in the thick of it," said Magowitz, who today uses his industry-wide connections as a way to persuade others to join in his fundraising efforts. Once again, his connections have paid off as the heads of some of the nation's most prominent home furnishings companies have signed on. "We're attracting a high-level group of individuals that otherwise would not have put any thought into pancreatic cancer."

The tournament started out small, raising about \$10,000 in 2002 when it was connected to another fundraiser, but grew to \$50,000 in 2003 during the inaugural Classic held exclusively in honor of his mother.

And it hasn't all been bright and sunny, though that is a draw of the event, held between Thanksgiving and Christmas each year on the first weekend in December. Magowitz has scheduled the 8th annual event for December 4.

Last year's event sold out a month in advance, and many golfers had to be turned away.

Much like his early days in the mattress business, Magowitz remembers the early years of the tournament, which he co-founded with business associate Ray Bojanowski, had its challenges as well.

It was so cold and rainy one year, they had to beg for tarps and heaters for the banquet tent. And there was so much rain, it leaked, dripping onto the huddled participants, including Dr. Von Hoff as he presented his annual research progress report.

"What was so great about that was, nobody cared," said Magowitz. "Sure, they came to have a beautiful day in Arizona, but we just had a great time and a great day, and it was as if the sky were sunny and blue."

A highlight of the 2009 Classic was a talk by

Honorary Chairperson Jai Pausch, the widow of Randy Pausch, the late Carnegie Mellon computer-science professor who died of pancreatic cancer in 2008. His now famous *The Last Lecture*, about the importance of achieving childhood dreams, has been featured on PBS, and more than 11 million viewers have seen it on YouTube.

"She's very poised, very passionate, and clearly carries Randy's passion to find a cure for this disease," said Magowitz, adding that Jai Pausch will return this year to the Classic in a key capacity. "The woman needs to get a lot of credit. She's a single mother — a widow with three young children — trying to lead a normal life. Yet she still is in this whirlwind of pancreatic cancer, with its fundraising and initiatives and interviews. It has to be an enormous challenge."

Magowitz said the annual event wouldn't be possible without the volunteer support of Tournament

Taking On the Spread of Cancer

Multi-institute Study Focuses on Metastasis to the Brain

As researchers and clinicians work toward developing new treatments for many of today's leading cancers, an area that remains challenging and poses far more questions than answers is how to stop cancer from metastasizing to the brain.

Today, improved drug treatments provide many cancer patients longer lives, and in many instances, these therapeutics knock down cancer cells at their point of origin.

But something else is happening, too: researchers are seeing these cancer cells change, adapt and migrate to the brain, where treatment options are limited and the disease is almost always fatal.

TGen Associate Investigator Dr. Nhan Tran leads a nationwide research team studying how to stop breast cancer cells from invading the brain.

"This will open up a huge research arena at TGen," said Dr. Tran, who is co-heading the Breast Cancer/Central Nervous System Metastasis (CNS Mets) Project, which eventually could affect all aspects of TGen cancer research.

A central goal of the project is to identify cellular pathways,

biomarkers and other key molecular mechanisms that will help scientists find ways to prevent this type of cancer — CNS Mets — from entering the brain.

"The translational component will be fast and real. We're going to start pointing our clinical partners in a more focused direction," said Dr. Tran.

Researchers in clinical trials are finding new drug treatments that are successfully shrinking tumors, allowing cancer patients to live longer, healthier lives. The downside, however, is that as patients live longer — sometimes years — their cancers often invade other parts of the body. When cancer invades the brain, doctors have few options.

Current chemotherapeutic regimens, often applied intravenously, have little impact on the course of CNS Mets, in part because of the blood-brain barrier, the

separation of circulating blood from the cerebrospinal fluid.

And cancers that migrate to the brain often erupt in multiple sites, making it almost impossible to remove them by surgery or radiation, or even a combination of both.

"This project has huge implications for patients in clinical trials," said Dr. Tara Iyengar, a co-Principal Investigator on the study with Dr. Tran and a Drug Development Scholar at TGen Clinical Research Services (TCRS) at Scottsdale Healthcare, where more than 30 clinical trials are underway. TCRS, at the Virginia G. Piper Cancer Center, is a partnership of TGen and Scottsdale Healthcare.

"Brain metastases, in general, are an under-funded area of research. Most clinical-trial protocols will not allow patients with brain metastases; the few that do have strict requirements about radiation treatment and steroid support. This makes it



DR. RESEAU

DR. IYENGAR

DR. TRAN

DR. CARPTEN

RESEARCHERS ARE FINDING NEW DRUG TREATMENTS THAT ARE SUCCESSFULLY SHRINKING TUMORS, ALLOWING CANCER PATIENTS TO LIVE LONGER.

very difficult for a large population of patients to receive new innovative drugs," said Dr. Iyengar, a board certified physician in hematology oncology, specializing in brain tumors.

"If we can highlight pathways that drive these metastases, we could potentially find drugs that could inhibit further growth," said Dr. Iyengar. "This would have a major impact on survival. We have made great strides in controlling systemic disease. But if we can't control CNS Mets, the patient succumbs to this disease."

This study, one of nearly 30 funded by an Integration Grant Program resulting from the recent alliance and affiliation between TGen and the Van Andel Research Institute, pairs a TGen scientist with a VARI scientist as a way to accelerate the research at both institutions, as well as leverage subsequent grants, mainly from the National Institutes of Health. The project also received funding from the Bruce T. Halle Family Foundation, and from the C.A.R.E. group at Desert Mountain.

Dr. James Resau, a project co-investigator and Senior Investigator at VARI, is providing validation research for this CNS Mets study.

"It is our hope that we would be able to objectively determine numbers and variations of labeled cells that

metastasize to the brain, and document how genetic manipulations and environmental/therapeutic interventions affect their growth and pathology," Dr. Resau said.

Other key project researchers are Dr. John Carpten, a project co-investigator and Director of TGen's Integrated Cancer Genomics Division, and Dr. Bodour Salhia, a TGen breast cancer researcher.

TGen researchers have enlisted the help of hospitals at the University of Iowa and University of Toronto, which are providing tumor samples for TGen analysis.

"We're going to have a comprehensive genomic analysis of all of the samples," Dr. Tran said. "That will allow us to dive into understanding the cellular pathways that are unique to driving brain metastasis, and whether those pathways are targetable. Are there drugs out there currently available to target this particular pathway?"

TGen's clinical partners should then be able to enroll patients, and immediately apply drugs already approved for treating other cancers to patients who have brain metastases, Dr. Tran said. Ongoing studies could also result in new drugs that could prevent CNS Mets from ever entering the brain.

Dr. Tran predicts that eventually the findings will be applied to other cancers, including lung, pancreatic, colon and renal cancers.

"It's a very interesting and unique study," Dr. Tran said. "Our hope is that we can have a very clear impact now, and a sustained clinical impact in the future."



Jai Pausch

*Roger Magowitz
continued from page 3*

Director Liz McBeth of Arlington, Va., his former Chief Financial Officer and family friend who he describes as "the backbone" of the Classic. Her duties include coordinating more than 300 people for dinner and more than 400 for lunch.

Going into its 8th year, the tournament has raised a total of more than \$1.7 million, and should easily eclipse \$2 million after this year's event.

"In a sad sense, we know that a cure for pancreatic cancer is equated to money. It's not going to happen by accident," Magowitz said. "It's going to happen through people like Dr. Von Hoff, his team in the lab, and his worldwide Pancreatic Cancer Research Team by developing new therapies; new drugs. That's how it's going to happen, and they need money for that. It becomes very difficult in today's economy to get people to fund programs. But, knock on wood, so far every year we've been able to reach higher levels."

Today, the kid from Brooklyn works harder than ever, but a life's worth of connections and the determination to conquer pancreatic cancer makes each day worth the effort.



DR. SALHIA



FOLLOWING IN HIS FATHER'S FOOTSTEPS

Dr. Lance Price helps TGen make new discoveries about wounds; infectious disease

Dr. Lance Price, Director of TGen North's Center for Metagenomics and Human Health, discovered science through his father's legacy.

Along with Dr. MacDonald Wood, Dr. William Ray "Bill" Price co-founded the Arizona Burn Center in 1965 at Maricopa General Hospital. Today, the Level I Burn Center, now part of the Maricopa Medical Center, is the second largest burn unit in North America.

Sadly, Bill Price died when Lance was 11 years old.

In his father's absence, the boy often found himself rummaging in his father's den, starting what would become a lifelong pursuit of discovery and service to others.

"In many ways," said Price, "my father's home office became a retreat for me after he died. I would play with his stuff and look at his old slides. I didn't know what I was looking at, but it planted in my mind the idea that I should be doing something to help people."

After graduating from Phoenix's Maryvale High School, Price began what he thought might be a pre-med track by earning a bachelor's degree in microbiology from Northern Arizona University (NAU). But it was in his first microbiology course at NAU that Price found his calling.

It was at NAU that Price first came to the attention of Dr. Paul Keim, an NAU Professor of Biology, the Cowden Endowed Chair in Microbiology, and Director of NAU's Center for Microbial Genetics and Genomics, and Director of TGen North.

When asked of that first meeting, Dr. Keim recalls a somewhat undisciplined 20-year-

old undergraduate student in his molecular genetics class with a passion for science. It wasn't long after that Dr. Keim hired Price as a graduate student technician to work on anthrax diagnostics and molecular epidemiology.

"Lance was great, both in the lab and at a keyboard. We co-wrote my very first RO1 grant submission on anthrax, which was one of the few funded National Institutes of Health grants on that subject prior to 2001," said Dr. Keim, one of the world's foremost authorities on infectious disease. "In addition, my most

THE NEW TESTS TGEN IS DEVELOPING ARE DESIGNED TO ENABLE PHYSICIANS TO DETECT SPECIFIC ORGANISMS IN HOURS, INSTEAD OF DAYS UNDER CURRENT TECHNOLOGIES.

highly-cited paper was one where Lance did lab work and co-wrote with me. Two decades later, he still has that wild passion for science, though now tempered with the discipline of a highly-driven scientist."

The prospect of working with experts on plague, anthrax and other deadly pathogens fascinated Price. "Working in Paul's lab provided an opportunity where I could actually accomplish something directly relevant to human health."

Others noticed Price's work, too. Johns Hopkins University in Baltimore recruited Price and it was there he earned a Ph.D. in Environmental Health Sciences. At Hopkins, he focused on the risks to human health from the use of antibiotics in food animal production, specifically on the threat of drug-resistant infections in people. His expertise in the area

eventually led to Congressional testimony on the subject in July 2009.

Even though he was back East, Price continued to collaborate and publish with Dr. Keim, who after TGen formed in 2002 became Director of the Pathogen Genomics Division at TGen North in Flagstaff.

"Paul kept telling me about TGen and I became excited," said Dr. Price. "I introduced him to the head of infectious diseases at Hopkins Bayview and it didn't take long before we looked at each other and said 'Hey, there are a lot of things we can do together.'"

Soon after, Dr. Price found himself splitting time between John Hopkins and TGen North. He traveled back and forth between the coasts for nearly a year before joining TGen full-time in March 2008.

"Paul had state-of-the-art equipment," he said.

"And TGen provided the support I needed to start taking the science in new directions."

In the past year, Dr. Price has made significant advancements in infectious disease research, especially in developing rapid microbial DNA tests and discovering the full extent of bacteria communities in chronic wounds, such as those that plague many diabetics.

Dr. Price conducts DNA sequence-based analyses, enabling him to determine all the forms of microbial life that exist in the wound. He discovered that wounds have as many as 30 different types of bacteria — complex microbiological communities heavily colonized by anaerobic bacteria, previously undetected using a microscope or cultures in a Petri dish.

His findings raise interesting questions about what should be done. Should we eliminate all

Scottsdale was still a small town in 1967 when Russ Jackson teamed with his friend Tom Barrett to auction a single car — a 1933 Cadillac V16 Town Car — raising funds for local charities, libraries and the arts.

Four decades later, the now-famous Barrett-Jackson annually stages four World's Greatest Collector Car Auctions across the United States, including one each January at Scottsdale's WestWorld events center.

Late last year, the Jackson name became synonymous with the fight against colon and prostate cancer, when Craig Jackson, Chairman and CEO of Barrett-Jackson, launched the Russ and Brian Jackson Cancer Research Fund at TGen in honor of his father and brother. In December 2009, Colorado Springs businessman

and car collector Rick Holland, whose own mother Bernice Holland had died of colon cancer, joined with Craig to establish a \$1 million named laboratory.

As a result, TGen's investigations into colon and prostate cancer will take place inside the Russ & Brian Jackson Research Laboratory, a salute to Craig's father, Russ, and brother, Brian, whose lives were cut short by colon cancer, which annually kills nearly 50,000 Americans. Money raised by the fund will support TGen's research into colon and prostate cancer.

"Establishing this fund and working in partnership with TGen is one of the most important things I have ever done," Jackson said. "Colon cancer is the second

leading cause of death from cancer in the U.S., and more than 100,000 men and women were diagnosed in 2009. I am thrilled to have found such an incredible and inspirational partner in TGen."

Cancer is a major focus of TGen's genomic studies, and with help from the Russ and Brian Jackson Fund, the staff will continue to push the boundaries of colon cancer investigation, further unraveling the genetic complexities of the disease.

"We will continue to push forward and conduct groundbreaking research, hopefully with accelerated results," said Dr. Jeffrey Trent, TGen's President and Research Director. "Craig came to me with the very specific goal of defeating colon cancer, and we will work



Photographs courtesy of Barrett-Jackson



hard to honor the memory of his family members whose lives were cut short by the disease.”

The Russ and Brian Jackson Cancer Research Fund will become a fundraising focus at each of the four Barrett-Jackson Collector Car Auctions in 2010. Craig Jackson will act as the national spokesperson, spreading the word about how the fund supports research into both diseases, and may one day lead to improved treatments and diagnostics.

“Working with TGen I learned about the number of research programs and time that are poured into finding cures to the many forms of cancer,” Jackson said. “The entire Barrett-Jackson family is behind this new effort to help TGen

fight colon and prostate cancer.”

Details of the fund and named laboratory came together just prior this year’s Barrett-Jackson Collector Car Auction in Scottsdale, where the original canvas painting of the event program cover was sold to help benefit the Russ & Brian Jackson Cancer Research Fund.

“Creating the Russ & Brian Jackson Cancer Research Fund will enable TGen to more swiftly develop better treatments for patients now, and perhaps provide important findings that could one day lead to a cure,” said Bennett Dorrance, Chairman of DMB Associates Inc. and Chairman of the TGen Foundation.

Barrett-Jackson also conducts annual collector car auctions in

Palm Beach, Florida, and in Las Vegas, Nevada. Barrett-Jackson recently announced the addition of a fourth auction in Orange County, California, June 25-27, where the company will continue its tradition of charity by giving collectors, sponsors and enthusiasts additional opportunities to support TGen research through the fund.

This year, nearly 340,000 Americans will learn they have colon or prostate cancer, and more than 85,000 will die. Craig Jackson’s support of TGen’s research to understand the genetic causes of colon and prostate cancer — two of the leading and most devastating cancer’s today— brings renewed hope to these individuals for improved diagnostics and treatments.



CRAIG JACKSON REVS UP TGEN CANCER RESEARCH

Fund memorializes auction chairman’s father and brother

Breaking The **Weight Loss** Cycle

TGen-Geisinger Health System Study Zeros in on the Genetics of Weight



The number of Americans who are overweight has increased dramatically in the past two decades. Today, 2 of 3 American adults suffer from obesity. Increasingly, many are reaching beyond diet and exercise to help stave off hunger and shed pounds — nearly 200,000 turned to bariatric surgery in 2009 as a means to achieve their weight loss goals.

But such surgery, which involves risky reconnections of the stomach and small intestines, is at times ineffective and can leave patients permanently dependent on calcium, iron, additional dietary supplements, and more susceptible to hernias, ulcers and other conditions.

Worst of all, for many the effects of surgery are fleeting, as they often regain the weight over a period of time.

In an effort to better understand how one's genetic make up influences weight gain and its many effects on the human body, TGen scientists have partnered with Geisinger Health System of Danville, Pennsylvania in a study potentially involving more than 4,000 patients. A disease, obesity stems from

more than overeating or lack of exercise; research has shown there is often an underlying genetic component leading to excess weight gain. This study is the first planned as part of a recently signed strategic research agreement between TGen and Geisinger that provides for a focused look at the gaps in clinical medicine where biomedical research can make a difference.

Leveraging Geisinger's wealth of clinical information — nearly 20 years worth of electronic health record data— the study will focus on identifying genetic markers that will enable physicians to determine who might be the best candidates for Roux-en-Y gastric bypass (RYGB), the most common bariatric procedure.

This long-term study, expected to last at least five years, and probably longer, also could assist in the development of new anti-obesity drugs, and lead to personalized weight-loss therapies.

"This study is unique in that a wealth of clinical and behavioral information is available on each patient," said Dr. Johanna DiStefano, Director of TGen's Diabetes, Cardiovascular and Metabolic Diseases Division. "Such information is critical for unraveling the links between genetic susceptibility

bacteria? Maybe not, he cautions.

"The body is a walking ecosystem. We cannot survive without the good bacteria that live on and in us," Dr. Price said. "When you apply a broad-spectrum antibiotic to a wound's microbial community, the susceptible bacteria are going to die off, but the resistant ones are going to rise up. You might modify the community in a bad way."

What Dr. Price seeks is a more targeted approach to treating wounds; to identify the good bacteria from

the bad; to find ways to enrich the good and exclude the bad. But for more than half a century, modern medicine has been dependent on broad-spectrum antibiotics.

And in his pursuits, he has high praise for his scientific team, which includes: Andrew Waters, Jordan Buchhagen, Tania Contente-Cuomo, Kim Pearce, Lindsey Watson, and Cindy Liu, a post-doc working with Dr. Keim at NAU and an adjunct faculty member at TGen North.

"The future may be to use more



Lance Price
continued
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and environmental exposures that determine individual risk of regaining weight following a RYGB procedure.”

The RYGB study is the first of many planned under an alliance announced in February between TGen and Geisinger.

“We have a common mission to make major advances against complex diseases, and are working together on strategies for applying the advanced genomic profiling technologies to individualized health care delivery, with an initial focus on diabetes, obesity and oncology,” said Dr. Jeffrey Trent, TGen’s President and Research Director.

The RYGB study will examine the genomes of 2,000 Geisinger patients, identifying upwards of 1 million variables in their DNA that could indicate an association with regaining weight after RYGB surgery.

In addition, as many as 2,000 controls (or non affected patients) will be examined, including patients from Geisinger, and study collaborators at Massachusetts General Hospital in Boston and Temple University’s Center for Obesity Research and Education in Philadelphia.



Johanna DiStefano, PhD

“Given our unique research structure and a patient population that overwhelmingly supports cutting-edge research, I am confident our partnership with TGen will allow us to test and apply new clinical translation theories to obesity and other areas of patient care,” said Glenn D. Steele, Jr., M.D., Ph.D., Geisinger’s President and CEO. “I look forward to the results of this first study, as I am confident we can greatly improve the outcomes for individuals coping with obesity and its many associated complications.”

More Americans are moving to RYGB after seeing only modest and

short-term results from diet and exercise, even those adhering to disciplined weight loss efforts.

In contrast, bariatric surgery — especially RYGB — yields more substantial and sustained weight loss. It is a more effective therapy for long-term weight loss in morbidly obese patients, and also as a surgical therapy for those suffering from type 2 diabetes. RYGB is the bariatric operation least likely to result in nutritional difficulties.

The amount of weight loss with RYGB varies. Clinical and physiological characteristics have so far failed to distinguish individuals who will maintain weight loss following bariatric surgery from those who will not.

“This study is especially innovative in that it seeks to incorporate environmental factors that interact with genetic variants to manifest a particular response, a complexity seldom examined in these kinds of studies,” Dr. DiStefano said.

The knowledge gained from this study ultimately may help physicians decide which patients are suitable candidates for RYGB and which are not.

narrow spectrum, targeted antimicrobial approaches,” Dr. Price said, especially with the rise of MRSA (Methicillin resistant *Staphylococcus aureus*) and other multi-drug-resistant infections.

“Resistance is changing the landscape of medicine. It’s changing the landscape of how you handle an infection. MRSA is just one organism. There’s lots of them, and we’re trying to get ahead of the curve.”

While it might take as much as a decade to produce the kinds

of targeted therapies envisioned by Dr. Price, he said the rapid assays, or tests, TGen is developing should be ready soon. They should enable physicians to detect specific organisms in less than 4 hours, instead of waiting as long as a week under current technologies.

Today, a portion of Dr. Price’s work has come full circle with his childhood and memories of his father. A recently begun project involves the study of bacteria on the wounds of patients at the

same burn center established by his father, where burn center collaborators Kevin Foster, Melissa Pressman and Karen Richey join him to eliminate the guesswork, and determine — definitively — what each patient is infected with.

“It’s a huge health problem that costs upwards of \$5 billion annually,” said Price.

If successful, Price would view it as a fitting tribute to his father and an enduring legacy to burn victims everywhere.



Dr. Raoul Tibes

High hopes for new therapy

Cancer researchers have high hopes for a new therapy for patients with certain types of lymphoma and leukemia. PCI-32765 is a new drug being assessed in a Phase I clinical trial at the Virginia G. Piper Cancer Center in collaboration with

controls (CMC), quality assurance and control, regulatory affairs and virtual business development.

A SOLiD look at tissue

Life Technologies Corporation is collaborating with TGen and US Oncology to sequence the genomes of 14 patients afflicted with triple negative breast cancer whose tumors have progressed despite multiple other therapies. The goal of this first-of-its-kind research collaboration is to demonstrate whether genomic sequencing of cancer tissue can provide clues for treatment strategies for these individuals. While genomic

Sciences of Milan, Italy's largest pharmaceutical research and development facility. It is designed to stop abnormal cell division and duplication, a common feature of cancer. "From the initial trial in patients with advanced cancers, this drug is well tolerated. We are now focusing on thymic cancer, based on our initial results, to hopefully find a treatment that is successful for this rare cancer, where there is no standard approved treatment," said Dr. Glen J. Weiss, principal investigator for this trial and Director of Thoracic Oncology at TGen Clinical Research Services (TCRS) at Scottsdale Healthcare. This Phase 2



Dr. Heather Cunliffe

Cunliffe joins Phoenix Komen for the Cure board

The board of directors of the Phoenix Affiliate of Susan G. Komen for the Cure recently named TGen Investigator Dr. Heather Cunliffe to its 15-member board. Dr. Cunliffe, a recipient of a National Komen Research Grant in 2005, began a close relationship with executive leadership and staff of Komen's Phoenix Affiliate, following her 2004 faculty appointment at TGen. Since that time, she has enjoyed participating in a variety of community outreach events with the local Komen affiliate, including their signature pink ribbon breakfasts, breast health awareness events, such as Channel 12's Buddy Check 12, and of course, the annual Komen Phoenix Race for the Cure. Board members provide guidance and leadership to staff and the more than 1,500 local volunteers, working together for a cure for breast cancer. The Phoenix Affiliate serves central and northern Arizona, including Maricopa, Apache, Coconino, Gila, La Paz, Mohave, Navajo, Pinal and Yavapai counties.

Training a new breed of physician

In early February, Life Technologies Foundation awarded TGen a \$300,000 grant to accelerate the education of doctors in the field of molecular medicine, and enable them to better understand how genomic research discoveries and might translate into improved treatments for their patients. The grant will fund two TGen

TGEN IN BRIEF

TGen Clinical Research Services at Scottsdale Healthcare. According to Dr. Raoul Tibes, a TGen Associate Investigator and Director of the Hematological Malignancies Program at the Virginia G. Piper Cancer Center, progress in developing new treatments for cancer has been painfully slow as only 2-4 percent of all cancer patients enroll in clinical trials. This is especially true for uncommon cancers such as leukemias and lymphomas.

Help me Rondaxe

TD2 and Rondaxe Enterprises recently forged a strategic alliance that will help emerging companies speed new high-quality treatments to cancer patients. Rondaxe, a drug development consulting company in Syracuse, N.Y., helps emerging pharmaceutical and biotechnology companies navigate through all phases of the drug development and commercialization process. The company specializes in drug chemistry, manufacturing and

sequencing has made great strides in helping researchers understand human disease, its clinical utility is not fully known. This research study brings together the accuracy of the Applied Biosystems SOLiD System, with US Oncology's expertise in cancer trials and TGen's Cancer Genome and Oncology programs, to provide additional information for oncologists and their patients.



Dr. Glen Weiss

Treating rare cancers

TGen and Scottsdale Healthcare are testing a new drug specifically for thymic cancer based on early promising results at Scottsdale Healthcare. PHA-848125AC is produced by Nerviano Medical

clinical trial of as many as 60 adults with advanced thymic cancer will help determine if PHA-848125AC is an active drug for this disease. The thymus is a small organ near the lungs and heart that is a key part of the body's immune system during fetal and childhood development.

Combating aggressive cancer

Researchers at TGen Clinical Research Services have identified a way to predict which patients with small-cell lung cancer may be resistant to first-line chemotherapy. The study, Tumor MicroRNA Biomarkers Associated with De Novo Chemoresistance in Small Cell Lung Cancer, was presented in San Diego at a joint conference of the American Association for Cancer Research (AACR) and the International Association for the Study of Lung Cancer (IASLC). This breakthrough is critical since patients with small-cell lung cancer (SCLC) often do not get a second chance at therapies to combat this aggressive type of cancer.

fellowships in genomic and molecular medicine, focusing on the treatment of rare cancers. The fellowships will be under the direction of Dr. Daniel Von Hoff, TGen's Physician-In-Chief and Chief Scientific Officer for TGen Clinical Research Services at Scottsdale Healthcare (TCRS), which provides a direct clinical research site for treating patients with rare tumors. TCRS enables molecular and genomic discoveries made by TGen and others around the world to reach the patient bedside as quickly as possible at the Virginia G. Piper Cancer Center at Scottsdale Healthcare. The goal, within three years, would be to identify three molecular targets in three rare cancers, and develop therapeutic agents to hit these targets, with the hope of immediately applying the results to patient care.



Dr. Daniel Von Hoff

Accelerating drug discovery

A research-collaboration and sub-licensing agreement between TGen and Horizon Discovery will allow TGen investigators to use Horizon's GENESIS™ and X-MAN™ technologies to accelerate the search for new drug targets, biomarkers and anti-cancer agents. Dr. Daniel Von Hoff, TGen's Physician-In-Chief and Senior Investigator is eager to partner with Horizon in the use of these new technologies, which should enhance TGen's research efforts to provide patients with significantly better outcomes. Horizon's core gene-targeting technology and human isogenic cell-lines are expected

to enable TGen to create a key center of excellence in translational medicine for generating and applying predictive human disease models in drug discovery.

And the winner is?

A team of TGen scientists won a \$1,000 prize for best scientific paper presented at BIBM09, a premier bioinformatics and biomedicine conference. Judges selected the paper, Identifying MiRNA and Imaging Features Associated with Metastasis of Lung Cancer to the Brain, from among 233 scientific submissions at the IEEE (Institute of Electrical and Electronics Engineers) International Conference on Bioinformatics & Biomedicine, held November 1-4 in Washington, D.C. According to conference judges, they made their selection based on the amount of work done for the study, including laboratory work, and the novelty of the research approach. "We (computational people) often focus too much on the elegance of computational modeling. This is a good paper to reach out to the computational community with a work by a large, collaborative team with a new idea."

Ending ESRD?

Researchers using a DNA analysis tool developed by TGen and UCLA have identified genetic markers that could help treat chronic kidney disease among diabetics. Study results, published in the December edition of *Diabetic Medicine*, show it is possible to identify biomarkers associated with end-stage renal disease (ESRD) from the pooled DNA of more than 1,000 diabetics. Specifically, TGen researchers identified genes that could potentially contribute to ESRD among those with Type 1 Diabetes. ESRD almost always follows chronic kidney failure and although treatable with dialysis

or transplantation, mortality rates remain high. While diabetic kidney disease is one of the most common complications of diabetes, it is currently not possible to determine who is at risk for ESRD.

Small molecule, big results if successful

TGen Drug Development (TD2) and Critical Outcome Technologies Inc. (COTI) of London, Ontario, Canada, are working to obtain approval of clinical trials for a promising new anti-cancer drug called COTI-2, an easily synthesized small molecule compound. TD2 will work with COTI to complete the Investigational New Drug (IND) process, enabling research necessary to gain U.S. Food and Drug Administration approval of clinical trials, perhaps by the end of 2010. COTI-2 works by inducing a brisk apoptotic response — the cancer cell kills itself — by targeting a pro-survival enzyme family called AKT. Initial tests have shown that COTI-2 can limit the growth of tumors in several types of cancer without the toxic side effects seen in other AKT inhibitors. It also may be even more effective when used in combination with other anti-cancer drugs.

An international effort

TGen Drug Development (TD2) and the Institut Paoli-Calmettes (IPC) have forged a strategic alliance that will enable both to maximize their worldwide contributions in the treatment of cancer patients. The partnership between TD2 and Marseille, France-based IPC's comprehensive cancer center will enable both non-profit institutes to speed research discoveries to patients with cancer. Both organizations will expand their clinical research network to evaluate new therapies in the U.S. and Europe in an effort to

more quickly introduce new drugs into clinical trials. Teams from TD2 and IPC will focus their efforts on discovering molecular alterations within cancers and finding biomarkers that will help identify new therapeutic targets to tailor treatments for individual patients.



Dr. Stephen Gately

Study: TD2 boosts Scottsdale economy

TGen Drug Development (TD2) is poised to play a significant role in the expansion of Scottsdale's biomedical industry, fostering new jobs and city revenues, and prompting the creation of more related businesses. That is the conclusion of a new report by the independent economic research firm Tripp Umbach of Pittsburgh about TD2's economic impact on Scottsdale. And while TD2's contributions to Scottsdale already are solid, its projected impact within 5 years will increase by nearly tenfold, the report concludes. TD2's direct annual economic impact on Scottsdale in 2009 was \$4.3 million. But when TD2's included, Tripp Umbach pegged the total economic impact in 2009 at more than \$26 million. That total economic impact is projected to reach more than \$239 million by 2015. "TD2 holds the promise of a brighter economic future for Scottsdale, and the promise of better healthcare for all Arizonans," said Dr. Stephen Gately, TD2's President and Chief Scientific Officer.

TAU THEY DO THAT?

TGen leads investigation into tau's affect on Alzheimer's disease

As we grow older, our bodies naturally produce less of the proteins our brains need to work, affecting one's recall. In most instances, this is a natural part of aging. When the proteins begin to dismantle connections within the brain cells, however, the rapid severity of memory loss is typically associated with Alzheimer's disease (AD).

A scientific group led by TGen recently identified three kinases, or proteins, that may offer insights into how memory functions and how scientists differentiate naturally occurring memory loss from Alzheimer's disease.

The findings, resulting from a multi-year TGen study, appeared in the January edition of *BMC Genomics*.

The study identified three kinases that trigger a malfunction in tau, a protein critical to the formation of the microtubule bridges within brain cells, or neurons. These bridges support the synaptic connections that, like computer circuits, allow the brain's neurons to communicate with each other.

"The ultimate result of tau dysfunction is that neurons lose their connections to other neurons, and when neurons are no longer communicating, that has profound effects on cognition — the ability

to think and reason," said Dr. Travis Dunckley, an Associate Investigator in TGen's Neurodegenerative Research Unit and the paper's senior author.

Tau performs a critical role in the brain by helping bind together microtubules, which are sub-cellular structures that create scaffolding in the neurons, allowing them to stretch out along bridges called axons. The axons support the synaptic, or chemical, connections with other neurons.

Under normal circumstances, kinases regulate tau by adding phosphates. This process, called tau phosphorylation, enables the microtubules to unbind and then bind again, allowing brain cells to connect and reconnect with other brain cells.

"That facilitates synaptic plasticity. It facilitates the ability of people to form new memories — to form new connections between different neurons — and maintain those memories. So, it's an essential function," Dr. Dunckley said.

However, sometimes the tau protein becomes hyperphosphorylated, a condition in which the tau creates neurofibrillary tangles, one of the signature indicators of Alzheimer's.

"When tau protein is hyperphosphorylated, the microtubule comes apart - basically destroying that bridge - and the neurons can no longer

communicate with each other," Dr. Dunckley said.

Investigators identified 26 proteins associated with the phosphorylation of tau, and found that three caused hyperphosphorylation of tau, permanently dismantling the microtubule bridges.


"This paper shows, for the first time, these three kinases affect Alzheimer's disease-relevant tau hyperphosphorylation, in which most of the tau protein is now driven into a permanently phosphorylated (or inactive) form," Dr. Dunckley said.

The next step will be to identify drug compounds that can negate the effects of the three kinases linked to tau hyperphosphorylation.

TGen's collaborators in the study included: the Department of Neurology at the Mayo Clinic in Jacksonville, Fla.; the Center for Alzheimer's Research at the Sun Health Institute in Sun City, Ariz.; Banner Alzheimer's Institute in Phoenix, Ariz.; the Department of Psychiatry at the University of Arizona; and the Arizona Alzheimer's Consortium, a group of nine institutes that cooperatively study Alzheimer's disease.



Travis Dunckley, PhD



WHEN THE TAU PROTEIN BECOMES HYPERPHOSPHORYLATED, THE TAU CREATES NEUROFIBRILLARY TANGLES — A SIGNATURE INDICATOR OF ALZHEIMER'S DISEASE.



TGen-VARI Alliance and Affiliation Finalized

In early February, TGen finalized its strategic alliance and affiliation agreement with the Van Anel Research Institute (VARI) of Grand Rapids, Michigan, a partnership that will maximize the research capabilities of both non-profit institutes.

The alliance and affiliation creates a robust basic-science-to-translational delivery platform aimed at developing new tests and treatments for patient benefit.

"We are excited to align with a prominent institute like Van Anel, a partnership that I fully expect to yield greater scientific and economic returns for both Arizona and Michigan," said Dr. Jeffrey Trent, TGen's President and Research Director, a title he also now holds at VARI.

TGen remains an Arizona-based 501(c)(3) non-profit biomedical research organization, headquartered in Phoenix with an Arizona-centric board.

Since making an initial alliance announcement in February 2009, TGen worked with key Arizona partners to ratify any needed changes

to funding or research agreements, including the Flinn Foundation, the Virginia G. Piper Charitable Trust, the Arizona Board of Regents, a number of the Valley's health care providers, and the State of Arizona.

"As one can imagine with a process of this scope, there were a number of technical and legal points to address," said Dr. Trent. "I can't thank our Arizona-based partners and members of our Board of Directors enough for their willingness to see the process through to completion. It was gratifying that the leadership of all organizations we worked with fully saw the long-term scientific and medical benefit the alliance and affiliation would offer."

TGen's final contract revision, signed Jan. 15, enabled the Arizona Biomedical Research Commission (ABRC) to continue funding TGen through state tobacco-tax revenues. The new state contract, facilitated through ABRC leadership and the Arizona Attorney General's Office, ensures continued state funding through fiscal year 2012.

"TGen is critical not only to our ability to find cures to cancer and

other diseases, but also to diversifying Arizona's economy and helping our state attract high-wage, cutting-edge, bioscience jobs. I am pleased that my office helped bring the parties together to secure TGen's future in Arizona," said Attorney General Terry Goddard.

VARI is the research arm of the Van Anel Institute (VAI), established in 1996 as a philanthropic research and educational organization by the late Jay and Betty Van Anel. VARI has more than 250 scientists and staff in 18 laboratories that study the genetic, cellular and molecular origins of cancer, Parkinson's and other diseases. VARI recently opened a 240,000 square-foot building expansion in downtown Grand Rapids.

"This agreement provides TGen and VARI a research platform from which to tackle many of today's leading diseases with greater strength of resources, and as important, redefines collaboration in a way that should enhance the biomedical sectors and provide economic benefit to both Arizona and Michigan," said David Van Anel, VAI Chairman and CEO.

TGen Foundation

Upcoming TGen Foundation events



Bernice E. Holland Golf Tournament
 Benefits colon cancer research
 Monday, June 14, 2010 • The Cheyenne Mountain Resort • Colorado Springs, Colorado



Terri Link Memorial Fund Golf Tournament
 Benefits adrenocortical cancer research • Saturday, October 2, 2010
 The Georgia Club • Statham, Georgia



StepNOut Run/Walk/Dash • Benefits pancreatic cancer research
 Sunday, November 7, 2010 • Kiwanis Community Park
 Tempe, Arizona

For more information, please visit www.helptgen.org or contact Erin Massey at 602-343-8411.



TGen Foundation is now on Facebook

The TGen Foundation is excited to announce the launch of its Facebook page. We invite you to follow us online and tell your friends and family to follow us, too.

Our mission is to positively impact the lives of patients and families by accelerating TGen's efforts to make and translate genomic discoveries into advances in human health. We hope that our Facebook page will be a resource for you. Join our community and receive updates about the cutting-edge DNA research taking place at TGen. To become a fan, login to Facebook and type 'TGen Foundation' in the search box. If you are not already a Facebook member, you can sign up for free at: www.facebook.com.



If you have any questions, please contact Dean Ballard, the TGen Foundation's Assistant Director of Development, at dballard@tgen.org or 602-343-8543. We hope to see you on our page!

SAFEWAY RAISES \$1.5 MILLION FOR TGEN



Second from right – Dan Valenzuela, Safeway. Far right – Cathy Kloos, Safeway, touring Dr. Cunliffe's lab.

Despite the economy and slower sales, Safeway Inc. recently donated more than \$317,000 to fund breast cancer research at TGen, bringing contributions by Safeway to TGen over the past three years to more than \$1.5 million.

"I'm grateful that Safeway leadership — Safeway management — is able to make all of this possible," Michael Bassoff, President of the TGen Foundation, told Dan Valenzuela, President of Safeway's Phoenix Division, which includes 115 stores across Arizona.

Valenzuela said that even in this challenging economic environment, Safeway's customers and employees succeeded in providing TGen with needed funds to support breast cancer patients.

"It's been a challenging year for us. Everybody has hardships that they see within their own families or among their friends," Valenzuela said. "It's great to see all these people at TGen coming together and working towards a common goal. It's a great partnership, because TGen is a local organization, here in our own state, and we can see the benefits of their scientists' hard work."

Because of the economy, Valenzuela said, Safeway is working harder than ever to help fund the needs of local organizations.

Dr. Heather Cunliffe, head of TGen's Breast and Ovarian Cancer Research Unit, said that, thanks to Safeway, TGen scientists are making significant progress against breast cancer.

"We are extremely proud to be partnering with Safeway, which is enabling these significant accomplishments within a short time frame. Your contributions are truly astonishing," Cunliffe told Valenzuela. "Your customers and employees are certainly crusaders in the war on breast cancer."



Foster & Lynn Friess

First unTEAL A CURE donations are expected to top \$124,000

More than 700 people turned out for the first unTEAL A CURE 5K run and walk supporting TGen's ovarian cancer research.

The inaugural event raised more than \$72,000 — nearly triple the original goal of \$25,000 — and will exceed \$124,000, thanks to an additional \$50,000 matching gift by international businessman and philanthropist Foster Friess and his wife, Lynn.

The National Cancer Institute estimates that this year more than 21,000 American women will learn they have ovarian cancer; more than 14,000 will die — that's one woman nearly every 37 minutes.

TGen Adjunct Sr. Investigator Dr. Stephen Anthony, who traveled from Washington State to attend the event, described the importance of ovarian cancer research, and how his partnership with Dr. Heather Cunliffe, Head of TGen's Breast and Ovarian

Cancer Research Unit, is leading to a better understanding of the disease and new treatments for patients.

Dr. Anthony also remembered two young women who lost their lives to ovarian cancer, Tiffanie Wyke and Taryn Ritchey, whose families were major participants in the event.

Michele Avery, a TGen employee-volunteer and herself an ovarian cancer survivor, chaired this year's unTEAL a Cure 5K, assisted by more than 50 volunteers.



'Taryn's Tigers' help raise funds in memory of young cancer victim

Taryn Ritchey (left) loved tigers. So when she arrived at TGen Clinical Research Services (TCRS), she latched onto a giant stuffed tiger and wouldn't let it go. Unfortunately, ovarian cancer wouldn't let go of Taryn, and at age 22 she succumbed to the disease in July 2007.

"Taryn's dying wish was to be able to help other young women so they won't have to go through what she went through," said her mother, Judy Jost of Cave Creek.

To help fulfill that wish, more than 40 supporters joined "Taryn's Tigers", running in the first unTEAL A CURE 5K run and walk on March 7, supporting TGen's ovarian cancer research.

"It means hope," Jost said of the event at Tempe's Kiwanis Community Park. "I'm trying to fulfill her final wish."

Jost works as a personal assistant

to international businessman and philanthropist Foster Friess, who splits his time between Jackson, Wyo., and Scottsdale. In Taryn's memory, Friess previously presented TGen with a gift of \$250,000 for ovarian cancer research. This year, for the inaugural walk, he pledged an additional \$50,000 matching gift.

Jost said it is important that women understand some of the telltale signs of ovarian cancer: backaches, constipation, bloated stomach and nausea. It is not detectable through routine Pap smears. Taryn had all those symptoms, but didn't know that they might be associated with cancer. Even if she had, her mother said, they might not have guessed that they could indicate cancer in someone so young.

When her doctor detected a lump during a routine medical exam, the results of an ultra-sound showed a cist

nearly 11 centimeters by 12 centimeters in size.

"At the time that we found it, we had no idea what the symptoms of ovarian cancer were," said Jost. "By the time doctors detected Taryn's cancer it was in an advanced stage."

Taryn received treatment at TCRS under the guidance of Dr. Stephen Anthony, who has since joined a practice in Washington State. Taryn fought her disease for nearly a year, maintaining an amazing attitude, even while enduring chemotherapy regimens. She even provided TGen her tumor tissue as part of their continued research efforts into small cell cancer of the ovary, in hopes of making a difference in the lives of any woman dealing with ovarian cancer.

"We need to raise awareness," said Jost, whose hopes were fulfilled by plans to continue unTEAL A CURE next year.



TGEN PRESIDENT HONORED FOR COMMUNITY SERVICE AT EVENING ON THE DIAMOND

Derrick Hall (left), President and CEO of the Arizona Diamondbacks, and Ken Kendrick (right), Managing General Partner of the Arizona Diamondbacks, present the 3rd annual Arizona Diamondbacks Foundation Community Leadership Award to Dr. Jeffrey Trent, TGen's President and Research Director.

Dr. Jeffrey Trent, TGen's President and Research Director, received the 3rd annual Arizona Diamondbacks Foundation Community Leadership Award on April 1 at a ceremony on the baseball diamond at Chase Field.

Dr. Trent received the award from Derrick Hall, President and CEO of the Arizona Diamondbacks, and Ken Kendrick, Managing General Partner of the Arizona Diamondbacks and a Board Member of the TGen Foundation.

The award was presented during the 4th annual Evening on the Diamond, a benefit for Diamondbacks charities attended by several hundred donors that included an appearance by comedian and television host Jay Leno.

Dr. Trent was honored with the Community Leadership Award for his longtime "dedication and commitment" to Arizona and to the Arizona Diamondbacks Foundation.

"I am deeply moved and honored by this award from the Diamondbacks organization, which has done so much to elevate the lives of those less fortunate," said Dr. Trent, noting that the Diamondbacks have raised more than \$15.5 million for a triple-play of charities: the homeless, indigent healthcare and children's programs. "I look forward to continuing our longtime partnership with the Diamondbacks in our mutual effort to enhance the health and quality of life of all Arizonans."