Translational Genomics Research Institute

TGen Today

TGen/Van Andel Alliance Creates National Footprint

Dr. Jeffrey Trent to Serve Dual Role PAGE 2

SPRING 2009

TGen
A Non-Profit Medical Research Institute

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Translational Genomics Research Institute

TGen Today

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About TGen

The Translational Genomics Research Institute (TGen) is a non-profit organization dedicated to conducting groundbreaking research 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 worldwide, TGen believes it can make a substantial contribution to the efficiency and effectiveness of the translational process.

TGen Alliance strikes a VARI GOOD CHORD

Alliance and affiliation allows both research institutions to maximize potential

TGen and the Van Andel Research Institute (VARI) will forge a strategic alliance that will enable both to maximize their worldwide contributions to science and health.

The non-profit research institutes jointly announced on Feb. 11 the initiation of an "alliance and affiliation agreement."

The partnership between TGen and Grand Rapids, Michigan-based VARI will enable both institutes to speed up their mutual goals of moving research discoveries about cancer and other debilitating medical conditions as quickly as possible from laboratories to patient care.

"Combining many of the scientific, educational, financial and business potentials of TGen and VARI will advance the research of both institutions and enhance the economic development of both Arizona and Western Michigan," said Dr. Jeffrey Trent, President and Scientific Director of TGen since its founding in 2002.

"This alliance will elevate both organizations in the world of scientific research," said Dr. Trent, who will retain his roles at TGen, but upon implementation of the agreement also will become President and Research Director of VARI.

VARI is the research arm of the Van Andel Institute (VAI), established in 1996 as a philanthropic research and educational organization by the late Jay and Betty Van Andel.

"We are excited to welcome Dr. Trent and TGen as they combine forces with us in our mission to conquer cancer and human disease," said VAI Chairman and CEO David Van Andel. "This alliance demonstrates that VARI and TGen are at the forefront of redefining a borderless, collaborative, national and international scientific community that transcends geographical limitations."

Dr. Trent will replace Dr. George Vande Woude, who in 1998 was appointed the founding Director of VARI. Dr. Vande Woude, a member of the prestigious National Academy of Sciences, will remain at VARI as head of the Laboratory of Molecular Oncology.

"This is a great moment for both Institutions. I have known Dr. Trent professionally for nearly 20 years and have always admired him as one of the nation's leading scientists. One of Dr. Trent's greatest attributes is bringing together researchers from many disciplines to work on problems that will improve human health," Dr. Vande Woude said.

Dr. Vande Woude, who held top-level administrative posts at the National Cancer Institute since the early 1980's, will be able to achieve a long-held desire to return to the lab full-time.

Dr. Jeffrey Trent, TGen's President and Scientific Director (left), and David Van Andel, VAI Chairman and CEO, are working to forge one of the nation's premier alliances among non-profit biomedical research institutes.

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Visiting TGen

The Anatomy of Collaboration

For Dr. Bart Williams, a Senior Scientific Investigator and Director of VARI's Laboratory of Cell Signaling and Carcinogenesis, two recent visits to TGen provided a first-hand opportunity to experience the research potential behind the TGen / VARI affiliation.

Williams' visits to TGen in August and February initiated collaborations with TGen faculty members and helped facilitate general interactions between scientists at both institutes.

Williams noted the complementary facilities between the institutes, and the depth of research faculty.

"The cadre of exceptionally talented scientists at TGen have particular strengths in translational research and are surrounded by technology related to that strength, including the infrastructure to perform and organize clinical trials,'' Williams said.

"As a researcher working in the basic sciences, I value input from those clinically-based researchers who can validate that our work at the basic level is relevant to important clinical questions,'' added Williams, who collaborated with TGen Drs. Nhan Tran, Pam Pollock, Mike Berens, Suwon Kim and David Duggan.

With experience in creating and characterizing mouse models to study human disease, Williams believes the combined forces of TGen and VARI will lead to improved models that make possible greater insight into the cellular mechanisms underlying human disease.

"Any time you can present your work to a strong group of scientists, the constructive criticism you will get will make your work better. Interactions with the TGen faculty and staff will be extremely helpful in improving the science at both institutes and moving clinically-relevant solutions forward in an accelerated manner," Williams said.

Dr. Williams earned his doctorate degree in biology in the Laboratory of Dr. Tyler Jacks at the Massachusetts Institute of Technology, Cambridge, Mass. He conducted his Postdoctoral fellowship in the laboratory of 1989 Noble Laureate Dr. Harold Varmus at the National Institutes of Health.

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The alliance combines the groundbreaking basic research expertise of VARI with the cutting-edge translational genomics and analysis of TGen.

"The search for a new director has ended with the best possible results – a renowned, research director in Dr. Trent, who will now lead VARI, and an alliance that strengthens two of the nation's fast-emerging leaders in biomedical research," David Van Andel said.

TGen is dedicated to conducting groundbreaking research with life changing results. Research at TGen is focused on helping patients with diseases such as cancer, neurological disorders, diabetes and infectious diseases. TGen is on the cutting edge of translational research, in which investigators unravel the genetic basis of complex diseases and medical conditions.

VARI opened its facility in 2000. Its 18 research laboratories are primarily dedicated to molecular cancer research, but it also focuses on conditions such as diabetes, Parkinson's disease, osteoporosis, and heart disease. VARI will open a 240,000 square-foot building expansion this fall, which will allow it to broaden its efforts to include additional neurological disorders and chronic illnesses. VARI's primary work has been in basic research – looking for what occurs to cause disease in individual cells, and using that information to identify "biomarkers" that can help predict and diagnose diseases, and lead to the development of safer, more effective drugs.

"VARI is on the verge of expanding its already strong basic research programs and implementing further translational research," said Dr. Daniel Von Hoff, TGen's Physician-In-Chief and a world-renowned cancer scientist.

"TGen is poised to translate the discoveries generated in laboratories from both organizations into real solutions for patients," said Dr. Von Hoff, who also is Chief Scientific Officer of TGen Clinical Research Services at Scottsdale Healthcare. "This is a terrific opportunity to work together and increase our chances of making a difference for our patients."

Both TGen and VARI are relatively young organizations that have triggered regional growth of the life sciences and biomedical industries in Arizona and Western Michigan. Both organizations have a strong focus on cancer, collaborations and expansion locally, nationally and internationally.

The "alliance and affiliation agreement" will become effective July 1, 2009.

Visiting VARI

Collaborating and Connecting

Dr. Bodour Salhia, a post-doctoral fellow under Dr. John Carpten in TGen's Integrated Cancer Genomics Division, visited Grand Rapids late last year to engage VARI scientists on two projects. Salhia, whose research focuses on breast cancer, prostate cancer and multiple myeloma, spent a month building new scientific collaborations and accessing VARI technology.

"From a research perspective, building these types of alliances allows for the integration of differing points of views and expertise into the research process, and often increases the efficiency of research while elevating the quality as well," Salhia said.

Working with VARI Scientific Investigator Dr. Jeff MaKeigan, Salhia conducted synthetic lethal screens using the human kinome — a subset of the human genome consisting of the protein kinase genes — in bladder cancer cells expressing a marker of advanced disease. Such screens are designed to identify various gene targets that reduce cell viability in the presence of another gene alteration or drug.

Salhia also spent time in the lab of VARI Distinguished Scientific Investigator Dr. James Resau testing breast cancer tissue specimens from Egypt to explore whether a molecular uniqueness exists within the cancerous tissue of Egyptian women. This study will be the largest molecular characterization study in this population.

Salhia described VARI's scientist, staff and facilities as "extraordinary" and left convinced a TGen / VARI alliance provides numerous opportunities for both institutes to achieve great success. She came away impressed with how similar the two institutes are in terms of collegiality and interaction.

"My trip was absolutely beneficial. It was scientifically productive and resulted in new and long-lasting scientific collaborations, paving the way for additional opportunities in the future — which as a post-doc are essential for career development."

Pay it Forward

A conversation with Diane Halle President, Bruce T. Halle Family Foundation, and Herbert K. Cummings Charitable Trust

Diane Halle, a member of the TGen Foundation Board, recently made two major gifts to fund important research efforts at TGen.

As President of the Bruce T. Halle Family Foundation, she made a substantial contribution to establish The Diane Halle Women's Health Initiative. As President of the Herbert K. Cummings Charitable Trust, she also made a major contribution to fund The Herbert K. Cummings Therapeutic Development Program – the next step in the development of a potential cure for pancreatic cancer.

This is on top of Mrs. Halle's generous past support of TGen. Her early and visionary support of the TGen Pancreatic Cancer Research Team (PCRT) helped create an unprecedented opportunity for 32 of the world's top medical institutions to work together. Dr. Daniel Von Hoff, TGen's Physician-In-Chief, has described the treatments generated by PCRT as "the most active regimen ever seen against pancreatic cancer."

The most recent contribution to TGen by Diane Halle (left), President of the Bruce T. Halle Family Foundation and Herbert K. Cummings Charitable Trust, will help fund research into woman's health and pancreatic cancer.

We asked Diane Halle about her philanthropic activities:

Question: How long have you lived in Arizona, and what do you like most about the Grand Canyon State?

Answer: I have lived in Arizona for 29 years. The main reasons that drive us all to the desert are its beauty and the weather. Being from Chicago, the weather might have had an upper hand. The unexpected plus was that a person could make a significant difference in the philanthropic world in this state in the '80s.

Q: Tell us how you became involved with TGen?

A: I became associated with the Arizona Cancer Center many years ago along with my late husband. I subsequently met Dr. Daniel Von Hoff while he was the Director in Tucson and immediately knew he was going to continue making a difference in cancer research. He has been a great help to my husband Bruce and me when we have needed information on cancer treatments for our friends and employees. Through Dr. Von Hoff, we met TGen President and Scientific Director Dr. Jeffrey Trent, and we were so impressed with his knowledge and devotion. The terminology of genomics was new to all of us, and it has taken time to understand its importance in the cure of all kinds of diseases as well as the establishment of our own genetic makeup. It fascinates me because the field is wide open, and TGen is going to be able to change how we think and feel and take care of our own bodies. Dr. Trent is on the brink of establishing new directives in the field of medicine. I have met many other amazing doctors at TGen, and we are so blessed to have them all on the TGen team.

Q: As President of the Bruce T. Halle Family Foundation, one of Arizona's Top 10 philanthropic organizations, and as President of The Cummings Charitable Trust, could you tell us how you first became involved in philanthropy and describe for us your charitable giving philosophy?

A: I started my philanthropic training through the Nathan Cummings Foundation in New York. This experience allowed me to participate in grant selections all through the United States, Israel and Russia. The broad base opened my eyes to a plethora of worldly needs. Upon arrival in Arizona, I concentrated mostly on the arts, then on healthcare issues and the needs of women and children. Today, I find myself again, through the Discount Tire Driven to Care Program, looking at the needs in the states that Discount Tire serves. The Bruce T. Halle Family Foundation is devoted to women's and children's issues, education, access to the underserved, healthcare issues and promoting spiritual awareness.

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PROGRESS AGAINST

Alzheimer's Disease

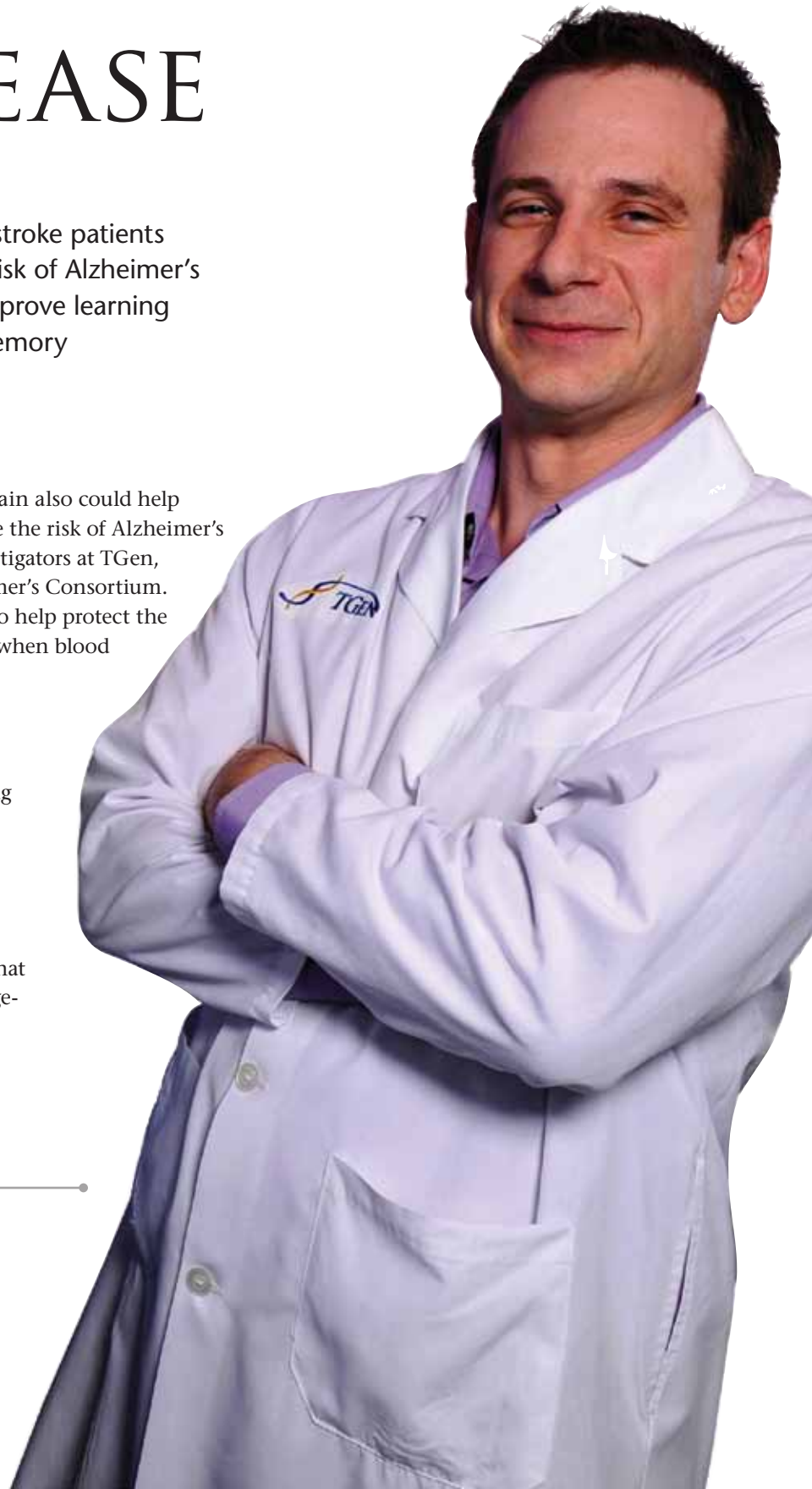
Drug used in stroke patients may reduce the risk of Alzheimer's disease and improve learning and memory

A drug used to improve blood flow to the brain also could help improve learning and memory and reduce the risk of Alzheimer's disease, according to a new study by investigators at TGen, Arizona State University and the Arizona Alzheimer's Consortium.

Fasudil has been used for more than 10 years to help protect the brain in stroke patients by dilating blood vessels when blood flow is curtailed.

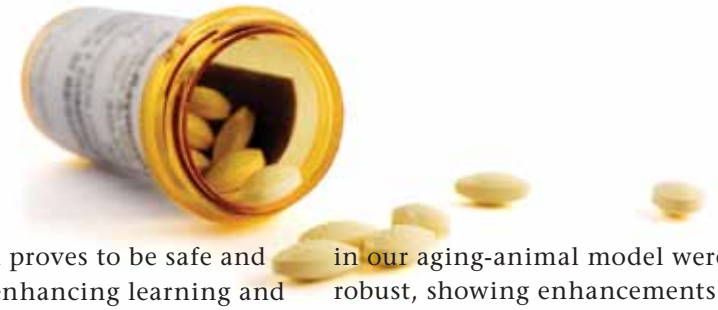
Arizona psychologists, geneticists and neuroscientists reported in the February edition of the journal *Behavioral Neuroscience* that hydroxyfasudil, the active form of the parent drug Fasudil, improved spatial learning and working memory in middle-aged rats when negotiating a complicated maze.

The findings suggest that hydroxyfasudil may influence similar cognitive processes in humans involving the hippocampus, a part of the brain that has been shown to deteriorate in patients with age-related disorders.



"Fasudil may be a new pharmaceutical weapon against Alzheimer's."

DR. MATTHEW HUENTELMAN, INVESTIGATOR - NEUROGENOMICS DIVISION



"If Fasudil proves to be safe and effective in enhancing learning and memory, it could represent a viable new option for the prophylactic treatment of disorders with a cognitive decline component. This could include diseases like Alzheimer's as well as general age-related impairment. In short, it may be a new pharmaceutical weapon that could be used even before the occurrence of symptoms," said Dr. Matthew Huentelman, an Investigator in TGen's Neurogenomics Division.

Clinical trials are being explored in the areas of cognitive impairment and dementia, said Huentelman, the scientific paper's first author.

Although far from proving anything about human use of the drug, the findings support the scientific quest for a substance that could treat progressive cognitive impairment, cushion the impact of aging, or even enhance learning and memory throughout one's life span.

"Fasudil shows great promise as a cognitive enhancer during aging," said Dr. Heather Bimonte-Nelson, an Assistant Professor in ASU's Department of Psychology and the paper's lead author. "The effects in our aging-animal model were robust, showing enhancements in both learning and two measures of memory. The possibility that these findings may translate to benefits to human brain health and function is very exciting."

In the study, the researchers gave daily injections of hydroxyfasudil to middle-aged, 17-18 month old, male rats. Injection made it easy to give the drug to rats, but people take it in the form of a pill.

Rats were tested on a water radial-arm maze, which assessed how well they remembered which of the radiating arms had a reward, a sign of accurate spatial learning and working memory.

Fasudil is used to protect the brain by dilating blood vessels when blood flow is curtailed. In the body, Fasudil breaks down into the more potent hydroxyfasudil molecule, which the authors hypothesized may alter memory by affecting the function of a gene called KIBRA.

The authors recently demonstrated that KIBRA might play a role in memory in healthy young and late-middle-aged humans.

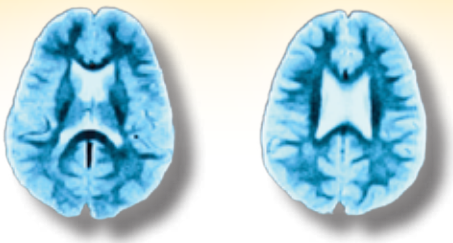
In September 2008, TGen investigators announced a link between the brain protein KIBRA and Alzheimer's disease, a discovery that could lead to promising new treatments for this memory-robbing disorder.

TGen researchers found that carriers of a memory-enhancing flavor of the KIBRA gene had a 25 percent lower risk of developing Alzheimer's disease.

The findings were reported in the *Neurobiology of Aging*, a Philadelphia-based peer-review journal that generally focuses on how aging affects the nervous system.

"This research suggests that KIBRA, and possibly some of the proteins with which it interacts, may play a role in Alzheimer's disease," Huentelman, that paper's senior author, said at the time.

The findings announced in September built on a previous TGen study published in 2006 in the prestigious journal *Science*, which showed a genetic link between KIBRA and memory in healthy adults. That pioneering study, led by collaborative teams from Arizona and Zurich, Switzerland, revealed a link between KIBRA and memory, in which healthy adults with the KIBRA T-allele performed better on memory tests than those without this gene.



"The possibility that these findings may translate to benefits to human brain health and function is very exciting."

DR. HEATHER BIMONTE-NELSON,
ASSISTANT PROFESSOR - ASU DEPARTMENT OF PSYCHOLOGY

Fighting the Good Fight

TGen's Dr. Haiyong Han is inspired by patients' stories in his quest to find a cure for the most deadly of all cancers

At first, Dr. Haiyong Han's scientific journey was a series of intuitively logical steps, starting from his hometown of Shaoxing, one of China's most culturally and historically significant cities.

But in more recent years, his epic battle against pancreatic cancer has been inspired by the desperate pleas of patients suddenly stricken by this most deadly form of cancer.

Growing up in the birthplace of silk making and Shao rice wine, Han was given a choice to pursue the arts or science.

"I liked to play with test tubes," said Han, who today not only commands his own research lab on the 4th floor of TGen's downtown Phoenix headquarters, but also manages the lab for Dr. Daniel Von Hoff, TGen's world-renowned Physician-In-Chief.

Han's career has followed Von Hoff's from Texas to Tucson to TGen.

After moving to nearby Hangzhou and attending Zhejiang University, one of China's oldest and most prestigious institutions of higher education, Han moved to Austin to attend the University of Texas.

In Texas, Han focused on Molecular Biology, which eventually led to his work in pre-clinical oncology drug discovery under Dr. Laurence Hurley, an award-winning biochemist who now is the Associate Director of the BIO5 Institute and the Howard J. Schaeffer Professor of Pharmaceutical Sciences at the University of Arizona.

Hurley introduced Han to Von Hoff, and both Han and Von Hoff moved to Tucson when Von Hoff was named Director of the Arizona Cancer Center. Han did his postdoctoral research under Von Hoff.

"Working directly with a clinician like Dr. Von Hoff provided me with a connection between laboratory research and making a difference with treatments for real-world patients," Han said.

> "SHE SAID SHE FELT LIKE SHE WAS GOING TO DIE IN THE ER," DR. HAN SAID OF ONE PATIENT WITH PANCREATIC CANCER.

The Tucson connection also was critical to Han's and Von Hoff's current investigations into possible cures for pancreatic cancer. Dr. Sydney Elias Salmon, the esteemed cancer investigator who in 1976 became the founding Director of the Arizona Cancer Center, died in 1999 of complications related to pancreatic cancer.

Han's early research in Texas addressed cancer by using small molecules to stop the unwinding of DNA during cell replication. Of course, such treatment had the side effect of affecting healthy cells as well as diseased ones.

His research at TGen today is more sophisticated, identifying cancer specific genetic changes, developing compounds that can selectively kill cancer cells harboring those genetic changes, as well as identifying biomarkers that can be used to detect pancreatic cancer.

One promising line of research in connection with the University of Georgia in Athens involves the analysis of "pancreatic juice," the bile-duct fluids, from patients with pancreatitis or related illnesses. In this study, Han and associates are looking at the glycosylation of proteins and other analytes to find pancreatic tumor markers, which are potentially more concentrated in the pancreatic juice than in the general blood circulation.

In his work, Han continues to collaborate with the top tier of UA investigators, including Hurley and Dr. Robert T. Dorr, another award-winning scientist whose most recent investigations into Imexon, a novel small-molecule, nonmyelosuppressive cytotoxic agent, has exciting possibilities in the treatment of metastatic melanoma, as well as lung and pancreatic cancer.

But it is the stories he hears from patients and their relatives – stories of desperation in fighting this difficult to detect cancer – that drives Han's research.

One woman he met told him that she went to a hospital emergency room three times, doubled-over with abdominal pain, before she was finally diagnosed with late-stage pancreatic cancer.

"She said she felt like she was going to die in the ER," Han said. "It's a tough disease. I think we are making small steps, and hopefully we will have a big impact in the near future."

Dr. Matthew Huentelman (right), an Investigator in TGen's Neurogenomics Division, explains genomics technology to the Honorable State Rep. Michele Reagan, Chairwoman of the Arizona House Commerce Committee.

Enquiring Minds

TGen tour for legislators provides insight into latest TGen research

State Rep. Michele Reagan knew there was something missing in her legislative life, and she was determined to find it.

The honorable Chairwoman of the Arizona House Commerce Committee knew generally about the Translational Genomics Research Institute. Reagan said she knew TGen was a positive force in the Arizona economy, that it was doing things to improve people's health, and that she already supported its funding.

But the four-term Scottsdale Republican said she had never seen the labs, the equipment and the people trying to discover the genetic origins of human disease.

"I had never visited what quite possibly is the most exciting thing to happen to our state in the last 10 years," Reagan said.

She often has ended many of her public speaking engagements listing TGen among the highlights of Arizona. But her constituents would pepper her with questions about the non-profit biomedical research facility, and many she just couldn't answer. "I've had some people ask questions afterwards: 'What do you mean? What are they doing?' "

"They (scientists) talk about proteins and plasmas and DNA and genomes like its just … these are words that most people … rarely use in a sentence," said Reagan, adding that she also realized that many other lawmakers also might want to know more.

In October, Reagan organized a legislative field trip to TGen, inviting all of the 60-member House of Representatives. To her

surprise, she said, 17 responded and eight, including Reagan, joined staff members from the Arizona Department of Commerce – as well as Sal Rivera, executive director of the Arizona Economic Resource Organization – for the trip to downtown Phoenix.

"We hear TGen talked about at the Capitol all the time. I'd never been to TGen, and that's embarrassing to say, especially since the funding for it was something I fought for in past budgets," Reagan said. "I thought to myself, 'If I've never been to TGen, then I wonder how many other representatives have never been there.' "

The highlight of their TGen visit was a presentation by Dr. Matthew Huentelman, a TGen Investigator in the Neurogenomics Division and a specialist in the possible genetic causes of age-related disorders. Huentelman has been a leading participant in several recent internationally recognized breakthroughs involving the possible genetic sources of age-related hearing declines and Alzheimer's memory lapses.

"Matt sold TGen," Reagan said. "You can hear all the numbers. But getting to meet somebody who actually is responsible for significant strides … I know that the doctors here are very, very busy … , but the 40 minutes that we took of Matt's time was invaluable to what we learned."

Huentelman, she said, was able to translate the many scientific concepts he uses into everyday language that the lawmakers could grasp.

Reagan said she and the other lawmakers were unexpectedly surprised at the breath of the research going on at TGen.

"Cutting-edge is probably a cliché, but it is just how amazing the scientific discoveries are. It was so far beyond what we thought you guys were working on that it was almost science fiction. We know you are working on cancer, and that you're working on Alzheimer's, but I don't think we realized the depth of how far you've come … some of the equipment that you have; its really like nothing we knew even existed."

The Honorable Rep. Laurin Hendrix, a Gilbert Republican and Vice-Chairman of the House Commerce Committee, described TGen as "very impressive," following a February visit to the research institute.

"I was not aware that we had a facility of this caliber in Arizona," said Hendrix, who was first elected to the Legislature in November.

The Honorable Arizona House Minority Leader David Lujan, a three-term Phoenix Democrat, said he was "thoroughly impressed and excited about the significant positive impacts that TGen is having not only in Arizona but (throughout) the world.

"TGen's investment in Arizona is creating spin-off companies that will help to diversify our economy and bring high-quality jobs to our state. In addition, TGen has shown a real commitment to partnering with high school and university students to develop outstanding future scientists, doctors and engineers. TGen is truly an asset to the state of Arizona," Lujan said.




The legislators' tour included opportunities to see working labs up close and personal. At left, State Rep. Laurin Hendrix gets a microscopic look at cancerous tissue.

Reagan added that a continued state investment in TGen is worthwhile for two major reasons:

— First, the jobs that TGen provides (now employing about 300 people) and the ancillary companies that are spinning off from TGen that she hopes will choose to stay in Arizona.

— Second, "From a real humanitarian (standpoint), and the one that struck most people as they walked out of here; you get the feeling after you've been here that you've just been in the place that they will discover the cure for cancer."

Reagan said she felt elevated when she called her secretary to check her next agenda item. "It was almost like this euphoric feeling; that I saw something really positive that our state was doing. So much of what lawmakers deal with are the negative issues of what our state's doing – how we're last in this, 49th in that, we just edged out Mississippi in this – and here was an area where we are clearly trendsetters. It was a feeling of pride when we left, and that was unexpected. A lot of us just didn't realize how amazing everything that is happening here is."

Reagan said she is planning more visits and wants to bring many more members of the Legislature to see what TGen is doing.

"With so many newly-elected people, I think it's really important. Would I like to come back? Absolutely," she said.

TGen In-Brief

"Dark fiber" link would accelerate data transfer

Plans for a new light-speed data line between TGen and Arizona State University's Tempe Campus could slash the time it takes to transfer raw genetic data between the two institutions. Speeding up information flow accelerates research into diseases such as Alzheimer's, autism, diabetes and various cancers. Currently, it can take as long as 12 days using conventional cables to transmit 7 terabytes of information from a typical experiment along the 10 miles between TGen's downtown campus and ASU's Tempe campus, home of the new Saguaro 2 supercomputer. The proposed data-line would trim the transmission time to 1 hour.

Helios Scholars launched

TGen began receiving applications for 45 internships in the 2009 Helios Scholars Program in late January. The program – with a 25-year funding commitment from the Helios Education Foundation – provides paid, eight-week internships to high school, college, graduate students and medical students who have an interest in developing research skills. Interns begin their tenure with biosafety and human subjects training and conclude with an oral or poster presentation showcasing their accomplishments. A recent survey of TGen's more than 200 past interns found that 94 percent of those who still are in school are pursuing degrees in science, with 25 percent pursuing doctoral degrees.

Berens, Guerra appointed to Tech Council

Dr. Michael Berens (above) and MaryAnn Guerra were appointed to new positions on the board of directors of the Arizona Technology Council. Dr. Berens, Director of TGen's Cancer and Cell Biology Division, was named Chairman Emeritus on the ATC board, one of four new executive officers named to two-year terms. Dr. Berens, who has served six years on the board – the past two as Chairman of the nearly 500-member organization – was one of five Director's Emeritus named to serve indefinite terms on the board. Guerra, TGen's Chief Business Officer and President of TGen Accelerators LLC, was one of 10 new directors appointed to three-year terms on the 33-member board, following its Oct. 23 meeting.

TGen spins off Catapult Bio™

Catapult Bio, a non-profit organization designed to help transform emerging research discoveries into business opportunities, accelerating the commercialization of life sciences in Arizona, recently announced its official launch. Initial funding for Catapult Bio comes from a grant of up to $14 million over five years by Los Angeles-based Abraxis BioScience. Catapult Bio's business model directly addresses funding gaps in Arizona's Bioscience Roadmap by providing the expertise, services and investment needed to develop and commercialize discoveries emanating from Arizona's life sciences research. Catapult Bio's vision emerged from TGen Accelerators, LLC (TGen Accel), to more fully develop research discoveries into new business opportunities that accelerate commercialization in the life sciences with an emphasis in the biomedical field.

Checking the Sixth Vital Sign

Physician-scientists from TGen and Scottsdale Healthcare presented their latest findings and techniques at a national conference in Phoenix Jan. 22-24, designed to provide cancer doctors with new treatments for their patients. "Molecular Oncology: The Sixth Vital Sign, What Every Oncologist Should Know" was intended to help cancer doctors provide better diagnosis, early detection as well as drugs and other treatments that in some cases can slow the growth or even shrink tumors. Dr. Ramesh K. Ramanathan, a Senior Investigator at TGen, was the co-program director of the conference, along with Dr. Daniel Von Hoff, TGen's Physician-In-Chief and the Chief Scientific Officer at TGen Clinical Research Services (TCRS) at Scottsdale Healthcare, a partnership of TGen and Scottsdale Healthcare Corp. The program included 7 other researchers and clinicians associated with TGen and Scottsdale Healthcare.

New cancer drug may boost patients immune system

Clinical trials of the drug VTX-2337 are underway at TGen Clinical Research Services at Scottsdale Healthcare and at Mayo Clinic in Arizona. Dr. Ramesh Ramanathan, Medical Director of TCRS at Scottsdale Healthcare, indicates the new drug appears promising.

Heather Cunliffe: a Woman on the Move

Arizona Foothills Magazine recently named Dr. Heather Cunliffe (above), an Investigator in TGen's Computational Biology Division and Head of TGen's Breast & Ovarian Cancer Research Unit, as one of 12 "Women Who Move the Valley." Cunliffe was recognized for her cancer research at TGen, as well as her advocacy of women's interests, work with graduate students, scientific publications, and efforts toward enhanced patient care. Breast cancer is the second leading

cause of death from cancer in American women. This sobering statistic is one of many motivating Cunliffe and other TGen scientists to translate powerful new research into effective clinical measures.

Von Hoff named Community Service Leader of the Year

Dr. Daniel Von Hoff (above), TGen's Physician-In-Chief, was named Arizona's Community Service Leader of the Year in October at the 2008 Governor's Celebration of Innovation. Dr. Von Hoff, who also is Chief Scientific Officer of TGen Clinical Research Services at Scottsdale Healthcare, won the William F. McWhortor Community Service Leader of the Year award, presented annually to an individual or organization from industry, government or academia that contributes to Arizona's technology industry through relentless community involvement, leadership, visibility and excellence in economic development activity.

One gene: duel roles

A January cover story in *Molecular Cancer Research* highlighted the continuing work of Dr. Pamela Pollock, researcher Michael Gartside and other TGen scientists and collaborators into the causes of melanoma. The gene, FGFR2, provides the body instructions for, among other tasks, making a protein that drives cell division, growth and development. The findings revealed that FGFR2 mutates in different ways in different kinds of cancer. The published results follow more than six years of research and involves at least 25 scientists from across the globe.

MedTrust Online is a new tool for cancer doctors

TGen spun off another company, MedTrust Online, in late January. For-profit MedTrust Online is a reliable one-stop medical information source for oncologists. MedTrust Online solution will help speed information to oncologists as they seek the best knowledge available about various diseases, especially quality information about potential drug therapies. MedTrust Online's Electronic Curbside Consult provides doctors with a platform for discussing difficult cases with experts and promotes peer-to-peer collaboration.

Teaching the teachers

TGen's Education Office hosted Arizona high school teachers Jan. 23-24 during a two-day scientific grants-writing workshop. The workshop was the second held as part of TGen's Biotechnology for Teachers program, funded through the Arizona Board of Regents. Working in partnership with Northern Arizona University's Department of Biological Sciences in the College of Engineering and Natural Sciences, and NAU's Center for Science Teaching and Learning in the College of Education, the program aims to provide teachers with skills to sustain biotechnology programs in the classroom.

TGen-led team identifies gene linked to age-related hearing loss

As reported in the December edition of *Human Molecular Genetics*, researchers led by TGen's Dr. Matthew Huentelman, an Investigator in the Neurogenomics Division, have identified a gene that could help explain why some people lose their hearing as they age. Finding the genetic causes of age-related hearing loss (presbycusis) could lead to treatments that would bring relief to millions of people worldwide who now suffer from social isolation, depression and even cognitive impairment as a result of not being able to properly understand what others are saying. Collaborators included teams from Los Angeles and Belgium.

Petritis named to head proteomics center

Dr. Konstantinos "Kostas" Petritis (above), a senior research scientist at the Pacific Northwest National Laboratory in Richland, Washington, will head TGen's new Center for Proteomics. The Center — a first-of-its-kind, industrial-scale proteomics biomarker discovery, verification, and validation facility — will work with world-recognized experts through the Partnership for Personalized Medicine, a joint initiative between TGen, the Biodesign Institute at Arizona State University, and the Fred Hutchinson Cancer Research Center in Seattle. The goal of the PPM is to translate our understanding of genomic variation to the diagnosis and treatment of disease. Initial efforts will focus on the discovery and validation of biomarkers in support of Luxembourg Project Lung Cancer, one of three programs linking TGen to the nation of Luxembourg.In addition, the new Center for Proteomics, housed on the 4th Floor of TGen's Phoenix headquarters, will provide a core resource to support collaborative proteomics studies within the TGen community. Dr. Petritis received his Doctorate and Master's degrees in Analytical Chemistry from the University of Orleans, in central France. He earned another Master's in Enology and Viticulture from the University of Bourgogne in Dijon, France, and a received a Bachelor's in Enology and Beverage Technology from Technological Educational Institution of Athens, Greece.

Clinical trial shows promise in treatment of solid tumors

TGen Clinical Research Services (TCRS) at Scottsdale Healthcare and Mayo Clinic are testing a new drug that may offer broad potential to treat solid tumors. Dr. Glen Weiss, Director of Thoracic Oncology at TCRS at Scottsdale Healthcare, said the new drug, TH-302, appears promising and may be more effective and less toxic to healthy tissues than conventional drugs. Phase 1 and Phase 1/2 trials are underway to investigate the safety and activity of TH-302 in patients with advanced solid tumors.



Special Event Highlights
Hot Cars, Sub-Par & Pavement Stars

StepNOut for Pancreatic Cancer doubles dollars

TGen's 3rd annual StepNOut for Pancreatic Cancer Research Walk/Run on Nov. 2, 2008, attracted over 750 people, nearly triple the previous year's participants — raising over $88,000, more than twice as much as the 2007 event.

Runners and walkers at Kiwanis Park in Tempe heard Honorary Chair Mark Curtis, co-anchor of *12 News*, describe how he lost his mother in September 2008 to pancreatic cancer.

TGen Physician-In-Chief Dr. Daniel Von Hoff provided an update about TGen's research and the advances being made against this most deadly form of cancer.

Nearly $8,000 was raised on the day of the event. One woman who had lost her dad to pancreatic cancer described how she read about the event in that morning's newspaper, put down her coffee and declared, "It looks like we're walking today."

Patients, families and community members from across the Valley and the nation joined with eight sponsors, including CWIE Holding Company, which had the largest employee turnout with more than 75 people. Brother and sister, Ron and Stephanie Cadwell, owners of CWIE, lost both their parents, Frank and JoAnn, to pancreatic cancer in 2008.

The top fundraising teams were: Roseanna Norman, $19,241; Suzanna Hilton, $15,650; Stephanie Cadwell, $4,380; Kathy Wills, $3,645; and Beth Katz, $3,251.

This year, the TGen Foundation introduced a new way of participating in the event, launching a software program that enables participants to create their own online fundraising pages to fight pancreatic cancer.

Alana's Champs 5K remembers TGen friend

The first Alana's Champs 5K, a run and walk to benefit TGen brain cancer research, drew more than 200 people Dec. 6, 2008, to the Arizona Capitol in downtown Phoenix.

The run and walk raised nearly $13,000 and included participation from nearly 100 TGen employees, thanks in part to the sponsorship of DPR Construction and the SmithGroup. The event was coordinated by TGen volunteer Brett Bernacchi and the Arizona Road Racers, and is named for Brett's wife, Alana Lysholm-Bernacchi, a TGen neurogenomics researcher, who died as the result of a brain tumor on Dec. 3, 2007.

Terri Link Memorial blessed with sunshine

The 2nd annual Terri Link Memorial Fund Golf Tournament raised $26,540 through the dedicated efforts of 80 golfers who played under sunny skies and ideal conditions Oct. 4, 2008, at the Georgia Club in Statham, Ga.

The tournament is named for Terri Link, who died in 2006 from Adrenocortical cancer. Her husband, Drew Link, a TGen volunteer, worked with nearly 20 volunteer friends and colleagues and 36 sponsors to plan the program and execute the event, which benefits TGen's adrenocortical cancer research.

Adrenocortical carcinoma is a rare cancer that forms in the outer layer of tissue of the adrenal gland, which is a small organ on top of each kidney that makes steroid hormones, adrenaline, and noradrenaline to control heart rate, blood pressure, and other body functions.

Seena Magowitz Golf Classic reaches $1 million

The Seena Magowitz Celebrity Golf Classic surpassed the $1 million mark in total contributions with its 6th annual fund-raiser for pancreatic cancer research on Dec. 6 at the Westin Kierland Resort & Spa.


This year's tournament raised more than $400,000 for TGen and the El Segundo, California-based Pancreatic Cancer Action Network.

Celebrities present included Arizona Diamondbacks' pitcher Brandon Webb, who was among the 168 golfers at the tournament, organized by Scottsdale resident Roger Magowitz – a member of TGen's National Pancreatic Cancer Committee – in memory of his mother, Seena, who died of pancreatic cancer in 2001.

Dr. Daniel Von Hoff, TGen's Physician-In-Chief, inspired a golf luncheon audience of 300 with a promising pancreatic cancer research update.

The event, themed "An Industry Unites," is known for bringing together such rivals as Sealy, Simmons, Tempur-Pedic, Stearns & Foster and Protect-A-Bed.

Many executives have lost colleagues or family members to the disease and the industry has rallied around the cause.

Despite a difficult economy, the event this year exceeded its goal of $350,000 by nearly 14 percent.

To learn how you can help support TGen research, please visit the TGen Foundation website at www.helptgen.org.

Q&A WITH

Laurie Carson, President & Founder Lung Cancer Research Foundation

Lung cancer is the leading cause of cancer mortality globally in both men and women. And yet it receives less federal research funding per death than any other major cancer. To help offset this disparity, the New York-based Lung Cancer Research Foundation (LCRF) recently donated $75,000 to lung cancer research and named a research bench at TGen.

Laurie Carson, President and Founder, created LCRF in 2005 after losing two relatives to lung cancer: a brother who never smoked, and an uncle who had quit smoking 20 years prior to his death.

Following a tour in 2008, Ms. Carson walked away impressed by TGen's responsiveness and scientific efforts, and within a few months submitted her organization's donation for the research bench as part of a larger plan to give LCRF a national reach.

Question: What does it mean for the Lung Cancer Research Foundation to name a research bench here at TGen?

Answer: LCRF is excited and honored to be able to name a research bench in lung cancer at TGen. One of the goals of LCRF is to continue building relationships with the country's leading research institutions and investigators. It is our hope that the naming of this bench will not only expand awareness for the disease, but also foster greater research connections and collaborations that will have a significant impact on patients with lung cancer.

Q: How would you best describe the significance of your generous action to the general public?

A: Historically, lung cancer has been a very overlooked and under-funded disease. At the LCRF, we believe that new scientific knowledge is beginning to provide new opportunities that will lead to new targets for therapies, as well as better diagnostic and prognostic tools. TGen's focus on translational genomics research puts them on the forefront of this new frontier.

Q: When it comes to lung cancer, many people "blame the victim" because of the popular assumption that it is a self-inflicted illness caused by smoking cigarettes. How do you convey to the general public the urgency of funding lung cancer research, as much or even more than other cancer research?

A: There is a great disparity in lung cancer research funding as it relates to the incidence of the disease. Health officials expected over 200,000 new diagnoses of lung cancer in the United States in 2008. With a very low survival rate, lung cancer claims more lives than breast, colon and all gynecological cancers – combined. While the link between smoking and lung cancer is well established, it is time to resist the "blame the victim" or "the one size fits all" mentality and focus on new discoveries that will lead to better lives for all lung cancer patients. This can only be achieved with increased funding for lung cancer research.

Q: Lung cancer in the U.S. has been the leading cause of cancer mortality. Do you see that changing any time in the future?

A: There are great challenges in the field of lung cancer. We know there are several types of lung cancer with a great deal of variability among the types. The good news is that attitudes toward lung cancer are shifting and there appears to be an increased interest in studying the disease.

Those of us at the LCRF hope that this pursuit of new knowledge will continue to take us down the path of progress. It will be a great day when survival rates are in line with the other major cancers.

TGen Foundation News

Community responds generously to accelerate research

In response to the nationwide outpouring of support from contributors at every possible level, the TGen Foundation has launched a special recognition program known as the President's Research Associates.

Members of this new program help accelerate TGen's mission of translating scientific discoveries made in the research laboratory to clinical treatments for patients. Members receive the *TGen Today* magazine, e-mails about our latest discoveries and special announcements.

Support comes from individuals, businesses, foundations and others. To learn more about how you can help, please contact Dean Ballard, the Foundation's Assistant Director of Development, at 602-343-8543 or e-mail dballard@tgen.org.

TGen gratefully acknowledges the following inaugural members of the President's Research Associates:

Ms. Jami P. Alire, Fervor Creative, Inc.
Luc E. Anselin and Emily Talen
Jeanne W. Archer
Mr. and Mrs. Brien C. Armstrong
Kay and Bill Baker
Dean and Carey Ballard
Mr. and Mrs. Richard I. Barr
Harry and Carol Beatty
Ms. Marilyn A. Beaver
Mr. Stephen Becker
Bruce D. Bevins
Dr. Robert A. Brooks
Mr. and Mrs. Maynard Carpenter
Lillian Cashman
Ms. Suzanne Chaillie
Marilynne J. Clancy
Wanda Clark
Ronald Cocciole
Debra Costa
Jo Crumbaker
James A. and Bonnie R. D'Aquila
Mr. Patrick Donahue
Ms. Gail E. Dunlap
Richard Edelman
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Dave Elrod, DPR Construction
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Mrs. Sherrill D. Koopot
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Mr. Matthew Lester
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Angela Weir
David and Sharon Weiss
Crissy and Lawrence Wells
Mr. and Mrs. Edward White
Colleen Wilkinson
Dennis Younes
Mr. Randall L. Yturri

Diane Halle — Continued from page 5

Q: At a time when many charities are struggling, how do you prioritize the funding requests you receive?

A: For 2009 and possibly 2010, our family is going to focus on those in need of food, shelter, healthcare and spiritual hope. The basic needs have always been a concern of mankind. It becomes difficult because the arts are another passion of ours. However, due to the economic times, we've had to shift priorities.

Q: We understand your late husband, Herbert K. Cummings, died of pancreatic cancer. What would be your hope for the funds you have dedicated to the efforts of Dr. Daniel Von Hoff to study this disease?

A: I lost my late husband, as well as many dear friends to pancreatic cancer. Bruce also lost his wife to pancreatic cancer.

For us both, uncovering the hereditary component to pancreatic cancer would be one of the most important aspects of our philanthropic work. Enabling Dr. Von Hoff and his team to find a cure for this disease is a paramount goal.

Sen. McCain Visits TGen

Engages staff about the economy, regulation, research and construction of ABC II

Sen. John McCain visited TGen in late February. His presentation — video-conferenced from TGen's headquarters to its labs in Scottsdale and Flagstaff — included the senator's views on the economy, international affairs, federal regulations and Congress' recent approval of the $787 billion federal economic stimulus package.

Dr. Paul Keim, a Senior Investigator and Director of TGen's Pathogen Genomics Division at TGen North in Flagstaff, shared with Sen. McCain that regulation proposed in the wake of the 2001 anthrax-letter attacks is having ripple effects across the entire research community.

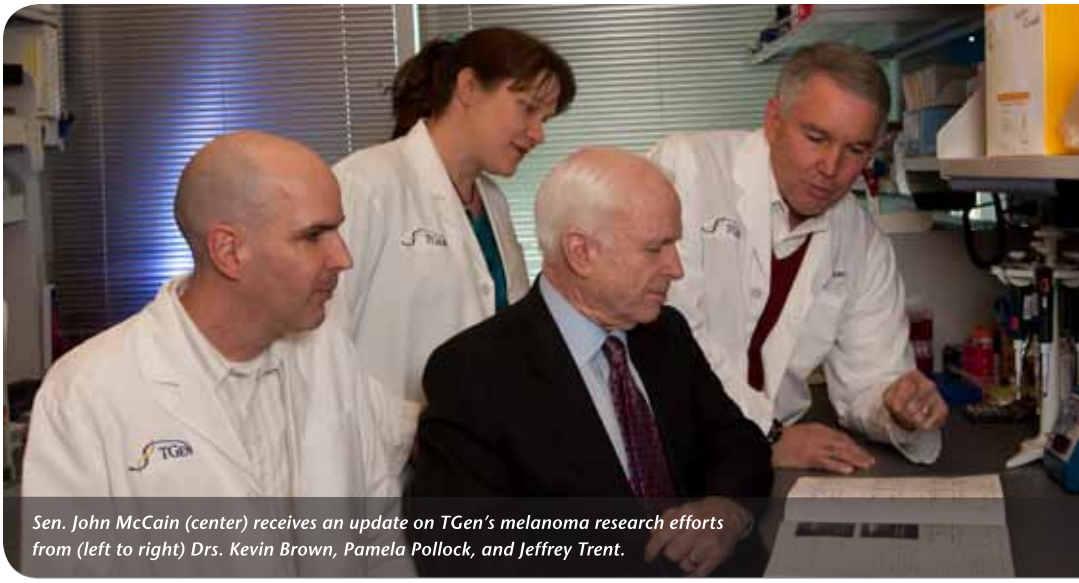
"We're afraid that there may be an over-reaction, and that this may, in fact, stifle the ability of dispersed research institutes like TGen to carry on in this area," Dr. Keim said.

Sen. McCain, recently appointed to the U.S. Senate's Committee on Homeland Security & Government Affairs, called bio-defense "part of the battleground of the future."

The senator also was asked if there was a chance that the planned Arizona Biomedical Collaborative II (ABC II) building near TGen headquarters could be considered under the $787 billion stimulus package passed by Congress. Sen. McCain deferred spending details to the State, but said he hoped it would be included. The $470 million ABC II biomedical research and education building was approved last year by the Arizona Legislature, the single largest part of a $1 billion plan for university construction. Those plans were recently put on hold because of questions about state financing in the face of a down economy.

On a related issue, Sen. McCain, who serves as Chairman of the TGen Foundation's National Advisory Council, said the federal stimulus package includes an additional $10 billion through the National Institutes of Health for scientific research.

Dr. Trent said that TGen's record of grant approvals is nearly double the national average. "All good ideas do not come out of Boston. We are competitive."



Sen. John McCain (center) receives an update on TGen's melanoma research efforts from (left to right) Drs. Kevin Brown, Pamela Pollock, and Jeffrey Trent.

Q: Why did you think it was important to dedicate funding for the study of diseases and conditions specifically affecting women's health?

A: Beyond pancreatic cancer, there have been other hereditary health concerns in both of our families. Some of these relate specifically to women. My passion personally for the last 15 years has been towards helping women and children. If we can stop certain diseases from following a generational path, wouldn't that be a miracle?

Q: What advice might you have for others who want to become involved in charitable giving?

A: To quote Scripture, "Suppose you see a brother or sister who needs food or clothing, and you say, 'Well, good-bye and God bless you; stay warm and eat well.' But then you don't give that person any food or clothing. What good does that do? So you see, it isn't enough just to have faith. Faith that doesn't show itself by good deeds is no faith at all." – James 2:14-17, *New Living Translation*

Safeway gives TGen $685,000 for breast cancer research

Arizona grocery chain increases contribution to TGen by 37 percent

Safeway presents a check for $685,236 to TGen for breast cancer research. From left are: Dr. Heather Cunliffe, a TGen breast cancer researcher; Dan Valenzuela, President of Safeway Inc.'s 116 Arizona stores; Cathy Kloos, Safeway's Phoenix Division Public Affairs Director; Erin Massey, TGen Foundation Director of Development; and Michael Bassoff, President of the TGen Foundation.

Safeway Inc. recently presented TGen a $685,236 check for breast cancer research. Dan Valenzuela, President of Safeway's Phoenix Division, which includes 116 stores throughout Arizona, thanked Safeway's customers and employees for stepping up for scientific research.

"We're very proud to donate to such an organization as TGen," Valenzuela told about 50 TGen employees gathered March 3 for the presentation. "Because of your research, and the things that you do, we're honored to support your efforts."

Safeway's donation represents a 37 percent increase from the $500,000 Safeway presented TGen last year. Safeway raises the funds each October through a month-long campaign at Arizona Safeway stores.

"You can't give enough credit to our customers and employees," Valenzuela said, adding that a major reason Safeway chose to support TGen was that the research dollars would stay in Arizona.

"The benefit (of TGen's research) is far-reaching. The big thing is, where do the funds go? It (TGen) is local," Valenzuela said.

Dr. Jeffrey Trent, TGen's President and Scientific Director, said the significant and timely contribution by Safeway is an example of the generosity repeatedly shown by local businesses and the people of Arizona.

"This donation will be put to immediate use to help develop treatments and, eventually, find a cure for breast cancer, a major priority for us at TGen and a goal that would benefit everyone," Dr. Trent said.

Michael Bassoff, President of the TGen Foundation, described Safeway's contribution as a special tribute to TGen researchers as they work to conquer cancer and other debilitating diseases.

"Contributors are looking hard at their charitable opportunities and are looking for the organizations that are run efficiently and produce results," Bassoff said. "Today's donation by Safeway is a tribute to you, the work you do in the laboratories, and the many Arizonans who came forward to support TGen," Bassoff told the assembled TGen employees.

Bassoff also credited the "extra gumption" and hard work of Safeway employees who were willing to ask customers if they would contribute to breast cancer research.

Dr. Heather Cunliffe, a TGen breast cancer researcher, said Safeway's donation helps accelerate work toward new treatments for breast cancer patients.

TGen
A Non-profit Medical Research Institute

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