

Translational Genomics Research Institute

TGEN TODAY

'1000 Genomes Project' 2
designed with patients in mind

Research: Dr. Kevin Brown 6
discovers blood cancer link

TGen & Van Andel retreats 8
boost Arizona-Michigan ties

Profile: Dr. Raoul Tibes is 10
a physician and a scientist

How to create your own 15
TGen fundraising page

'DREAM TEAM' SEEKS CURE FOR PANCREATIC CANCER

DR. DANIEL VON HOFF
STANDS UP TO CANCER

PAGE 4

SUMMER 2009

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Find out more by contacting Denise A. McClintic, J.D., LL.M., at 602-343-8611 or dmclintic@tgen.org.

Translational Genomics Research Institute
TGEN TODAY

Page **2** — Next Generation Genomic Research

Page **4** — \$18 Million Grant Funds TGen Pancreatic Cancer Research

Page **6** — Cancer Research Collaboration

Page **8** — TGen / Van Andel Retreats Highlighted

Page **10** — Dr. Raoul Tibes - A Rare Breed



12 TGen In Brief, **14** TGen Foundation Events Highlights,
16 Mountains of Hope Funds Breast Cancer Research, **17** Anne Rita Monahan
Back Cover TGen Helios Scholars Program Highlights

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. For more information, visit: www.tgen.org



Life: It's Variations of A Theme

1000 Genomes Project provides an in-depth look across multiple genomes

In 2003, after 13 years of research and a cost of nearly \$3 billion, the federal government's Human Genome Project sequenced — spelled out — the complete DNA code of an entire human genome. That effort produced a massive amount of data about one person, mapping the more than 3 billion base pairs of alleles that make each of us unique.

But, it was data from just one genome.

What researchers need is genomic data from many people to better understand the variations that form the basis of human health – and human disease. In another effort, the International HapMap Project (2002-07) studied 269 individuals from across the globe, producing more valuable data about genetic variation, but only in selected areas scanned in each genome.

A new international effort launched in 2008 – the 1000 Genomes Project – aims to sequence, or spell out, the complete genomes of more than 1,000 individuals, establishing by far the most detailed catalogue of human genetic variation as a tool for medical research.

Such research will lay the groundwork for the personal genomics era of medicine, in which people routinely will have their genomes sequenced to predict their individual risks of disease and response to drugs, according to the National Institutes of Health, which is helping fund this study.

The 1000 Genomes Project aims to considerably reduce the time and cost of sequencing individual genomes by using faster and less costly technologies. And TGen is playing a substantial role in guiding this objective.

Dr. David Craig, Acting Director of TGen's Neurogenomics Division, said the result of this massive project should be a nearly exhaustive accounting of the common genetic changes among healthy individuals.

"If the Human Genome Project provided a blueprint of our genetic code, the 1000 Genomes Project should provide detailed annotation for researchers and clinicians that hopefully translates into vastly improved patient care," Dr. Craig said.

TGen recently was awarded one of five data processing grants; \$1.6 million to fund a data processing pipeline for the 1000 Genomes Project.

As the project ramps up, Dr. Craig led a day-long discussion June 12 at TGen. Included were representatives from UCLA and Life Technologies – collaborators on TGen's grant – and colleagues from Baylor College of Medicine, Amazon.com, and the Van Andel Research Institute.

Technology saves time and money

To reduce the time and cost of mapping each genome, researchers will rely on new technology, so-

called next generation sequencing, which will require highly coordinated collaboration by multiple research groups.

In addition to three other next-generation sequencing platforms, TGen will process data using the SOLiD 3 systems produced by Life Technologies. TGen will help develop software tools for the vast amounts of data that will be generated, while adhering to common data and analytical standards so the results can be accessed by researchers across the globe.

THE 1000 GENOMES PROJECT SHOULD PROVIDE RESEARCHERS WITH THE DATA THEY NEED TO MAKE TREMENDOUS PROGRESS IN TRANSFORMING LABORATORY DISCOVERIES INTO WAYS OF PREVENTING, DETECTING AND TREATING COMMON DEBILITATING DISEASES

"We have three main goals," said John Pearson, Head of TGen's Bioinformatics Research Lab. "Developing tools for monitoring data quality. Developing tools for aligning the data and detecting genetic variation across the genome. And developing a suite of software capable of simultaneous viewing of sequence data across multiple sites for the purpose of quality control and variant inspection."

Those gathered at TGen agreed that they should: establish a "gold standard" of reliability and verification, ensure that – while identities of the DNA donors remain confidential – the sequencing results will be freely available via the Internet, and process the data in a way that is useful not only for academic study but also for

commercial applications.

This is the first large-scale project to use the next-generation sequencing platforms for extensive human re-sequencing; machines that produce millions of DNA sequence reads in a single pass at a fraction of the original cost.

How the project will proceed

The project will include three steps: a detailed scan of six individuals (a mother, father and child from two families); a less detailed scan of 180 individuals; and a scan of exons, or coding regions in the genome, among 1,000 individuals.

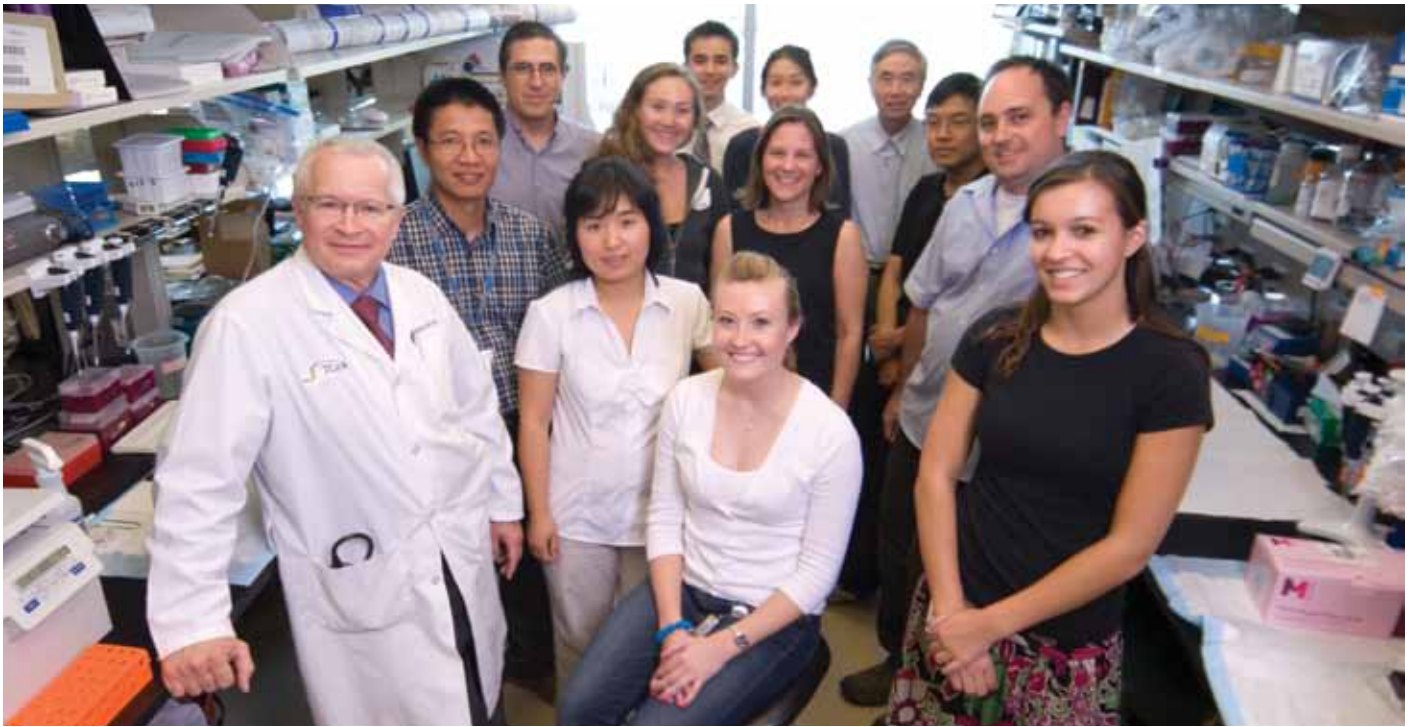
Scientists hope that by layering the information, the sequences from the six in-depth scans will fill any gaps in the less detailed scans, providing a comprehensive view of more than 1,000 human genomes.

Dr. John Carpten, Director of TGen's Integrated Cancer Genomics Division, said TGen's goal is not only to reduce the time and expense of sequencing individual genomes, but also to process data in a way that leads to the best verifiable results.

"We want to do it right. We're excited about this new technology and where it's going, and how we can help patients," Dr. Carpten said. "It's never been done before."

Dr. Craig said that the 1000 Genomes Project should provide researchers with the data they need to make tremendous progress in transforming laboratory discoveries into ways of preventing, detecting and treating common debilitating diseases such as Alzheimer's, autism, diabetes and many types of cancer.

"Four hundred years after Galileo invented the telescope, and 40 years after landing on the moon, we stand at the threshold of major discoveries into the inner-space of molecular biology that will benefit humankind forever," Dr. Craig said.



Dr. Daniel Von Hoff (left), TGen's Physician-In-Chief, is joined by his laboratory staff.

TGEN LANDS \$18 MILLION GRANT TO STAND UP TO CANCER

TGen and the University of Pennsylvania (Penn) have received a three-year, \$18 million grant from Stand Up to Cancer (SU2C) to research pancreatic cancer.

Dr. Daniel Von Hoff, TGen's Physician-In-Chief, and Dr. Craig B. Thompson, Director of the Abramson Cancer Center at Penn, are co-leaders of SU2C's pancreatic cancer "Dream Team," which will investigate new approaches to treating patients with pancreatic cancer, the fourth leading cause of cancer death in the U.S.

"We want to do something dramatic. It is going to take a tremendous amount of real thinking power to make that difference, so it is a dream come true to be able to put this team together to work towards this goal," said Dr. Von Hoff, who also is Chief Scientific Officer for TGen Clinical Research Services (TCRS)

at Scottsdale Healthcare, a primary clinical research site for TGen and the SU2C grant.

The \$18 million to TGen and Penn was the largest single grant among five awards, totaling \$74 million, announced by SU2C, a philanthropic group created by members of the entertainment industry and cancer scientists a year ago to quickly turn scientific discoveries into ways to care for cancer patients.

The goal of the pancreatic cancer Dream Team research project – "Cutting Off the Fuel Supply" – is to develop tests, using advanced imaging techniques, to determine what nutrients pancreatic cancer cells require to fuel their growth and survival. Understanding the cell's fuel supply will help scientists develop more individualized treatments with fewer side effects.

TGen and its clinical partner at TCRS

will launch a series of innovative clinical trials in advanced pancreatic cancer. These clinical trials will be designed to deprive pancreatic tumors of crucial nutrients, thereby cutting off the fuel supply. This approach will be added to the already promising and clinically effective treatment regimes at TCRS.

TCRS is located at the Virginia G. Piper Cancer Center at Scottsdale Healthcare Shea Medical Center in Scottsdale. Other clinical sites in the study are at Penn in Philadelphia and at John Hopkins University in Baltimore.

The TGen-Penn team will combine translational methods developed at the University of Pennsylvania with individualized-therapies developed by TGen to rapidly move laboratory findings to bedside treatments, benefiting pancreatic cancer patients as quickly as possible. They will test

the drugs in combination with existing standard chemotherapy, with the hope of improving quality of life while increasing the percentage of patients surviving beyond one year.

In addition to his positions at TGen and Scottsdale Healthcare, Dr. Von Hoff is a Clinical Professor of Medicine at the University of Arizona. His major interest is in the development of new anticancer agents. Dr. Von Hoff's work focuses on the development of molecularly targeted therapies for patients with pancreatic and other advanced cancers. He is serving a six-year term on the National Cancer Advisory Board and has served on the FDA's Oncology Advisory Committee. Dr. Von Hoff is a past president of the American Association for Cancer Research, was on the AACR and the American Society of Clinical Oncology's Board of Directors, and is a fellow of the American College of Physicians.

Since its inception in 2002, TGen has pioneered cutting-edge research in genomic medicine, enabling physicians to design targeted and individualized therapies for patients suffering from cancer and other debilitating diseases.

The five Dream Teams – culled from 237 submissions – are comprised of seven leaders, four co-leaders and 27 principal researchers from more than 20 leading institutions, with more than 300 individuals participating.

Collectively, the research that will be done through the Dream Team projects could impact the diagnosis and treatment of a wide range of cancers in adults and children, including — but not limited to — pancreatic, breast, ovarian, cervical, uterine, brain, lung, prostate, rectal and colon. These represent two-thirds of all U.S. cancer

deaths; 562,340 people are expected to die of cancer this year in the U.S.

On average 1 in 3 women and 1 in 2 men in the U.S. will be diagnosed with cancer in their lifetimes. Worldwide, cancer annually kills nearly almost 8 million.

On behalf of Stand Up To Cancer, the 28,000-member American Association for Cancer Research (AACR) will be responsible for administering the grants.

AACR is the oldest and largest

**THE TGEN-PENN TEAM WILL
COMBINE TRANSLATIONAL
METHODS DEVELOPED AT THE
UNIVERSITY OF PENNSYLVANIA
WITH INDIVIDUALIZED-THERAPIES
DEVELOPED BY TGEN TO RAPIDLY
MOVE LABORATORY FINDINGS TO
BEDSIDE TREATMENTS, BENEFITING
PANCREATIC CANCER PATIENTS AS
QUICKLY AS POSSIBLE**

scientific organization in the world focusing on every aspect of high-quality, innovative cancer research from the bench to the bedside. Lauded internationally for its scientific breadth, innovation and spread of new knowledge about cancer, the AACR is on the front lines in the quest for the prevention and cure of cancer.

The Stand Up To Cancer movement raises funds to hasten the pace of groundbreaking translational research that can get new therapies to patients quickly and save lives. It was begun in 2007 by a group of women whose lives have all been affected by cancer in profound ways. They began working

together to marshal the resources of the media and entertainment industries in the fight against the disease.

The Entertainment Industry Foundation has distributed hundreds of millions of dollars to support critical health, education and social issues.

Pancreatic cancer remains one of the most deadly forms of cancer. More than 75 percent of patients die within the first year of diagnosis. Recent advancements have had little impact, and a new approach is desperately needed.

Using modern tumor imaging, it is possible to monitor a tumor's glucose utilization and such tests are now routinely used in clinical practice. In most cases, the more glucose a tumor is using, the more advanced the tumor and the greater likelihood of spread. Similarly, if a tumor is using less glucose as a response to chemotherapy, then it is a good indication that the tumor is responding to treatment.

Pancreatic cancer presents a unique challenge because it is addicted to another molecule, glutamine, rather than glucose. Glutamine is an amino acid that helps build muscle mass and is used by some cells for energy. When cancer feeds or metabolizes excess amounts of glutamine, it can lead to extreme weight loss by robbing other cells of this important nutrient, a condition from which many pancreatic cancer patients suffer.

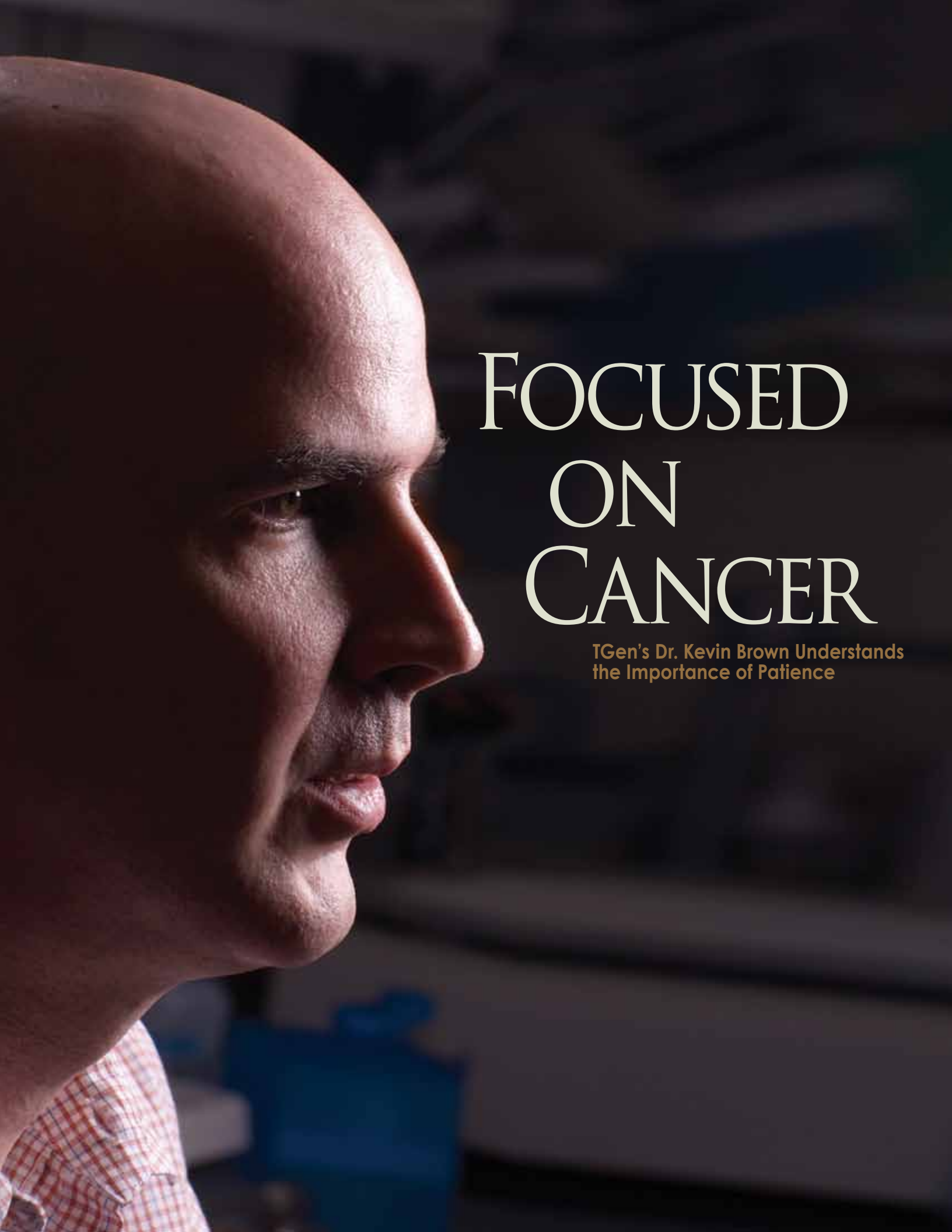
In addition, the waste that is a by-product of this process generates an intense reaction from surrounding normal cells, which then secrete growth factors that help tumor cells grow. Cancers that use excess glutamine are often resistant to standard forms of chemotherapy, another characteristic of pancreatic cancer.

**CBS NEWS ANCHOR
KATIE COURIC IS A
PANCREATIC CANCER
RESEARCH ADVOCATE**



Couric explains Stand Up to Cancer
www.youtube.com/watch?v=0dh60lq2IK0

TGen-Penn Dream Team:
www.cbsnews.com/stories/2009/05/27/earlyshow/health/main5043867.shtml?source=related_story



FOCUSED ON CANCER

TGen's Dr. Kevin Brown Understands
the Importance of Patience

TGen Research

TGEN AND UC BERKELEY SCIENTISTS USE 'POOLED' METHOD TO DISCOVER GENE ASSOCIATED WITH NON-HODGKIN LYMPHOMA

It was a little outside of his scientific comfort zone, but TGen's Dr. Kevin Brown jumped at the chance to help researchers at the University of California Berkeley conduct the first genome-wide association study of non-Hodgkin lymphoma.

After all, Dr. Brown once studied the behavior of salamanders during his undergraduate studies, so he's used to taking on new and unusual tasks.

Dr. Brown, one of the first scientists to join TGen after the biomedical research institute was formed in 2002, has studied skin cancer for most of the past seven years.

But recently, Dr. Brown, an Associate Investigator in TGen's Integrated Cancer Genomics Division, was asked to work with Dr. Christine Skibola, an Associate Adjunct Professor of Environmental Health Sciences at UC Berkeley's School of Public Health.

What resulted July 20 was the publication of a scientific paper in the journal *Nature Genetics*, which identified a gene that carries nearly twice the risk of developing an increasingly common type of follicular lymphoma.

"One of the primary goals of doing a study like this is to be able to look at prevention and early detection strategies. There's clearly a genetic component to the disease," said Dr. Brown, the study's co-lead author. "This is a starting point. This gives us new insight into how the disease works. It gives us some potential to target the gene."

The investigative team led by Drs. Brown and Skibola identified a single

nucleotide polymorphism, or SNP, strongly associated with the risk of developing follicular lymphoma, a cancer whose rates have nearly doubled in the past 30 years.

TGen and UC Berkeley scientists identified the SNP – a particular DNA variant within the more than 3-billion base human genome – as rs6457327.

One of the keys to the study's success was the use of a "pooled" genome-wide association study, a method of

CARRIERS HAVE NEARLY TWICE THE RISK OF DEVELOPING FOLLICULAR LYMPHOMA

identifying genes championed by Dr. David Craig, Associate Director of TGen's Neurogenomics Division, and contributor to the *Nature Genetics* study.

The method has been successfully used at TGen to discover genes associated with other diseases, including Alzheimer's and metabolic diseases.

This technique allowed the TGen-UC Berkeley team to screen more than 500,000 SNPs. The nearly 90 most significant SNPs were then genotyped to more closely examine their association with lymphoma.

Researchers found that for SNP rs6457327, the presence of the G allele – a DNA letter that varies within the genome – was protective against follicular lymphoma, while the presence of the A allele was predictive of an increased risk of

developing follicular lymphoma. Dr. Brown said individuals who had the A variant were nearly twice as likely to develop follicular lymphoma.

Follicular lymphoma accounts for as much as 30 percent of all non-Hodgkin lymphoma (NHL), a cancer of the lymphatic system involving the blood, bone marrow and lymph nodes. In NHL, tumors develop in lymphocytes, a type of white blood cell. Follicular lymphoma arises from B-cells, a specific type of white blood cell. NHL is the fifth most common type of cancer in the U.S., and is newly diagnosed in about 66,000 Americans each year, and annually kills nearly 20,000, according to the National Cancer Institute.

Dr. Skibola said more studies would be needed to determine the biological importance of other SNPs linked to rs6457327 that might change the function of the gene. This could help determine how they might influence risk of the disease.

The scientists also want to know if genetic susceptibility to follicular lymphoma is associated with:

- Environmental factors, such as exposure to the sun.
- Conditions such as psoriasis – a chronic, autoimmune skin disease closely associated with a similar region of the genome.
- Exposure to viruses. Follicular lymphoma is associated with HIV infection, occurring in as many as 10 percent of all HIV-positive patients, according to the Lymphoma Research Foundation.



Above: Dr. Jeffrey Trent (upper left), TGen's President and Research Director, welcomes the faculties of TGen and the Van Andel Research Institute on June 4 at the Phoenix Convention Center during the 2009 TGen Scientific Retreat.

Below: TGen staff traveled to the Crystal Mountain Resort in Thompsonville, Mich., May 12-15, to attend the first joint scientific retreat between TGen and the Van Andel Research Institute.



"The Van Andel faculty members are not only impressive with regards to their publication records, but they are all clearly entrenched in the education of the next generation of scientists." – Dr. Matthew J. Huentelman, Investigator in TGen's Neurogenomics Division

"I'm convinced that we can realize much more translational impact together than independently." – Dr. Spyro Mousses, Director, TGen Pharmaceutical Genomics Division

TGEN-VARI SCIENTIFIC RETREATS

More than 30 members of TGen's staff traveled to the Crystal Mountain Resort in Thompsonville, Mich., May 12-15, to attend the first joint scientific retreat between TGen and the Van Andel Research Institute. Nearly 300 people participated in this retreat, including staff from TGen and Van Andel and from several Michigan universities and other institutes.

That was followed June 4 with 20 members of the Van Andel staff participating in TGen's annual scientific retreat, which also drew nearly 300 participants at the Phoenix Convention Center.



KEYNOTE SPEAKER HIGHLIGHTS ARIZONA-MEXICO RESEARCH

Dr. Gerardo Jimenez-Sanchez, M.D., Director General of Mexico's National Institute of Genomic Medicine, addresses TGen retreat.

Differences in the DNA among Mexico's 65 ethnic populations must be identified to significantly advance that developing nation's public health, a top Mexican official said June 4 at TGen's 2009 Scientific Retreat.

Dr. Gerardo Jimenez-Sanchez, M.D., Director General of Mexico's National Institute of Genomic Medicine (INMEGEN), told more than 300 assembled scientists that such information might one day explain why a greater proportion of Mexicans, than those in other countries, got sick and died during the recent worldwide outbreak of swine flu.

"This is when science can make a life-changing impact," Dr. Jimenez-Sanchez said during his keynote address at the day-long conference at the Phoenix Convention Center. He also was

interviewed by TGen Board Chairman José Cárdenas, host of the KAET-TV, Channel 8, public-affairs program, *Horizonte*, which was broadcast June 11.

Discovering the unique genetic biomarkers within Mexico's surprisingly diverse populations could lead to development of more specific, safer and effective drugs to combat such disabling conditions as diabetes, heart disease and cancer – especially as Mexico moves to join the ranks of the world's developed nations, he said.

Currently, many drugs sold in Mexico are manufactured in Europe, and are designed for generic populations, Dr. Jimenez-Sanchez said. "We are believers in personalized medicine. We need to develop our own (scientific) tools and our own products through genomic medicine."

Dr. Jeffrey Trent, TGen's President and

Research Director, joined Dr. Jimenez-Sanchez in predicting that genomic research would not only benefit Mexicans, but also would improve the health of Hispanics living in the U.S.

"If we are not developing drugs specifically for individuals based on their genetic make-up, we might not be giving them the right drugs at the right time in the right dosages," said Dr. Trent, who until TGen's start in 2002 held a similar U.S. post to Dr. Jimenez-Sanchez's position in Mexico. Dr. Trent is the former Scientific Director of the National Human Genome Research Institute at the National Institutes of Health in Bethesda, Maryland.

Dr. Trent served at NHGRI when it was directed by Dr. Francis Collins, who in August was confirmed by the U.S. Senate as President Obama's director of the National Institutes of Health.

TGen Profile

A Double Threat to Cancer

TGen physician-scientist propels advances in ‘personalized medicine’ at TCRS

The paw of a golden-mane lion hangs playfully from the reception desk, striking a disarming pose, at TGen Clinical Research Services at Scottsdale Healthcare.

Nearby are other stuffed toys – zebras, a cheetah, a tiger and a 4-foot-tall giraffe.

“A lot of patients want to take them home,” and sometimes they do, said Dr. Raoul Tibes, one of a rare breed of physician-scientists with one foot at the bench of his laboratory and one foot at the bedside of his patients.

Tibes is riding the wave of the future in medicine. He is a doctor able to stay on top of the latest science, while expertly guiding his cancer patients through the rigors of clinical drug trials.

It isn’t easy. Few cancer specialists are willing to shoulder the burdens of both the lab and the clinic. Most want to specialize as scientists, or doctors.

But a few, like Dr. Tibes, are both.

He works as a doctor at the clinic in Scottsdale, where he also focuses on prostate cancer. And he conducts laboratory research for TGen in

Phoenix, where he supervises a translational laboratory research program in leukemia.

Dr. Tibes is a board certified internist, hematologist and oncologist. His patients have already been through the medical wringer by the time they see him. They must have already exhausted other treatments, including surgery, radiation or conventional chemotherapies. Many have had remissions, only to have their cancers recur.

WE TAILOR EACH PATIENT’S NEW TREATMENT BASED ON THE MOLECULAR CONTEXT OF THE DISEASE

“Unfortunately, cancers come back. They know they have advanced disease,” said Tibes, who encourages cancer patients and their doctors to contact him as soon as possible when patients qualify for clinical trials.

Physicians at the Scottsdale clinic are at the forefront of creating personalized therapies for individual patients, based

on each cancer’s genomic profile. Tumors are tested by TGen scientists using state-of-the-art technologies as part of the process of developing specific drug treatments.

Personalized therapy is the new frontier in medicine. Genetic information is not only what makes us unique individuals, but helps TGen’s scientists discover the unique causes of our ailments, as well as specific new treatments.

This is the basis of what has come to be known in health circles as “personalized medicine,” and it is key to the success of TGen’s efforts; finding a specific drug treatment targeted to the individual needs of each patient, easing their suffering and, hopefully – some day – discovering a cure.

“We aim to tailor each patient’s new treatment based on the molecular context of the disease,” said Tibes, who received his medical degree from the Ludwig-Maximilians-University in Munich. He trained in internal medicine at the New York University Medical Center in New York. He served a fellowship in medical oncology/

Clinical trials participation

If you, or someone you know, would like more information about participating in TGen-sponsored clinical trials, please visit: www.tgen.org and click on ‘Clinical Trials’ or call 480-323-1339.

Dr. Tibes Is Active In Science And ...

TGen researcher Dr. Raoul Tibes is not only active in world scientific circles, but is also a volunteer in the Valley’s hematological community.

In June, Dr. Tibes made two oral presentations at the 14th Congress of the European Hematology Association in Berlin. The EHA is Europe’s largest hematological network and is the equivalent of the American Society of Hematology. Both of his talks focused on genes identified through RNAi screening that could affect the development of Acute Myeloid Leukemia (AML) and whose further study could eventually lead to improved patient therapies.

hematology at the world-renowned MD Anderson Cancer Center in Houston, prior to joining TGen and Scottsdale Healthcare in 2006.

Unlike conventional drug therapies, which use a broad spectrum of agents to attack diseases, targeted therapies help avoid toxicities and can result in fewer side effects, while increasing the effectiveness against cancers.

“We emphasize quality of life,” said Dr. Tibes, adding that extending the life of the patients, as well as maximizing their comfort, are paramount concerns.

Since opening in 2005, TGen Clinical Research Services at Scottsdale Healthcare has become one of the nation’s prominent sites for early phase clinical trials. It has experienced steady growth, with more than 3,000 patient-visits in the last year, said Dr. Ramesh K. Ramanathan, Medical Director of TGen Clinical Research Services.

“TGen in Scottsdale provides a unique opportunity for cancer patients in the greater Phoenix area and the Southwest,” said Dr. Ramanathan, who also is a senior investigator and Deputy Director of TGen’s Translational Research Division and a clinical professor of medicine at the University of Arizona College of Medicine-Phoenix in partnership with Arizona State University. “Patients no longer have to travel to Los Angeles, Houston or New York to avail themselves of cutting edge cancer therapies.”

TGen Physician-in-Chief Dr. Daniel Von Hoff initiated the clinical trials program. He is Chief Scientific Officer of TGen Clinical Research Services, Clinical



Dr. Raoul Tibes confers with patient Jerry Coffman of Phoenix who is undergoing treatment for basal cell cancer.

Professor of Medicine at the University of Arizona, and a member of the Mayo Clinic’s Comprehensive Cancer Center.

TGen Clinical Research Services, part of the Virginia G. Piper Cancer Center at Scottsdale Healthcare Shea, conducts Phase I and Phase II clinical drug trials:

- Phase I trials establish the safety, toxicity and best way to administer new drugs.
- Phase II trials continue safety evaluations and more precisely attempt to determine the effectiveness of a new drug on a particular disease.

At all stages, Dr. Tibes said, patients are consulted along with their oncologists. The patients are seen several times the first week, and often

weekly after that.

“We keep the patient and their primary oncologist in the loop at all times,” Dr. Tibes said of the clinic’s work with patients and their doctors.

If one line of treatment does not work, patients can join another clinical trial. Often the drugs administered under the guidance of Dr. Tibes and his colleagues at the Scottsdale clinic are being given to humans for the first time.

“We are among the first in the world to push the concept of personalized medicine in cancer therapies,” Dr. Tibes said. “The overall goal of personalized medicine is to make therapy more specific, less toxic, and the treatment outcome for the patient, better.”

... In The Community

In January, Dr. Tibes participated in the 10th Annual Leukemia Cup Regatta, a three-day fundraising event for the Desert Mountain States chapter of the Leukemia & Lymphoma Society, the world’s largest voluntary health organization dedicated to funding blood cancer research. The Arizona Yacht Club hosted the event at Lake Pleasant.





TGen-led team receives \$1 million skin-cancer grant

An international scientific team led by TGen received a \$1 million grant July 30 to study skin cancer from the Melanoma Research Alliance.

"There are situations in which there is a strong family history of melanoma. If you can identify the genes, or mutations, that put people at risk for melanoma, you can implement targeted screening or prevention efforts," Dr. Brown said.

"Identifying the genes that mediate development of melanoma will give you an understanding of the basic biology, and conceivably could give you some clues into ways that you could do chemo prevention, or other things, for people who are at strong risk of getting melanoma," Dr. Brown said.

with significant investments. At the same time, it holds the promise of furthering scientific investigations on a global basis," said Dr. Jeffrey Trent, TGen's President and Research Director. "We've already made a lot of progress."

The IBBL is part of a five-year plan to help turn Luxembourg into one of Europe's foremost biomedical centers – one uniquely focused on diagnostic biomarkers. The effort is wide-ranging and dynamic in its goals of improving patient care while lowering healthcare costs.

The project already has expanded in scope since it was announced last

Health and Research Center includes a tumor biorepository for TGen that will aid in discovering new ways to diagnose and treat breast cancer, which affects 1 in every 8 American women.

The new center is located in John C. Lincoln's Medical Offices 3, 19646 N. 27th Ave., in northwest Phoenix.

Breast cancer patients at the new center may donate tumor tissues, boosting TGen's abilities to use genomic and proteomic research to develop new ways to combat breast cancer.

TGen's role at the new center will be for research; not for TGen clinical trials.

The new center provides TGen with yet another avenue of assisting local hospital and research networks, including Arizona's three major universities, St. Joseph's Hospital and Medical Center, Banner Health and Scottsdale Healthcare.

TGEN IN BRIEF

The grant was made to a team led by Dr. Jeffrey Trent, TGen's President and Research Director, who is the Team Lead among the Principal Investigators in the study: Identification of Novel Melanoma Risk Genes Using High-throughput Genomics.

"The world-wide team of investigators on this project has worked together for a decade to identify individuals and families who are at increased risk for this deadly disease. While the team includes investigators from Europe and Australia, the research is particularly important to Arizonans who are disproportionately affected," Dr. Trent said.

Dr. Kevin Brown, an Associate Investigator in TGen's Integrated Cancer Genomics Division, also described the TGen-led team as part of an ongoing collaboration with the International Melanoma Genetics Consortium (GenoMEL), which has identified families worldwide that are predisposed to getting skin cancer.

The other Principal Investigators in the TGen-led research are: Dr. Nicolas Hayward of the Queensland (Australia) Institute of Medical Research; Dr. Goran Jonsson of Lund (Sweden) University; and Dr. Graham Mann of the University of Sydney (Australia).

IBBL takes shape in Luxembourg

A partnership between TGen and Luxembourg began in earnest July 6 with the arrival of a new CEO and the advent of a new building for the Integrated Biobank of Luxembourg (IBBL).

The IBBL is seen as an international collection, repository, analysis and distribution point for blood, serum, saliva, tumors and other biospecimen samples to assist investigators worldwide in scientific research.

"I think it's fantastic. This project helps Luxembourg with their long-term goals, while providing Arizona

year. For example, while initial plans focused on collecting tissues for cancer research, the IBBL is studying an international project involving the collection of biospecimens across Europe and Africa in an investigation of cardiovascular disease.

And, the information technology needed to process tissue samples has resulted in new computer software – developed jointly by TGen and Luxembourg investigators at the Institute Henri Tudor that could have commercial uses, said Tess Burleson, TGen's Chief Operating Officer.

John C. Lincoln facility helps TGen research

The May 4 opening of a new breast health center next to John C. Lincoln Deer Valley Hospital is providing significant research opportunities for TGen.

The 9,000-square-foot Breast



Diabetes breakthroughs described in New Orleans

TGen scientists have identified five genetic biomarkers that could help lead to improved treatments, with fewer side-effects, for patients with diabetes.

Senior Investigator Dr. Johanna DiStefano presented the findings in New Orleans on June 6, at the 69th Scientific Sessions of the American Diabetes Association.

"We identified genetic variants that may predict how well someone will respond to the common anti-diabetes drug, Actos," said Dr. DiStefano, Director of TGen's Diabetes, Cardiovascular & Metabolic Diseases Division. "The implications of these findings include determining which patients will best respond to the drug for the prevention or treatment of diabetes. In addition, this work lays the foundation for personalized medicine for patients with this disease."

Personalized medicine involves the rapid application of laboratory discoveries to therapies, depending on the individual genetic make-up of each patient.

A TGen-led team, working with scientists from the University of Southern California's Keck School of Medicine, investigated why as many as 30-40 percent of diabetes patients treated with thiazolidinediones (TZDs), such as Actos, fail to respond to the drug with the expected improvement in insulin sensitivity.

First complete myeloma genomes are sequenced

The Multiple Myeloma Genomics Initiative of the Multiple Myeloma Research Consortium (MMRC) has completed two high-resolution genomics profiling studies at TGen on the full reference collection of multiple myeloma tumor tissues from 250 patients.

And, in work at the Broad Institute of the Massachusetts Institute of Technology and Harvard, the MMRC has sequenced the first multiple myeloma whole genomes.

Sequencing, or spelling out, the multiple myeloma whole genomes

will help enable scientists to identify key genetic targets for new cancer treatments, the MMRC and the Multiple Myeloma Research Foundation said July 27.

The Multiple Myeloma Genomics Initiative is a comprehensive genomic analysis program designed to accelerate progress against multiple myeloma by significantly improving the understanding of the biology of the disease.

"The Multiple Myeloma Genomics Initiative has created an unprecedented opportunity to examine an extraordinary breadth of genomic information to pinpoint the most important genes and cellular processes driving the disease," said Dr. Jeffrey Trent, TGen's President and Research Director, and co-principal investigator on the Multiple Myeloma Genomics Initiative. "Such a remarkable dataset exists for very few other cancers. It will no doubt pave the way toward personalized medicine for multiple myeloma patients."



TGen North assists with Arizona swine flu tests

Following April's worldwide outbreak of swine flu, also known as the H1N1 virus, TGen assisted state and federal authorities as part of a

coordinated effort to prevent a flu pandemic.

The Arizona Department of Health Services (ADHS) sent samples of suspected Arizona cases of swine flu to TGen's Pathogen Genomics Division (TGen North) in Flagstaff.

David Engelthaler, Director of Programs and Operations for TGen North, said analysis by TGen eventually could track how the flu is moving and mutating.

TGen's work in producing disease-detecting genotyping tools has potential national and global significance in tracking potential drug-resistant mutations of swine flu, said Engelthaler, a former Arizona State Epidemiologist and former Arizona Biodefense Coordinator.

In addition to assisting ADHS, TGen is working with a pharmaceutical company to help discover ways to track and prevent anti-viral drug resistance. Strains of influenza eventually become resistant to anti-viral drugs.

"We've maintained and developed a really strong relationship with the state Health Department, and we've helped them with other disease outbreaks in the past. We have all this cutting-edge technology, so we want to bring that to bear on these public health emergencies," Engelthaler said.

"At ADHS, our primary concern is to quickly identify these cases to take the appropriate public health measures. Our partnership with TGen is a crucial part in responding quickly to any potential cases," said Will Humble, Interim Director of ADHS.

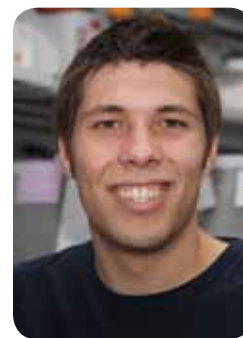
Intern cleans up with yet another award

Eric Anderson, a TGen intern who already has secured several major academic awards, has received a

\$15,000 grant for his proposal to develop a better way of detecting breast cancer.

Anderson was awarded \$15,000 from Arizona State University's Edson Student Entrepreneur Initiative, which he will put toward his efforts at TGen to validate a molecular diagnostic test for 'basal-like' breast cancer, a highly aggressive tumor subtype that accounts for nearly 15 percent of all breast cancers diagnosed.

In May, *USA Today* named Anderson one of the nation's Top 40 students. A senior at ASU, he was named to the national newspaper's prestigious annual All-USA College Academic Second Team.



Intern earns elite science scholarship

Joshua Niska, a TGen intern, has won a \$7,500 national Goldwater Scholarship from the Barry M. Goldwater Scholarship and Excellence In Education Foundation.

Niska is among five TGen interns who have won this prestigious national award including his brother, Jared Niska. Goldwater Scholarships are considered the nation's highest undergraduate award in science, math and engineering.

Josh Niska, a student at Arizona State University, plans to attend medical school, teach and pursue a career in cancer research.

TGen Foundation News

TGen Recognizes Major Investments In TGen; Arizona Bioscience Sector



Arizona Sen. John McCain presented TGen's John S. McCain Leadership Award to Jeannot Krecké, Luxembourg's Minister of the Economy and Foreign Trade.



Catherine Ivy, Founder and President of the Palo Alto, Calif.-based Ben and Catherine Ivy Foundation, accepted TGen's Collaborative Spirit Award.



Bennett and Jacquie Dorrance hosted TGen's Founder's Dinner in Scottsdale.

Advances in brain tumor research and the creation of an international biosciences consortium were celebrated at the TGen Foundation's fifth annual Founder's Dinner.

The Ben and Catherine Ivy Foundation received TGen's Collaborative Spirit Award. In 2008, the Foundation awarded \$3 million to TGen to lead the Ivy Genomics Based Medicine (GBM) Project.

The Grand Duchy of Luxembourg received TGen's John S. McCain Leadership Award. In 2008, that nation announced collaborations with TGen and three other U.S. biomedical groups to help make Luxembourg a key biotechnology center of Europe.

Both awards were announced April 14 at the Founder's Dinner, an annual event celebrating TGen's achievements.

"These awards highlight the importance of government, academic and private-sector investments that are helping TGen make Arizona one of the emerging national and international players in biomedical research," said Dr. Jeffrey Trent, TGen's President and Research Director. "Through their foresight, the investments made by the Ben and Catherine Ivy Foundation and by the Grand Duchy of Luxembourg will pay significant dividends in the future for medical advances and patient benefit."

Dr. Trent referred to a report issued during April's annual meeting of the Arizona BioIndustry Association, which showed that in 2007 Arizona's non-hospital bioscience sector accounted for \$3.6 billion in annual revenues and more than 13,500 jobs. When hospitals and university research was included, that study

showed, Arizona's bioscience sector numbers jumped to \$12.5 billion in revenues and more than 87,400 jobs.

Dr. Trent presented the Collaborative Spirit Award to Catherine Ivy, Founder and President of the Palo Alto, California-based Ben and Catherine Ivy Foundation, a foundation dedicated to improving survival and quality of life for people diagnosed with brain tumors.

"The Ivy GBM Project represents our priority of keeping the patient and relevant clinical issues at the center of every research project we support" Catherine Ivy said. "The Ivy Foundation is proud to be part of this collaborative effort led by TGen. Not only are we creating synergy with TGen and other participating medical and research institutions, we are also minimizing duplication and maximizing transparency of data to achieve outcomes that would not otherwise be possible."

Arizona Sen. John McCain presented the John S. McCain Leadership Award to Jeannot Krecké, Luxembourg's Minister of the Economy and Foreign Trade.

"When searching for a partner to help us establish what we hope will be Europe's premier biotech infrastructure in Luxembourg, we sought out TGen because it is a world-class model of how high-quality science programs can be created in a relatively short period of time," Minister Krecké said.

The Founder's Dinner was hosted at Scottsdale Airport's Hangar One by Jacquie and Bennett Dorrance. Bennett Dorrance, Chairman of Scottsdale-based DMB Associates Inc., also is Chairman of the TGen Foundation Board of Directors.

Boston Marathon Runner Creates Personal Fundraising Page Benefitting TGen's Pancreatic Cancer Research

Amy Lownds, a Massachusetts scientist, raised \$5,724 for TGen's Pancreatic Cancer Research Team (PCRT) by creating her own personal fundraising web page.

Lownds, a Clinical Research Associate at the Lahey Clinic in Burlington, Mass., organized her personal fundraising around her successful April 20 completion of the Boston Marathon.

"I decided I was going to run this marathon last spring when I lost my grandma, Claire Serio, to cancer," Lownds said. "I wanted to do something to honor her memory, and do so while helping and thinking of others, an action very characteristic of the amazing, inspiring, and loving person she was."

Lownds discovered the TGen Foundation through her job at the Lahey Clinic, which is a member of PCRT, a network of research and pancreatic cancer clinical drug trial sites. Since she was already committed to running the marathon, she decided it might be a good way to raise money, too.

"Amy contacted me in late January



Amy Lownds runs in the Boston Marathon.

about her plan to run the Boston Marathon in April, and her hope to raise support for pancreatic cancer research," said Erin Massey, the TGen Foundation's Director of Development.

Lownds worked with the TGen Foundation to launch the Personal Fundraising program. She was the first person to test the program. Lownds set a goal of \$5,000 and invited her

friends, family and colleagues to visit her page, where they made donations, wrote personal messages, and viewed her progress toward her fundraising goal.

The web site makes it possible for anyone, anywhere to raise money to support research at TGen. Just follow the simple instructions provided on the TGen Foundation's web site, www.tgenfoundation.org. Look for the Fundraising Made Personal link.

"Working with TGen and running the Boston Marathon was one of the most amazing experiences of my life. I was completely overwhelmed and touched by the help and encouragement from TGen, and the love, generosity and support from my family and friends. I can't wait to do it again!" Lownds said.

Lownds surpassed her goal, raising \$5,724 online through her personal fundraising page. Along with additional offline donations, Lownds collected a total of more than \$6,000 for pancreatic cancer research.

And her time in the marathon? — 4 hours, 36 minutes and 26 seconds.



BUILD YOUR OWN WEB PAGE AND SUPPORT TGEN RESEARCH

The TGen Foundation has launched a Personal Fundraising web program, enabling anyone to raise funds for TGen's cutting-edge research.

Each personalized fundraising page may be customized for the individual's specific disease interest or can be designated to support TGen's overall research efforts.

Your Personal Fundraising Page can also be easily integrated with social networking applications such as Facebook.

It's easy. Just set a goal — a dollar amount — then follow these simple steps:

- 1 - Go to www.helptgen.org and click on "Fundraising Made Personal" (see image at left).
- 2 - Select the research you wish to support and click on it.
- 3 - Fill out your information and click on "next."
- 4 - Follow the steps to personalize your web page.

You will receive an e-mail from the Foundation thanking you for your support and providing you with additional information.

Once you have created your page, you can add pictures, track your fundraising progress, leave messages, invite family and friends to visit your web page where they can donate and track your progress, thank your supporters, and more.

TGEN BREAST CANCER RESEARCH RECEIVES \$50,000

Mountains of Hope Foundation Launches New Web Site

The Marilyn B. Gula Mountains of Hope Foundation recently donated \$50,000 to the TGen Foundation, bringing the total amount the Phoenix-based organization has raised for TGen to fight advanced stages of breast cancer to \$250,000.

The Mountains of Hope Foundation was established in 2003 by Marilyn (Lynn) B. Gula, who died of breast cancer in 2006, following a decade-long battle against the disease.

In appreciation of her Foundation's support, TGen dedicated a laboratory research bench July 9 "In Loving Memory of Marilyn B. Gula."

The additional \$50,000 was matched with other donations to the TGen Foundation, enabling TGen to hire a bioinformatician. This new position will help speed research in TGen's Molecular Characterization of Circulating Tumor Cells Project, which aims to guide chemotherapy choices among women with the most advanced stages of breast cancer.

Mountains of Hope plans to continue its fundraising efforts for TGen and other major research

facilities across the nation, aided by the July 10 launch of a new website.

Lynn loved wine, cooking, jewelry and purses, all items that her husband Allen Gula Jr. said will be for sale at www.mountainsofhopefoundation.org, including:

- Four new specialty wines from Scottsdale's Su Vino Winery, made

"WE'D BUILD A BUILDING IN SOME NICE PLACE. PUT IN THE ABSOLUTE BEST TECHNOLOGY ON THE PLANET. FIND THE ABSOLUTE BEST PEOPLE. ELIMINATE ALL THE BUREAUCRACY. AND TURN THE SCIENTISTS LOOSE AND LET THEM SOLVE THE PROBLEM," GULA SAID. "WHEN I FIRST HEARD ABOUT TGEN, I IMMEDIATELY REMEMBERED THAT CONVERSATION."

from grapes grown in Napa Valley, north of the San Francisco Bay Area where Lynn and Al spent time when not at home in Phoenix.

- "Handbags for Hope" purses.
- Bangle bracelets.
- A cookbook with all the favorite recipes of Lynn, who worked from hundreds of cookbooks and "loved to experiment," Al said.

In addition, the Mountains of Hope Foundation recently conducted its second annual golf outing in Ohio, where the Gula's lived before

moving to California and Phoenix. A fundraising walk is planned soon in Cleveland, and other events are planned in the Bay Area and Phoenix.

"Sight, Sound & Taste for a Cure" is a wine-tasting and dinner fundraiser planned from 6-9 p.m. Oct. 23 at L&M Home Entertainment Ltd., 15507 N. Scottsdale Road, Suite 135, in

Scottsdale. Tickets are available through the Mountains of Hope web site.

Gula, a Phoenix businessman and Chairman of the Mountains of Hope Foundation, recalled a talk he and Lynn had during her cancer treatment that helps explain why the Foundation is

so committed to TGen.

The Gula's thought about what they would do if they had the resources, and almost simultaneously they came up with the same ideas.

"We'd build a building in some nice place. Put in the absolute best technology on the planet. Find the absolute best people. Eliminate all the bureaucracy. And turn the scientists loose and let them solve the problem," Gula said. "When I first heard about TGen, I immediately remembered that conversation."



TGen scientist named to Medical Advisory Board

Dr. Heather Cunliffe, Head of TGen's Breast & Ovarian Cancer Research Unit, has been named to the Marilyn B. Gula Mountains of Hope Foundation's Medical Advisory Board.

Dr. Cunliffe joins three other respected doctors and scientists on the Mountains of Hope Foundation's Medical Advisory Board: Dr. Cliff Hudis, Chief of Breast Cancer Medical Service, Memorial Sloan Kettering; Dr. Hope Rugo, Co-Director of the Breast Oncology Clinical Trials Program and Professor of Medicine, UCSF Breast Cancer Center, San

Francisco; and Dr. Cliff Reid, President and CEO, Complete Genomics, Mountain View, Calif.

"We're honored to have Dr. Cunliffe as the newest member of the Mountains of Hope Medical Advisory Board," said Allen Gula Jr., a Phoenix businessman and Chairman of the Mountains of Hope Foundation. "Her expertise and unwavering commitment to the research and treatment of advanced breast cancer will be instrumental as the Foundation continues its mission of making inroads to improve the detection, treatment and management of this deadly disease."

MONAHAN'S BATTLE CONTINUES AGAINST CANCER

Anne Rita Monahan — who with her initials urged women to “ARM yourself against ovarian cancer” — passed away May 19 after valiantly battling the disease she fought to eradicate.

The Anne Rita Monahan (ARM) Foundation will continue Anne’s efforts to educate woman about the signs and symptoms of ovarian cancer, encourage early

detection, minimize misdiagnosis and fund research into developing a reliable screening test.

“She fought to bring awareness to other women about the disease that was ravaging her body so that they could avoid her fate. She also fought to raise money to fund research to find a screening process so that this ‘silent killer’ would be easier to detect,” according to the ARM Foundation.

Anne, a Phoenix resident, was an avid supporter of TGen. She established the ARM Foundation in 2007. She had been diagnosed nearly eight years earlier with ovarian cancer after having been misdiagnosed for 10 years prior to that.

The ARM Foundation’s principal goal is to raise awareness about the disease, teaching women how to detect it as early as possible.

Anne worked tirelessly to raise money in support of new diagnostic tests so that patients will receive earlier treatments

resulting in better outcomes.

On May 20, the ARM Foundation presented a check for \$20,000 to TGen’s Dr. Heather Cunliffe to continue TGen’s ovarian cancer research. The funds were raised in February during the Foundation’s inaugural Tea For Teal event, which was held at the new Sheraton Hotel in downtown Phoenix. Teal is the color associated with ovarian cancer awareness.

The ARM Foundation has raised more than \$35,000 towards Anne’s goal of \$100,000 for TGen’s ovarian cancer research.

“The tremendous courage shown by

Anne Rita Monahan in her brave struggle with ovarian cancer is an example to all who face adversity. We at TGen are honored to carry on her fight to stop this terrible disease,” said Michael Bassoff, President of the TGen Foundation.

Even after her death, Anne’s amazing efforts were recognized by Soroptimist International of the Kachinas, the Glendale branch of the worldwide organization

dedicated to improving the lives of women and girls. The Soroptimists presented its Making A Difference for Women Award in honor of Anne to Gayle Parker, a board member of the ARM Foundation.

“It was an incredibly warm and sincere group of women who gave (the award). A framed certificate was awarded to Anne Rita Monahan ‘for ARMing women in the fight against Ovarian Cancer.’ It was an honor for me to receive the award on her behalf,” Ms. Parker said.

“THE TREMENDOUS COURAGE SHOWN BY ANNE RITA MONAHAN IN HER BRAVE STRUGGLE WITH OVARIAN CANCER IS AN EXAMPLE TO ALL WHO FACE ADVERSITY. WE AT TGEN ARE HONORED TO CARRY ON HER FIGHT TO STOP THIS TERRIBLE DISEASE.”

Upcoming Foundation Events



Terri Link Memorial Fund Golf Tournament

Benefits adrenocortical cancer research

Date: Oct. 17

Time: 9 a.m. registration; 10 a.m. shotgun-style start

Location: The Georgia Club in Statham, Ga.



Step N Out Walk/Run

Benefits pancreatic cancer research

Date: Nov. 1

Time: 8 a.m. Registration; 9 a.m. Run/Walk

Location: Tempe’s Kiwanis Park. Enter off Guadalupe Road at All American Way.



Seena Magowitz Golf Classic

Benefits pancreatic cancer research

Date: Dec. 5

Location: Phoenix’s Westin Kierland Resort & Spa, 6902 E. Greenway Parkway

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



A Non-profit Medical Research Institute

Translational Genomics Research Institute
445 N. Fifth Street
Phoenix, AZ 85004

44 HELIOS SCHOLARS GRADUATE FROM TGEN INTERN PROGRAM

Future leaders in science and medicine graduated July 31 from an intense summer internship program at TGen.

The 44 members of the Helios Scholars Program at TGen wrapped up eight weeks of investigations with a symposium of scientific posters and discussions at Arizona State University's Walter Cronkite School of Journalism and Mass Communications.



Helios Scholar Troy Trevino and Paul J. Luna, Helios Foundation President and CEO.

This was the third year of TGen's Helios Scholars Program, funded by the Helios Education Foundation, the largest philanthropic foundation in Arizona and Florida solely focused on education. The foundation has donated \$6.5 million toward the Helios Scholars Program at TGen.

This innovative program helps

students from all backgrounds sharpen their research skills as they prepare for careers in science or medical fields.

Selected from a competitive pool of applicants – many at the top of their class – their backgrounds ranged from bioengineering to business to international studies. The program includes high school, undergraduate and graduate level students, including those in medical school.

Under the guidance of research investigators – who provide closely-supervised, one-on-one instruction – Helios Scholars use cutting-edge technology while learning about the genetic causes of diseases such as melanoma, prostate cancer, diabetes and Alzheimer's disease.

Past interns boast an array of impressive accomplishments – publishing scientific abstracts, scientific articles, and acceptance into medical and graduate schools.

TGen will begin accepting online applications for next summer's Helios program in early 2010.



Above: TGen President Dr. Jeffrey Trent discusses a scientific point with Megan Russell, a Helios Scholar.



Center: Vince Roig, Chairman of the Helios Board of Directors addresses the symposium.

Below: Helios Intern Rachel Stringer discusses her scientific poster.

