Translational Genomics Research Institute

TGENTODAY



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10 CANINE DNA OFFERS
GENETIC INSIGHTS INTO
CANCER, DEAFNESS, HEART
DEFECTS, OBESITY, NEUROLOGIC
DISORDERS AND MORE





Supporting TGen
You, too, can make a difference

In this issue of *TGen Today*, we feature Chip and Daryl Weil. We are truly fortunate to have received their generous planned gift to fund our cutting-edge pancreatic cancer research.

By naming TGen as a beneficiary of his life insurance policy, Chip ensures that he will leave a legacy in the area of research that he cares about – one that personally has touched his family.

You, too, can make a difference by considering a planned gift to TGen. Whether you name TGen as a beneficiary in your life insurance policy, or as a charitable beneficiary of your will or trust, you will have the satisfaction of knowing that your gift will fund research into a broad range of human diseases, the results of which help shape the future of medicine and lead to new diagnostics and improved treatments for patients.

If you or someone you know would like to learn more about making a current or planned gift to TGen, please contact Denise A. McClintic, J.D., LL.M., Associate Vice-President at 602-343-8611 or at dmcclintic@tgen.org.

TGEN TODAY



Cover Story Page 10 — Canine Consortium Initiates Research

The DNA of Bernese mountain dogs like this one will be studied at Michigan State University to better understand malignant histiocytic sarcoma, a type of cancer.

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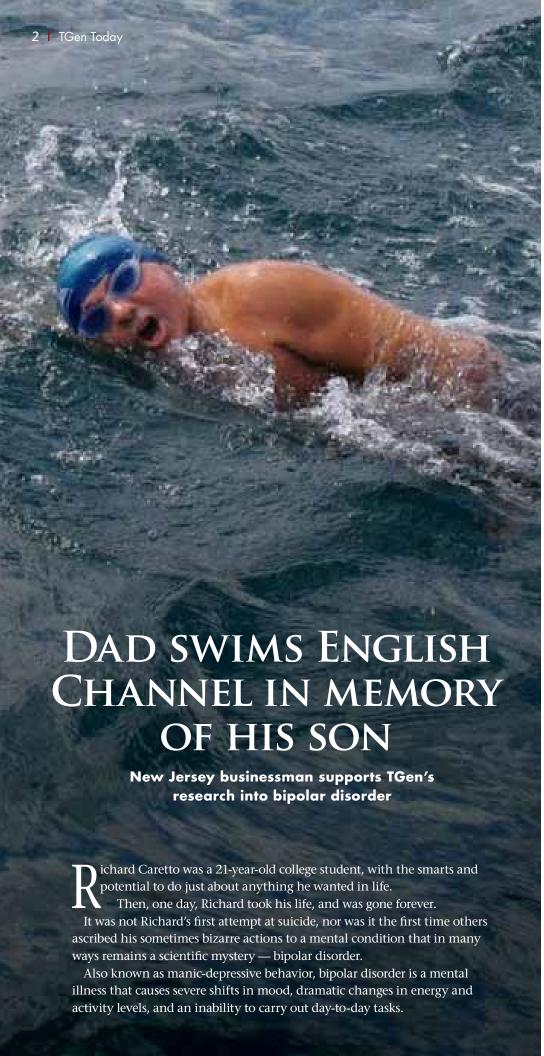


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About TGen

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



Unlike the normal ups and downs that everyone goes through, the radical symptoms of bipolar disorder can result in damaged relationships, poor job or school performance, and even suicide. It often starts in the late teens or early adult years. But it is not easy to detect, and some people suffer for years before they are properly diagnosed and treated.

Martino Caretto, Richard's father, wants to change that. Following Richard's death on April 30, 2009, the Caretto family identified TGen's genetic research into bipolar disorder as the nation's most promising.

And Martino — a 59-year-old Italian-born executive of Ferrero, an international confectionary business — wanted to do something extraordinary to bring attention and funding to this cause

On August 8, after waiting eight days for a break in the weather, Martino and his swimming companion, Michele Drocco, began a relay swim of the English Channel.

It was a first for a two-person Italian-American team, and the first as an international fundraiser for TGen's bipolar disorder research.

"For open-water swimmers, the English Channel is like what Mount Everest is to climbers," said Martino, who has always been an avid swimmer and even competed in his youth in water polo.

In recent years, he swam the Hudson River, not far from his family's U.S. home in Basking Ridge, N.J., and earlier this year he swam with two friends in a 24-mile marathon charity relay race in the warm waters off Tampa, Fla.

But swimming the more than 28 cold-water miles from Dover, England, to Calais, France — even as a part of a one-hour-in, one-hour-out, relay — presented a greater challenge.

"It is extremely challenging," Martino said. "We had enough endurance to cover the distance, but we were not adequately prepared for the cold and rough waters."

The water was a cool 62 degrees. But the temperature onboard their boat, on a mostly overcast day, was an even chillier 57 degrees, causing Martino to shiver uncontrollably at times when he would exit the water as Michele took over swimming.

"The impact of the cold water is brutal," Martino said afterwards. "Once on board, I suffered from hypothermia with uncontrollable tremors in various parts of my body."

Martino said he would not have been able to complete the relay swim without the nurturing and encouragement of his wife, Phyllis, who helped him put on warm clothes and provided him with hot drinks in between his six, one-hour swims.

Crossing the channel was not without its own mysterious beauty: "We saw wonderful, enormous jellyfish around us in the sea, which was rich with plankton that reflected in the water when the sun hit it, creating a beautiful kaleidoscope of colors."

Still, there are tremendous obstacles to overcome: "The cold has a cumulative effect, making it increasingly difficult to restore normal body temperature. We began to encounter huge cargo ships and merchant vessels that passed us, completely unaware of our presence, creating enormous waves that tossed us around in the water and prevented us from swimming properly."

There were times, especially when the winds kicked up, that he wanted to quit. But he kept his mind focused on his strokes — 3,000 per hour — and on the memory of his son, Richard. "I didn't want to let him down."

After 12 hours and 8 minutes, the official observer blew his whistle as Martino reached shore. Tears flowed down his cheeks as he alternately hugged Michele and Phyllis.

Martino chokes up when asked what he misses most about his son: "Touching him. Hearing his voice. Seeing him. Pretty much everything."

Richard, who is remembered as a generous person with a sharp wit and sensitivity to social problems, was always an outstanding student and athlete. A varsity athlete, he ran cross country and

track, wrote for the school magazine, and performed volunteer work with underprivileged children and patients with dementia.

"He had always been a stellar student; at the top of his class," his father said.

But in 2005, towards the end of his senior year, Richard failed a physics test and ran away. His parents found him in



Thinking back to the end of his swim, while returning to England, Martino remembered looking up and seeing a single star in the east, and thinking of his son, Richard: "One lonely star shines in the night sky, showing us the way. I see your face in that star, smiling."

Atlantic City. "He was not coherent," his father said. "We realized that he was not well. That's when he started psychiatric treatment."

Still, Richard graduated on the dean's list and enrolled at Duke University in North Carolina. But toward the end of his freshman year, he was hospitalized after contemplating suicide.

The next fall, he transferred to Stevens Institute of Technology, closer to home in Hoboken, and seemed to get better. But during a visit home in January 2009, Richard overdosed on pills — his first suicide attempt — which, again, required hospitalization.

Living at home and attending college, Richard thrust himself into acting, and

even starred in a play the night before he died. So, why did Richard take his own life?

"I wish I knew," said his father. "That's why we would like the genetic research, to come to some kind of findings."

Martino's other son, Carlo, a senior this fall at Harvard, suggested that the family work with TGen after conducting a nationwide search of research institutes. "We were extremely impressed," Carlo said, "by the scientific advances made by TGen, by its technological and research leadership, and by its dedication to making discoveries in the very area that concerned our family — bipolar disorder."

The Caretto family cemented their decision to support TGen following a New Year's Eve visit and tour, hosted by Dr. David Craig, Associate Director of TGen's Neurogenomics Division. The division studies the genetic basis of brain disorders, including Alzheimer's, autism and bipolar, to find new and better ways to treat patients.

"They were very enthusiastic. The emotions were strong. They were really positive," said Dr. Craig, who would like TGen's bipolar disorder research to better enable clinicians to get beyond trial-and-error efforts. Instead, understanding the genetic basis of the disorder could provide more exacting diagnosis and treatment. "If we get there, that would absolutely be a win."

Because Martino's father was manicdepressive and a cousin suffered from bipolar disorder, Martino believes there may be a hereditary link.

With Dr. Craig and others at TGen, Martino said he believes he has found scientists who are truly dedicated to improving patients' lives.

"I am not a scientist. I don't profess to understand it all," Martino said. "But I had a very good impression from the people I met. I saw them as very committed and genuinely interested in improving the lives of other people. I really liked the people I met."



Tackling bipolar disorder

TGen research delves into the genetic origins of mental illness

B ipolar disorder is an extremely complicated psychiatric condition that will require sophisticated analysis and state-of-the-art technology to discover its genetic origins and develop new treatments for patients.

TGen is one of the few biomedical research facilities in the nation ready to capture the nuances of this disorder, which affects nearly 1 of every 100 Americans, including more than 2 million of the nation's adults.

TGen's high-level examination is possible through its next-generation sequencing technology, which can analyze the entire 3 billion chemical letters of an individual's genetic code within a few weeks, a process that once took years to accomplish.

Researchers will need to examine millions of DNA data points unique to each patient that might be associated with increased susceptibility to this condition, especially because bipolar disorder is likely due to a combination of many different genetic variants.

Dr. David Craig, Associate Director of TGen's Neurogenomics Division, is one of the nation's leaders in the effort to define, develop and implement tools and methods necessary for generating and interpreting whole genome sequencing data.

The next major step at TGen is to sequence the entire genomes of thousands of individuals with bipolar disorder.

"Together, with the Bipolar Genetics Consortium and other institutes, we hope to begin this study within the next year," Dr. Craig said.

Symptoms vary among individuals with bipolar disorder and there is no blood test to detect this condition.

But patients generally suffer from episodes of extreme mania and depression, affecting their energy and ability to function. Tragically, suicide occurs in as many as 15 percent of individuals diagnosed.

"Lithium treatment is one of the few treatments shown to lower occurrence of suicide," Dr. Craig said. "TGen is part of new initiative to uncover the molecular mechanism for how lithium works and who would most benefit from this type of therapy."

The type of medications and dosages needed to treat bipolar disorder usually are based on trial-and-error. However, this condition tends to run in families, so the identification of specific DNA variants presents a clear path for discovering new ways to predict, diagnose and treat this disability. Especially needed is the identification of genes that can better predict drug-response.

TGen also works with the National Institute of Mental Health's Genetics Initiative for Bipolar Disorder to provide genetic profiling of DNA samples from bipolar disorder patients.

Caretto family creates first international fundraising page



Martino Caretto set no particular fund-raising goal when he decided to swim the English Channel in memory of his son, Richard. He simply wanted to tell his family and friends about his plans to swim.

"I don't want to put people under pressure. I want people to feel that they have the opportunity to give, but not an obligation," said Martino, who worked with the TGen Foundation to create a personal fundraising web page.

Such fundraising pages allow donors to contribute to the specific research areas at TGen that are most important to them. Martino's personal fundraising page for bipolar disorder research, presented in both English and Italian, is the first international fundraising effort led by an individual on behalf of TGen.

See his progress, and consider making a contribution, at www.tgenfoundation.org/netcommunity/martinocaretto.



DR. DANIEL VON HOFF Wins top award

r. Daniel D. Von Hoff, TGen's Physician-in-Chief, received the top award in June from the American Society of Clinical Oncology (ASCO) for his lifetime achievements in cancer research: The 2010 David A. Karnofsky Memorial Award and Lecture at ASCO's 46th Annual Meeting at the McCormick Place in Chicago.

ASCO — with 28,000 members the world's largest society of clinical oncologists — presented the award to Dr. Von Hoff "for his outstanding achievements in cancer research and for his impact on the treatment of patients with cancer."

Dr. Von Hoff is an internationally recognized physician-scientist who has contributed to the development of numerous anticancer agents, including paclitaxel, docetaxel, irinotecan and gemcitabine. He also is the Chief Scientific Officer of TGen Clinical Research Services at Scottsdale Healthcare and at US Oncology, and is a Clinical Professor of Medicine at the University of Arizona College of Medicine.

Each year through its Special Awards Program, ASCO recognizes quality researchers, patient advocates and leaders of the global oncology community who through their work have made significant contributions to enhancing cancer care. These recipients of ASCO's highest, most prestigious awards collectively represent significant strides in cancer treatment and leadership in the oncology community.

"The work of this year's awardees collectively represents decades of commitment to improving the care and quality of life for people living with cancer," said Richard L. Schilsky, M.D., ASCO's Immediate Past President and Chair of the Special Awards Selection Committee.

"Our understanding of the biological basis of cancer and our ability to transform that knowledge into better treatments for patients have been enhanced by their contributions and it is an honor to present them ASCO's highest awards."

The David A. Karnofsky Memorial Award, first presented in 1970, recognizes outstanding contributions to cancer research, diagnosis and/or treatment. Each year's recipient delivers a keynote lecture during the opening session of the ASCO Annual Meeting.

ASCO named the award after David A. Karnofsky, 1914-1969, an American clinical oncologist and specialist in cancer chemotherapy, known for developing the Karnofsky scale, an index for determining a patient's suitability for therapy and for estimating a patient's physical state, performance and prognosis after a therapeutic procedure.

TGEN STIMULUS IMPACT ESTIMATED AT NEARLY \$42M

The 12 grants received by TGen from the National Institutes of Health (NIH) under the American Recovery and Reinvestment Act (ARRA) could produce nearly \$42 million in new business activity and help Arizona's economy and beyond.

Besides its headquarters operations at the downtown Phoenix Biomedical Campus, TGen's economic and business presence also is felt surrounding its operations in Scottsdale and Flagstaff.

Many of TGen's stimulus-grant projects involve collaborations with other institutions — including the Van Andel Research Institute in Grand Rapids, Mich. — an alliance that helps bring funds to Arizona that otherwise might be lost to institutions in other states.

The benefit to Arizona includes projects at Arizona State University in Tempe and the University of Arizona in Tucson.

TGen's 12 grants totaled \$18.9 million. Under a federal formula, TGen's NIH grants could result in as much as \$41.9 million in new business activity.

Details of the 12 grants include:

- **\$7.6 million** to establish the Southwest Comprehensive Center for Drug Discovery and Development (SCCDDD) in conjunction with the University of Arizona in Tucson and Van Andel Research Institute (VARI) of Grand Rapids, Mich.
- \$4.3 million for the nationwide Canine Hereditary Cancer Consortium (CHCC) in collaboration with VARI, the National Cancer Institute, Michigan State University and the University of Pennsylvania.
- **\$474,000** for research in conjunction with Mayo Clinic Arizona into how to best detect coccidiodes, the causative agent in Valley Fever, and track its resistance to anti-fungal agents.
- **\$404,000** for research into how nerve growth factor (NGF) influences the spread of pancreatic cancer.
- \$240,000 for research into unhealthy lipid metabolism, the leading cause of coronary heart disease among patients with Type 2 diabetes.
- \$118,000 for an analysis of next generation sequencing data to identify genetic variants associated with prostate cancer, the most common malignancy among American men.
- **\$3.6 million** through Ohio State University to study the genetic causes of why 2 out of 5 Americans, age 55 and older, have osteoarthritis in their knees.
- **\$1.1** million through the Fred Hutchinson Cancer Research Center in Seattle to determine the genetic makeup of nearly 53,000 DNA samples as part of a nationwide Woman's Health Initiative.
- \$707,000 through the House Ear Institute in Los Angeles to look for the genetic causes of age-related hearing loss.
- \$225,000 through the Fred Hutchinson Cancer Research Center to, in part, expand the analytic and information management capabilities associated with the Women's Health Initiative.
- \$207,000 through the University of Michigan to evaluate, in part, associations between a breast cancer gene and prostate cancer.
- \$47,000 through Arizona State University to help design new computer algorithms for genetic studies.

Breast cancer focus of research partnership



Dr. Heather Cunliffe

A recently signed research partnership between TGen and the John C. Lincoln Breast Health and Research

Center offers women diagnosed with breast cancer an opportunity to donate tissue samples for studies exploring better ways to diagnose and treat breast cancer.

"This agreement will double our local access to valuable research resources, accelerating our goal to molecularly characterize highly aggressive forms of breast cancer," said Dr. Heather Cunliffe, head of TGen's Breast and Ovarian Cancer Research Unit. "The more biospecimens available for study, the more evidence we have to develop rationalized approaches for precision treatment selection for all breast cancer patients."

Alisa Domb, R.N., B.S.N., clinical research coordinator for John C. Lincoln Health Network, oversees the collection process. Women who meet the requirements and give consent will have tumor tissue, healthy tissue and blood samples prepared and sent to TGen for the research.

Samples can be as small as 2 mm, she said. Only leftover tissue, not needed to diagnose the case, will be used. The patient's health history will be followed for 20 years.

John C. Lincoln is one of several facilities working on this study with TGen.

"We want to be part of the team," Domb said. "It's really about the collaboration, joining together, pooling our resources and really finding a way to treat breast cancer so women don't have to suffer."



1 BIKE, 3 DAYS, 165 MILES

TGen researcher participates in coast-to-coast relay set to end on the steps of Congress

lone on a heart-pounding bike ride up some of Arizona's steepest highways, TGen's Dr. Matthew Huentelman kept thinking about patients with Alzheimer's disease.

Their suffering from this memory-robbing disease was his motivation.

Dr. Huentelman traded test tubes and lab coat for a bike helmet and shorts as he rode his bicycle 165 miles July 29-31 from Phoenix to Holbrook as part of Breakthrough Ride 2010.

Sponsored by the national Alzheimer's Association, the first of more than 60 scientists and researchers started the coast-to-coast ride July 17 in San Francisco. Their goal is to encourage Congress to more than quadruple federal funding for Alzheimer's disease research.

The 4,500-mile ride through 13 states ends Sept. 21 — World Alzheimer's Day — in Washington, D.C., where advocates will present at least 50,000 petition signatures in support of S. 1492 and H.R. 3286, paired bills that comprise the Alzheimer's Breakthrough Act.

Dr. Huentelman, an Investigator in TGen's Neurogenomics Division, will be on the steps of the nation's Capitol when the petition is delivered.

"As the Baby Boom generation enters their twilight years,
Alzheimer's has an even greater potential to become a major health issue facing this country. An increase in research funding would greatly advance our understanding of Alzheimer's and could potentially

push onset of the disease out by a number of years," Huentelman said.

This single disease could devastate our healthcare system within our lifetimes. Spending more now on research, Dr. Huentelman believes, could fend off the anticipated escalating costs of Alzheimer's disease. This is especially important as the first of more than 70 million

The Breakthrough Act would:

Authorize

\$2 billion annually (from \$460 million) for Alzheimer's disease research.

Create

An integrated federal campaign to overcome Alzheimer's disease.

Provide

Medicare reimbursement to increase the detection and diagnosis of Alzheimer's disease and other dementias.

Baby Boomers — those born 1946-1964 — begin next year to turn 65, the age when late-onset Alzheimer's risk begins to significantly rise.

According to the Arizona Alzheimer's Consortium — a leading research collaboration that includes TGen — more than 5 million Americans have Alzheimer's, a number projected to grow to 16 million within 30 years.

Two other researchers in the Arizona Alzheimer's Consortium rode in the Breakthrough Ride before and after Dr. Huentelman. Dr. Michael Sierks of Arizona State University biked from Palm Springs to Phoenix; and Dr. Lee Ryan of the University of Arizona rode from Holbrook to Albuquerque, N.M.

Dr. Huentelman's part of the

relay was not easy, given triple-digit temperatures in the deserts, and a nearly 6,500-foot climb the first day between Phoenix and Payson. Add to that monsoon-driven rain on the second day between Payson and Heber, which included a 1,300-foot elevation gain in less than 5 miles to get to the top of the Mogollon Rim.

"I felt pretty lonely on the long climbs during the Phoenix to Payson leg," said Dr. Huentelman, who is used to riding long distances with partners. With no one to keep him company or pace him, his thoughts turned to Alzheimer's patients and the suffering he wants to alleviate.

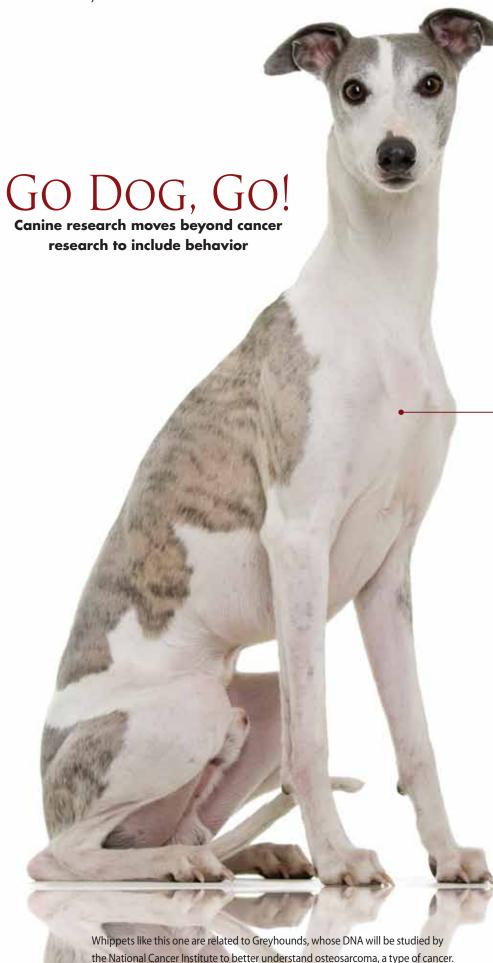
Wherever Dr. Huentelman stopped, well-wishers wanting to know more about the Breakthrough Ride and Alzheimer's research approached him and his support team from the Desert Southwest Chapter of the Alzheimer's Association.

"Along the whole ride people were very responsive. When we talked to anyone, the first thing out of their mouth was, 'Oh, my mother ...' or 'Oh, my father ...'

On the third day between Heber and Holbrook, Dr. Huentelman was rewarded with cooler temperatures and even roads.

"The whole thing just had a nice memorable feel to it. For this brief period of time, over a couple of days, you were carrying the torch for this really important cause," he said. "That night, we had a beautiful double rainbow."

How could someone forget that?



Gen and the Van Andel Research Institute (VARI) have embarked on an unprecedented research project, using the genomic studies of naturally occurring cancers in canines to not only help treat dogs, but to learn more about treating cancer in humans, too.

The Canine Hereditary Cancer Consortium (CHCC) includes veterinarians, scientists and clinicians from across the nation, including investigators at the National Cancer Institute, whose efforts will retrieve genetic information from cancers that are common in certain breeds of dogs to treat similar cancers that are rare in people.

But the study of dogs will not only be useful in understanding cancer.

Additional research has begun into dog behavior, and how their genetic propensity to herd, fetch - and even chase their tails — can beg new questions and point to new answers about the behavior of their owners.

And future research is planned in the areas of deafness, heart defects and obesity.

Dr. Mark Neff, a VARI Scientific Investigator and Director of the TGen-VARI Program for Canine Health and Performance, also is head of VARI's Laboratory of Neurogenetics and Canine Behavior.

"What's unique about dogs is that they get the same disorders and diseases that we do," Dr. Neff said. "My laboratory aims to marry dual aspects of dog biology." First, tackling the basis of neurological and behavioral disorders in the dog, and how this information can help treat human diseases. Second, exploring the adaptive variation in dogs. This will shed light on the evolution of instinctive patterns and tendencies. The heritable variation underlying selectively bred behaviors, such as pointing and herding, can provide a unique window on how the central nervous system works.

"By approaching the mechanics of the mammalian mind through both the positive and negative behaviors that result from genetic variation, we hope to better understand the general rules governing the brain and behavior, and how these basic rules are broken in the context of human mental illness and psychiatric disease," Dr. Neff said.

Dr. Nick Duesbury, a Senior Scientific Investigator at VARI and a Lead Investigator within the CHCC, said VARI and TGen are perfectly positioned to lead this highly promising field of canine research into the genetic causes of cancer.

"There's a really strong synergy

diversity of purebred dogs coupled with their predisposition for particular cancers to identify the underlying genetic causes that contribute to disease, and then translate those discoveries to humans.

Dr. Jeffrey Trent, President and Research Director for TGen and VARI, and also a CHCC Principal Investigator, emphasized that no dog will be harmed; that all research is supervised by animal care and use committees and by protocols established by the National Cancer Institute.

"In most cases, a simple saliva sample provides a sufficient amount of DNA for study," Dr. Trent said.

WE HOPE TO BETTER UNDERSTAND THE
GENERAL RULES GOVERNING THE BRAIN AND
BEHAVIOR, AND HOW THESE BASIC RULES ARE
BROKEN IN THE CONTEXT OF HUMAN MENTAL
ILLNESS AND PSYCHIATRIC DISEASE

between the two institutes. TGen has this incredible expertise in genomic technologies, and Van Andel is really good at functional biologies," said Dr. Duesbury.

One of the initial goals of the CHCC will be to study a group of cancers called sarcomas, which are easier to study in dogs than in humans.

"The sad realities of sarcoma, because it is such a rare disease, is that very few people take the time to do any research on it because it is not possible to get the number of (human) samples you need for those kinds of studies," Dr. Duesbury said. "We've got an incredible advantage here with the dogs, because these diseases are much more common in dogs than they are in humans. We can get some insight into the biology. Our strongest hope and desire is that we can translate that into therapies we can use for people."

This strategy leverages the low genetic

The same processes used to study the genetic origins of diseases in humans will be used to study dogs.

"We're making decisions on individual patients by looking at their genome, taking that information and building around it all the knowledge that we can find, and then adding that into the armamentarium of the clinician that can help in the treatment of patients."

Similarly, dog genomes will be mapped to understand how they influence cancer outcomes, influence metastatic rates, the progression of diseases, and the effectiveness and safety of new treatments.

Dr. Trent said that, if his pet dog Honey Bear — his fifth Labrador retriever — is any indication, it should be easy to get plenty of DNA material to study. "A little slobber? Trust me, with my Labrador, you can get plenty of it."



Van Andel's Neff earns scientific pedigree in dog genetics

For Van Andel investigator Dr. Mark Neff, Director of the Program for Canine Health and Performance, his research into the various aspects of dog biology is a "feel-good project" in three ways.

"We're going to help dogs. We're going to help people. And were looking at cancers that have unique, unmet needs," said Dr. Neff, who also heads Van Andel's Laboratory of Neurogenetics and Canine Behavior.

Dr. Neff, who previously served as associate director of the Veterinary Genetics Laboratory at the University of California, Davis, will draw on the strengths of both TGen and Van Andel colleagues to tackle the basis of neurological and behavioral disorders in the dog as such studies will inform work on human disease counterparts.

Currently, Dr. Neff is developing genetic screens, diagnostic tests and treatments

PETSMART ANTICIPATES EXPANDING ROLE IN CANINE CANCER PROJECT

DNA samples from dog saliva would help discover genetic origins of disease

ometime next year, dogs could get more than their coats shorn, teeth cleaned and toenails clipped at PetSmart.

One day, with the permission of their owners, dogs groomed at PetSmart could receive cheek swabs — Q-Tips with little sponges on the ends — that would sample DNA from dog saliva, part of the nation's largest genetic study of canine cancer.

Because cancer in dogs and humans are similar, the DNA samples from dogs will be used by researchers at TGen and the Canine Hereditary Cancer Consortium (CHCC) to not only determine the genetic origins of cancer in dogs, but also in humans.

Phil Francis, Executive Chairman of PetSmart Inc., said the CHCC program should provide better health and longer life for pets, as well as speed up and minimize costs associated with cancer research in humans.

"The mission of our company is total lifetime care for every pet, every parent, every time, and I saw the completion of the dog genome as a way to go to a higher level of science to help pets live longer and have healthier lives," said Francis, whose company earlier this year pledged \$500,000 towards the CHCC.

Researchers will analyze dog DNA for cancer biomarkers that could lead to better ways to prevent, diagnose and treat diseases.

"We are going to advance dog medicine," Francis said. "But an equally important societal benefit is: We are going to collapse timetables and reduce costs to make faster advances in cancer research for humans."

Pet owners who have their dogs cared for at Banfield, The Pet Hospital whose clinics are in most of



HERE IS WHAT YOU SHOULD TELL YOUR HUMAN: "BRING ME INTO THE GROOM SHOP. BECAUSE I WANT TO GET INTO THIS STUDY. AND THEY'LL SEND ME UPDATES IN A NEWSLETTER THAT I'LL LET YOU READ."

PetSmart's 1,164 stores across the U.S. and Canada — also may allow DNA blood samples taken of their pets.

Francis predicts that Banfield will be able to provide a wealth of scientific data for TGen and CHCC researchers, since specific dog breeds have propensities for certain diseases, and many cancers that are rare in humans are common and easier to study in dogs.

In turn, new medicines for dogs, including chemotherapy, could be part of new lines of prescription dog food available through PetSmart, which already carries medicinal pet foods made by Hill's Pet Nutrition, which also contributed \$500,000 to the CHCC.

There is no start date yet for the saliva and blood sample programs, but Francis said they would begin when practical. Customers, he added, likely would receive e-mail notifications, addressed to their dogs, that read something like this, "Here is what you should tell your human: 'Bring me into the groom shop, because I want to get into this study. And they'll send me updates in a newsletter that I'll let you read."

TGen President Dr. Jeffrey Trent said he believes TGen and the CHCC would receive a substantial number of DNA samples from PetSmart, considering that the company on average grooms more than 80,000 dogs each week.

"You can imagine having a partner with a national footprint is going to be a critically important part of the CHCC project," Dr. Trent said. "PetSmart is a Phoenix-based company with a real heart for helping pets and their pet parents."

Francis is dedicated to local and national philanthropy. For example, in 2006 he and his wife, Nita, were the first husband-wife co-chairs of the annual campaign of the Valley of the Sun United Way.

In all, PetSmart charities last year gave more than \$30 million to petrelated causes — mostly for spaying, neutering and adoption — making it the world's largest contributor to programs involving companion animals.

Francis also set an example in 1998 by adopting a mix-breed puppy with mange and worms from a shelter, saving it from being euthanized.

"She's cured of mange, cured of worms, and sleeps on the bed," Francis said. "Her name is Bit O' Honey, but it could just as well be Lucky."

Van Andel's Neff...continued

for rare human cancers by studying these cancers in dogs, using simple, easy-to-obtain samples of dog saliva or blood.

"The technologies that have been put in place over the last two or three decades to study human genetics, can now be slightly refocused and accommodate

the biology of the dog," said Dr. Neff, who wants to apply the best practices discovered in dogs to people. "More importantly, no dogs are kept for research. We only collect samples of naturally

occurring cancers, and all samples are contributed on a volunteer basis."

The American Kennel Club and the Morris Animal Foundation endorse Dr. Neff's research, and the studies in no way harm dogs and rely

In many ways, he says, the genome of the dog makes

a perfect research subject. Because the lifespan of a dog is relatively short, researchers can identify genetic risk factors in puppies, and then follow the same dogs over a decade through the progression of their diseases as adults.

Another positive is that pet owners freely share their dogs medical history, and this helps researchers better understand the disease. "That knowledge provides a much clearer picture of the animal over time," Dr. Neff said, "and it makes it easier to recruit canine samples for the various studies we have."

Dogs are relatively easy to study, because specific dog breeds are genetically predisposed to specific cancers, even to the extent of what parts of their bodies the cancers attack.

"With these dogs, we stand to deliver really outstanding medicine," Dr. Neff said.

The Canine Hereditary Cancer Consortium by the numbers

Number of CHCC studies, including melanoma in dobermans, labs, cockers and schnauzers, hemangiosarcoma in clumber spaniels, malignant histiocytic sarcoma in Bernese mountain dogs, osteosarcoma in rottweillers and greyhounds, and lymphoma in several breeds of dogs.

Age at which nearly half of all dogs die of cancer.

solely on the consent of the owners.

Number of dog breeds that might eventually be included in the study.

Number of researchers expected to contribute to the study, including scientific investigators at nearly a dozen institutions.

Dollars each, from PetSmart and Hill's Pet Nutrition:

Dollars in federal stimulus funds over two years.



Listen Up: Here's How Your Dog Can Participate

Together, we can make progress in fighting cancer. If your vet suspects, or has already determined your dog has cancer, please contact us if you are interested in becoming a study participant. For those dogs awaiting surgery

to remove a tumor, we will provide a collection kit. If the surgery has occurred and test results confirm a conclusive diagnosis, a simple, onetime blood sample will enable us to study their DNA. In some cases a saliva sample will help as well.

In the unfortunate event that your dog has a surgically untreatable tumor and you elect for euthanasia - a sample from your dog can still significantly advance the science and understanding of similar cancers to aid future generations of dogs.

All dogs with cancer can help future generations by donating a sample.

If your dog is affected with one of the cancers currently under investigation, or you would like to donate samples for future studies, please visit the CHCC website and complete the on-line form — www. tgen.org/sample — to learn how.

Protein inhibitor revives chemotherapy



TGen investigators have discovered a treatment method that may help ovarian cancer patients who no longer respond to conventional chemotherapy.

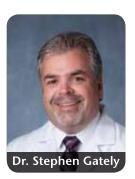
women in the U.S. annually. The standard treatment for cancer of the ovaries, which produce human egg cells, is surgical removal of the cancer, followed by chemotherapy.

Partnership advances pancreatic cancer research

TGen and Asuragen Inc. announced in April a research agreement that could lead to ways of detecting cancer before it spreads.

Dr. Glen Weiss, an Associate Investigator in TGen's Cancer and Cell Biology Division, plans initially to

TD2 partners with Horizon Discovery



A strategic alliance announced in April between TGen Drug Development (TD2) and Horizon Discovery Limited will significantly advance personalized medicine.

The partnership will create a

to what drug," said Dr. Stephen Gately, TD2's President and Chief Scientific Officer, referring to the goal of personalized medicine, treating patients with drugs tailormade for their specific diseases. "This partnership is the engine that will actually make this work and allow for the design of shorter and less-costly clinical trials that enroll the patients most likely to respond to a given drug," Gately said.

Van Andel Research Institute plans clinical trial



TGen's sister institute in Grand Rapids, Mich., the Van Andel Research Institute (VARI), will provide cancer patients in West Michigan opportunities to access new drugs to fight their disease.

VARI is joining with Spectrum Health and with Cancer & Hematology Centers of Western Michigan to develop a Phase I clinical trial program, which will link labs and clinical research, providing patients with enhanced access to potentially life-saving diagnostic and treatment options.

Phase I clinical trials are initial studies to determine the safety and effectiveness of drugs in humans. TGen has had such a program in Scottsdale since 2005.

"The ultimate focus of VARI's

TGEN IN BRIEF

A scientific paper that will be published in the September issue of the journal Gynecologic Oncology describes how the inhibition of a protein, CHEK1, may be an effective element to incorporate into therapies for women with ovarian cancer. The research led by TGen's Dr. David Azorsa, a Senior Investigator, and Dr. Shilpi Arora, a Staff Scientist, found that inhibiting CHEK1 by a small molecule known as PD 407824, enabled ovarian cancer cells to be attacked again by cisplatin, a widely used platinumbased chemotherapy drug for

The TGen team proved their method in the research laboratory, which is very encouraging, considering that the use of protein inhibitors in combination with cisplatin, is also proving to be effective in clinical trials with cancer patients. The prognosis remains poor for patients with ovarian cancer, which kills nearly 14,600

women with ovarian cancer.

work with Asuragen to search for new ways to screen patients for pancreatic cancer, one of the fastest moving and

deadliest types of cancer.

The project will combine the microRNA expertise and diagnostic development experience of Asuragen with TGen's strengths in basic and clinical research. TGen moved to partner with Asuragen on this project because of its reputation as an excellent assay development partner, demonstrated market success and research compatibility with Dr. Weiss' work with microRNA technology.

Currently, there is no screening test in common use for pancreatic cancer, which in the U.S. is the fourth leading cause of cancer death, annually killing more than 35,000. Also, there is no diagnostic test, other than examining diseased tissue. As a result, pancreatic cancer often is not detected until the cancer is in advanced stages, when patients face diminishing treatment options.

beginning-to-end solution for pharmaceutical and biotechnology companies to more rationally design and tailor their drugs to specific patient populations based on the unique genetic variations that define a given disease.

TD2 will use Horizon's panel of more than 200 geneticallydefined human isogenic cell-lines - designed to accurately mirror cancer patient genetics — in its comprehensive pre-clinical service as a prelude to performing selected in-house clinical trials. This will provide clients with a fully integrated drug discovery service that will accelerate the isolation and optimization of appropriately targeted therapeutic agents and attain their rapid market approval. And it will save time and money in the development of more effective cancer treatments.

"The future of oncology drug development will require us to predict which patients will respond translational research program is always on the patient," said Dr. Jeffrey Trent, President and Research Director of both TGen and VARI. "Our goal is to move scientific discoveries as quickly as possible into clinical diagnostics and treatments. VARI's emphasis on precision medicine, joining with physicians and scientists at TGen, makes it possible to target specific problems in the treatment of individual patients."

The initiative also will reunite two former colleagues. Dr. Daniel Von Hoff, TGen's Physician-in-Chief, will serve as the VARI project's interim Physician-In-Chief. He is teaming up with Dr. Timothy J. O'Rourke, who is the Betz Family Endowed Chair for Cancer Research at Spectrum Health. Working together, they have produced significant results in the field of pancreatic cancer research.

Study helps predict success with cancer drugs



Researchers at TGen, the Van Andel Research Institute (VARI) and the Virginia G. Piper Cancer Center at Scottsdale Healthcare have discovered a biomarker that could help in the treatment of patients with an aggressive type of lung cancer. Using a particular biomarker, researchers might better predict which patients with small cell lung cancer (SCLC) are resistant to existing drug therapies, and which ones could benefit from new therapies tailored to their specific needs, according to a scientific paper published June 14 in the Journal of Thoracic Oncology.

"There is a need for predictive biomarkers that can aid investigators in designing future clinical trials, to help identify treatments that might be effective for these patients who most likely will be resistant to existing drug therapies, " said Dr. Glen J. Weiss, the paper's senior author and Director of Thoracic Oncology at TGen Clinical Research Services at Scottsdale Healthcare, a partnership between TGen and Scottsdale Healthcare.

Of all lung cancer patients, an estimated 33,000 are diagnosed with SCLC. This is a particularly aggressive disease that usually goes undetected until it is in an advanced stage and treatment options are limited. More than 95 percent of SCLC patients eventually die from the disease. Researchers focused on identifying microRNAs, which are single-stranded RNA molecules that regulate how genes and proteins control cellular development.

Because microRNAs are so resilient, they are relatively easy to detect, a limitation for other biomarkers.

TGen intern one of nation's top 20 students

Joshua Niska, a 5-year intern at TGen, capped a string of major academic honors June 9 by being named one of the nation's top 20 college students by USA TODAY.

Niska and other members of

the newspaper's 2010 All-USA College Academic (First) Team each received a \$2,500 cash award. They were selected, according to the newspaper, based on their leadership, activities and, most importantly, how the students extended their intellectual talents beyond the classroom.

Meanwhile, another recent 4-year TGen intern, Eric Anderson — who last year was named to USA TODAY's list (Second Team) of the nation's top 40 college students has received a Fulbright Scholarship to pursue genomic cancer research at the Academic Medical Center at the University of Amsterdam.

Both Niska and Anderson recently graduated with honors and at least 4.0 grade-point averages from Barrett, the Honors College at Arizona State University. Niska majored in Biochemistry. Anderson majored in Bioengineering, Biochemistry and Biological Sciences.

Studies identify genetic links to kidney disease; kidney failure



TGen researchers made two presentations at this year's 70th Scientific Sessions of the American Diabetes Association (ADA), June 25-29, in Orlando, Florida.

One presentation described a DNA study of American Indians in Arizona, in which a TGen-led team discovered a genetic biomarker with a significant association to kidney failure.

The study showed "the strongest evidence" for association with End Stage Renal Disease (ESRD), or kidney failure, in marker rs13315275, and also found evidence of some lesser associations between ESRD and four other markers. "This study could someday lead to better treatment options for those patients suffering from diabetic kidney disease," said Dr. Johanna DiStefano, Director of TGen's Diabetes, Cardiovascular and Metabolic Diseases Division, and lead author of the study's abstract.

All five biomarkers are genetic variants of the gene SUCNR1, which is located in a chromosomal region of the human genome identified as 3q24-q27. This region has been linked to diabetic nephropathy, or diabetic kidney disease, in previous studies.

In another TGen study presented at the ADA, researchers initiated an investigation into the ways that the PVT1 gene impacts development of diabetic kidney disease.

Previous studies have shown an association between PVT1 and kidney failure in patients with both type 1 and type 2 diabetes. In the new study, research by Dr. Lucrecia Alvarez, a TGen Post-Doctoral Fellow, found that PVT1 was expressed in mesangial cells - specialized cells around blood vessels in the kidneys — at a rate up to five times higher in conditions of high glucose (high blood sugar), compared to normal glucose levels. High blood sugar is a signature symptom of diabetes.



ouis A. "Chip" Weil III and his wife, Daryl, (above) are no strangers to philanthropy. They understand the importance of supporting non-profit organizations, and over the years they have been major supporters of numerous non-profits throughout the Valley.

One recent day at their Flagstaff home, Chip, the retired chairman, president and CEO of Central Newspapers Inc., and former publisher of The Arizona Republic, was busy working as a volunteer member of the USO World Board of Governors. Chip also has served as campaign chairman for the Valley of the Sun United Way, led the Board of Trustees as Chairman of the Phoenix Art Museum, and sat on the boards of both the Rodel Charitable Foundation of Arizona and the Thunderbird School of Global Management.

Now, TGen is among the many organizations that can thank Chip for

TGen Foundation

STRONG VOICES FOR PANCREATIC CANCER RESEARCH

Legacy Society member advances TGen's work with planned gift

his counsel and financial support.

Chip has made provisions for TGen to receive a major gift supporting research into the underlying genetic causes of pancreatic cancer and driving an unprecedented number of new therapeutic approaches —through clinical trials— to patient care.

"My sister was taken by pancreatic cancer at the age of 51," said Chip. "Public awareness of this horrible disease has not been very high. We need to change that while Dr. Dan Von Hoff (TGen's Physician-In-Chief) and his associates coordinate worldwide efforts to find the answers."

Chip chose to make a planned gift to fulfill his goal of supporting pancreatic cancer research. He did this by naming TGen as a beneficiary of his life insurance policy — a smart move easily accomplished by submitting a change of beneficiary form to your policy provider.

This giving technique is one that is becoming increasingly popular with mature donors who want to provide for the long-term support of their favorite charities. There are several ways to make such an insurance gift without changing one's current estate plan.

Because it is such a versatile gift, Chip hopes that others will follow

his example and make similar contributions to TGen. In addition to supporting TGen's pancreatic cancer research, a donor might consider making a gift to breast, prostate or ovarian cancer, to diabetes research, or to support TGen's work in neurological diseases such as Alzheimer's, ALS, autism or Parkinson's disease.

To commemorate Chip's gift, TGen has added his name to the Legacy Society, which is chaired by The Honorable Skip Rimsza, former Mayor of Phoenix and current TGen Foundation board member. The Society serves as an honor roll of donors who have made various types of planned gifts to TGen.

"TGen is honored to be the recipient of this wonderful planned gift from Chip, and we are encouraged that this will spur on others in our community to contribute to the area of research that they would most like to support," Mayor Rimsza said when he learned of Weil's generous gift.

If you or someone you know would be interested in discussing a life insurance gift, a bequest or other planned gift to benefit TGen, please contact Denise A. McClintic, J.D., LL.M., Associate Vice President, at 602-343-8611 or at dmcclintic@tgen.org.

The Marilyn B. Gula Mountains of Hope Foundation donates additional research funds to TGen

The Marilyn B. Gula Mountains of Hope Foundation continued its fight against advanced breast cancer in July with a \$50,000 donation to TGen, for a total contribution over two years of \$300,000.

"Our sole mission is to enable research that allows for earlier diagnosis and better treatment for patients with advanced breast cancer," said Allen J. Gula, Chairman of the Mountains of Hope Foundation.

The Foundation's support furthers research into the genetic components of common and complex diseases, including advanced breast cancer. TGen matched this most recent donation with other philanthropic contributions, enhancing the Institute's bioinformatics expertise to accelerate a project to molecularly characterize circulating tumor cells in stage IV breast cancer patients.

The Mountains of Hope Foundation was established in 2003 by Marilyn B. Gula, who ultimately lost her decade-long battle with advanced breast cancer, but not before she established the Foundation with the intent of making inroads to improve the detection, treatment and management of this deadly disease for others.

Spirit of ovarian cancer advocate keeps fundraising drive on track

The Anne Rita Monahan Foundation presented \$15,000 in support of ovarian cancer research to TGen.

That amount brings to \$50,000 the total raised by the organization named for Anne Rita Monahan, a Phoenix woman whose initials encouraged women to "ARM yourself against ovarian cancer."

The Foundation raised the funds at the 2nd annual Tea for TEAL, the color associated with ovarian cancer. The English-style tea for 160 people occurred February 2 at the Sheraton Phoenix Downtown Hotel, the first event held since Monahan lost her battle to ovarian cancer in May 2009. She was 47.

Monahan started her foundation in 2007, six years after receiving her diagnosis of ovarian cancer. Her mission: eradicate the disease. Today, her foundation continues her efforts to make women aware of the signs and symptoms of ovarian cancer, to encourage early detection, minimize misdiagnosis and fund research into developing evidence-based rationales for precision therapy and a reliable screening test.

Plans are underway for the 3rd annual Tea for TEAL, 2 p.m. Feb. 19 at the Sheraton Phoenix Downtown Hotel, 340 N. Third St.

Rachel Busch, President of the ARM Foundation said, "I'd like to see us continue with Anne's dream." That includes eventually reaching Monahan's fundraising goal of \$100,000 for TGen's ovarian cancer research.



'Strides for Life' event nets \$25,000 for Lung cancer research

Following its first major Arizona fundraising event, the national Lung Cancer Research Foundation (LCRF) pledged \$25,000 for lung cancer studies at TGen.

The first Strides for Life-Arizona event, held April 11 near Tempe Town Lake, drew 175 participants to a family-friendly 3-mile fun run-walk and children's dash.

It was so successful, the New York-based Lung Cancer Research Foundation already has scheduled its 2nd annual Arizona fundraiser at the same location, Tempe Arts Park, at 7:30 a.m. April 10, 2011.

"We were thrilled with the turnout and success of our inaugural Strides for Life – Arizona," said Laurie C. Carson, the Founder and President of the Lung Cancer Research Foundation. "LCRF would never have been able to accomplish our initial goal and establish a footprint for this event without the encouragement and support that TGen provided. It is an honor and a privilege to be affiliated and to support their groundbreaking biomedical research in lung cancer."

Lung cancer is the leading cause of cancer death worldwide, annually claiming 1.3 million lives. The National Cancer Institute estimates that nearly 220,000 new cases of lung cancer occur annually in the U.S., while more than 159,000 individuals succumb to the disease.

Given that no practical way to screen for lung cancer exists, nearly 75 percent of all patients diagnosed have advanced-stage disease, leaving few options for treatment.

TGen's Lung Cancer Research Lab is at the forefront of efforts to improve lung cancer detection, develop new therapies and enhance our understanding of tumor biology.

TGen Foundation

Upcoming TGen Foundation events



Oct. 2, 2010 · 4th Annual Terri Link Memorial Golf
Tournament · The Georgia Club, Stratham, Ga.
This golf tournament celebrates the life of Terri Link and benefits Adrenocortical Cancer Research (ACC). The tournament includes raffles, on-course contests, and a lunch reception. Registration begins at 9 a.m. with a shotgun start at 10 a.m. Visit www.terrilinkmemorial.com



or call (404) 580-9803.

Oct. 21, 2010 · 12th Annual Key to the Cure · Saks Fifth Avenue, Phoenix

Join us for this highlight of the fall social season — a wonderful morning of fashion, friendship and fundraising — as we raise awareness and funds for women's cancers including breast and ovarian cancer research. The morning includes shopping, a runway fashion show and breakfast.

Saks will generously donate 2 percent of all sales from Oct. 21–24 to TGen. Visit www.helptgen.org to learn more.



Nov. 7, 2010 \cdot 5th Annual stepNout Run/Walk/Dash \cdot Kiwanis Park, Tempe

This year your participation will take us one step closer to a cure. Every step you take and each dollar raised will be used in the fight to prevent and cure pancreatic cancer. The event includes a change drive, lively (but silent) auction and awards ceremony. Registration begins at 7 a.m. Visit www.helptgen.org to register and learn more.

Seena Magowitz

The Face and Voice for Pancreatic Cancer

Dec. 4, 2010 · 8th Annual Seena Magowitz Celebrity Golf Classic · Talking Stick Resort, Scottsdale

Join us at one of the premier charity golf tournaments in Arizona. In the past four years the tournament has raised more than \$780,000 in support of pancreatic cancer research at TGen. Registration begins at 6 a.m. and includes a silent auction and 19th Hole luncheon and awards ceremony. Golf slots fill up fast. Visit www. seenamagowitzcelebritygolfclassic.com or e-mail liz@seenamagowitzfoundation.com for more information.





Translational Genomics Research Institute 445 N. Fifth Street Phoenix, AZ 85004 "Address service requested"

A TRANSLATIONAL EXPERIENCE

2010 Helios Scholars gain hands-on training

omorrow's leaders in science and medicine graduated July 30 from the Helios Scholars Program at TGen, one of the nation's most advanced biomedical research internship programs.

The 44 interns concluded eight weeks of hands-on investigations with a daylong symposium filled with discussions and scientific poster presentations.

"The beauty of this program is that students are immersed in the genuine essence of science," said Brandy Wells, TGen's Education and Outreach Specialist. "They work on the frontier of research, actively practicing concepts such as the scientific method and experimental design, and seeking answers to the questions they formulate. This journey into the unknown is what ultimately fuels their desire to pursue a career in the biosciences."

Among this year's graduates, 93 percent said they will pursue careers in science or medicine, and 89 percent said they planned to attain an M.D. or Ph.D.

"This innovative partnership with TGen not only helps students explore the biosciences, but it takes them beyond the classroom and into state-of-the-art laboratories, where they partner with TGen scientists to conduct independent scientific research on the genetic causes of certain diseases. That experience and exposure to the TGen scientists is invaluable to these students," said Paul Luna, Helios Education Foundation President and CEO.

The program allows high school, undergraduate and graduate level students, including those in medical school, to conduct independent scientific research affecting real-world patients.

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

The program began in 2008 through a 25-year, \$6.5 million grant from the Helios Education Foundation, the largest philanthropic foundation in Arizona focused solely on education. Applications for next summer's Helios Scholars Program at TGen opens in January, 2011.

