THE LATEST ALLY IN THE FIGHT AGAINST DISEASE

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.
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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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

Dad swims English Channel in memory of his son

New Jersey businessman supports TGen’s research into bipolar disorder

Richard Caretto was a 21-year-old college student, with the smarts and potential to do just about anything he wanted in life. Then, one day, Richard took his life, and was gone forever.

It was not Richard’s first attempt at suicide, nor was it the first time others ascribed his sometimes bizarre actions to a mental condition that in many ways remains a scientific mystery — bipolar disorder.

Also known as manic-depressive behavior, bipolar disorder is a mental illness that causes severe shifts in mood, dramatic changes in energy and activity levels, and an inability to carry out day-to-day tasks.
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.


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 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 manic-depressive 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.”
Bipolar 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

Dr. 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 physical state, performance and prognosis after a therapeutic procedure.
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.”

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**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.
A 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 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?

Read details about Dr. Huentelman’s bike ride at his blog: http://actionalz.blogspot.com/2010/08/alzheimers-breakthrough-ride-journal.html

More information about the Breakthrough Ride is available at www.alz.org/breakthroughride.
Go Dog, Go!
Canine research moves beyond cancer research to include behavior

TGen 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.

Whippets like this one are related to Greyhounds, whose DNA will be studied by the National Cancer Institute to better understand osteosarcoma, a type of cancer.
“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 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 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.

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.”
PetSmart Anticipates Expanding Role in Canine Cancer Project

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

S
ome time 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
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

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.

“Yet you 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 pet-
related 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 solely on the consent of the owners.

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

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>5</td>
<td>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.</td>
</tr>
<tr>
<td>10</td>
<td>Age at which nearly half of all dogs die of cancer.</td>
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<tr>
<td>20</td>
<td>Number of dog breeds that might eventually be included in the study.</td>
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<tr>
<td>200</td>
<td>Number of researchers expected to contribute to the study, including scientific investigators at nearly a dozen institutions.</td>
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<tr>
<td>500,000</td>
<td>Dollars each, from PetSmart and Hill’s Pet Nutrition:</td>
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<tr>
<td>4,300,000</td>
<td>Dollars in federal stimulus funds over two years.</td>
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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, one-time 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.
TGen investigators have discovered a treatment method that may help ovarian cancer patients who no longer respond to conventional chemotherapy.

**Protein inhibitor revives chemotherapy**

Dr. David Azorsa

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 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.

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

The future of oncology drug treatments.

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...
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 with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair with Dr. Timothy J. O’Rourke, who is the Betz Family Endowed Chair.

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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.

Studies identify genetic links to kidney disease; kidney failure

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.

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.

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.
Louis 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 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.
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.
Tomorrow’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.