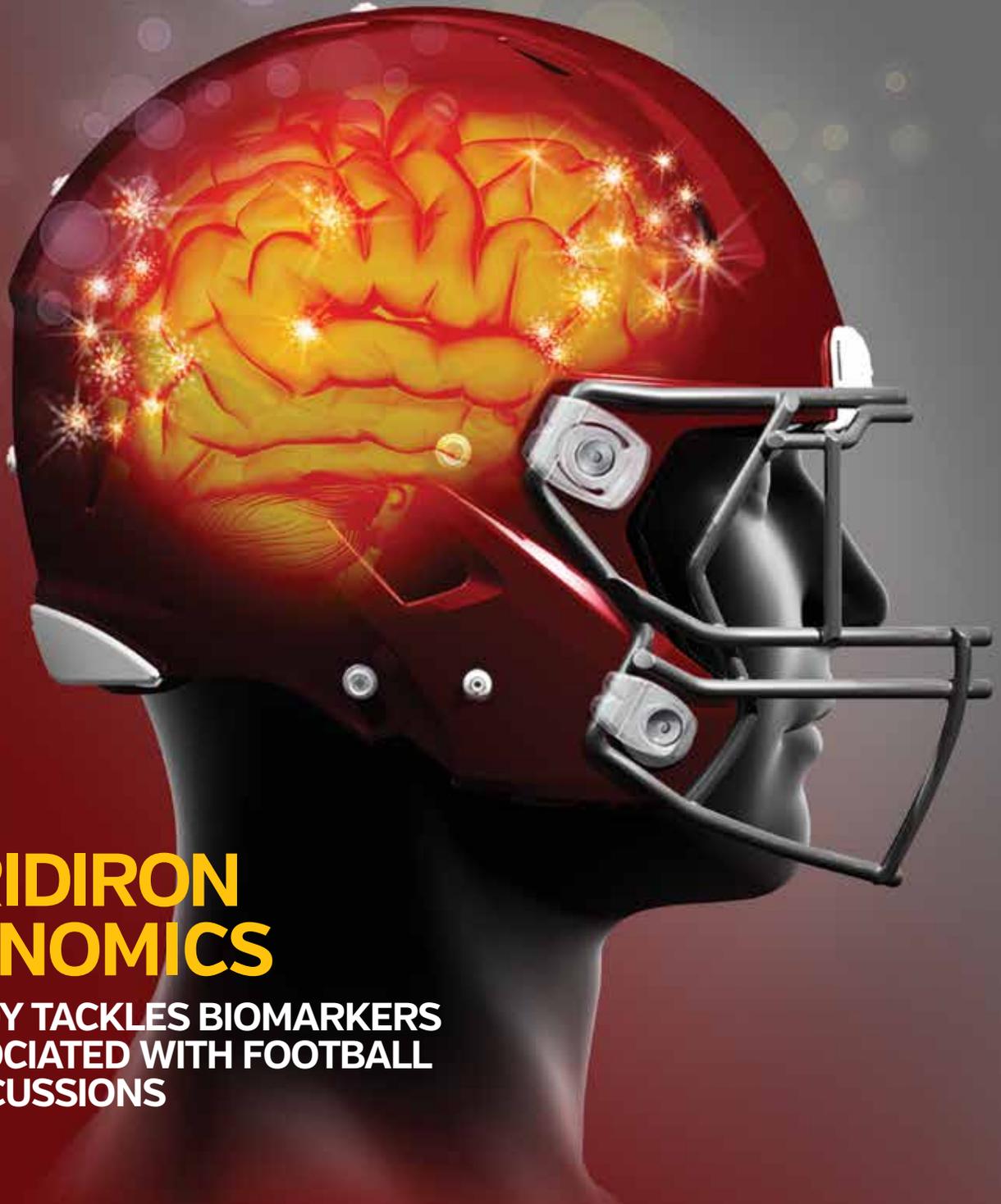


FALL | 2013

TGen Today

A PUBLICATION OF THE TRANSLATIONAL GENOMICS RESEARCH INSTITUTE



GRIDIRON GENOMICS

**STUDY TACKLES BIOMARKERS
ASSOCIATED WITH FOOTBALL
CONCUSSIONS**



A Non-Profit Biomedical
Research Institute

Follow the Crowd
In Support of
Alzheimer's
Research

Center provides
new hope for
children and
families

TGen Clinical trials
provide immediate
patient benefit



A Look Inside...

Dear Friends,

TGen scientists and doctors work tirelessly to provide those patients and their families who need our help the most with **hope and answers**. Of equal importance – and worthy of our thanks – are those civic-minded individuals and companies beyond the walls of our Institute who support our work through funding, events, and service on our Boards and Committees; a few are highlighted within these pages.

Whether you are a child born with an unknown genetic disorder, a woman battling pancreatic cancer, a football player suffering from a concussion or a family coping with Alzheimer's disease, by focusing on each individual's unique genetic signature, TGen's researchers are leading the way in the delivery of precision medicine, a bold new approach to more accurately diagnose and treat human disease.

In this issue, you will read how precision medicine helped Pam Ryan, a Phoenix woman given just a few weeks to live following her pancreatic cancer diagnosis and how TGen physicians brought her **hope and answers** in the form of a breakthrough new treatment. The article detailing the benefits of this TGen-led clinical study appeared in the prestigious *New England Journal of Medicine*.

Kendall Bayne's story details the fight of a beautiful and talented South Carolina high school student whose family turned to TGen for help in her fight against adrenocortical carcinoma, a rare and aggressive cancer. Kendall's family found **hope and answers** at TGen. Having successfully fought this disease for more than two years, Kendall has rallied her entire school and community through an effort called *Team Kendall: Fight Like a Knight*.

Our cover story details how a collaborative of scientists from TGen, Arizona State University, Barrow Neurological Institute and A.T. Still University have teamed up to tackle the issue of sports-related concussions. Funded by Riddell, the industry leader in football helmet manufacturing, the study employs Riddell technology worn by ASU's Sun Devil players that monitors and records head impacts and transmits it in real time to the scientific team working the sidelines of each ASU game.

Perhaps no technology has connected people globally more than the Internet. The story of MindCrowd is more than an Internet story, though, it's how scientists at TGen and the University of Arizona **hope** to attract 1 million people from around the world to participate in a unique study of short-term memory, the results of which may bring **answers** to the millions of families dealing with the heart break and loss created by Alzheimer's disease.

In closing, I hope you will consider your own role in bringing **hope and answers** by financially supporting TGen's work through a gift to the TGen Foundation. I assure you that there is no better investment of your charitable dollars.

On behalf of everyone at TGen, thank you for helping us make a difference – one patient at a time.

Michael Bassoff
President, TGen Foundation



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Gridiron Genomics

Study tackles biomarkers associated with football concussions

[Photo of ASU player by Peter Vander Stoep, Sun Devil Athletics]



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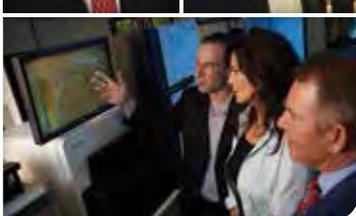
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'Wonder Woman' Lynda Carter advocates TGen 'MindCrowd.org' study; urges everyone to take the test



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About TGen |

Translational Genomics Research Institute (TGen) is a Phoenix, Arizona-based non-profit biomedical research organization dedicated to conducting groundbreaking research with life changing results. TGen is focused on helping patients with cancer, neurological disorders and diabetes, through cutting edge translational research (the process of rapidly moving research towards patient benefit). TGen physicians and scientists work to unravel the genetic components of both common and rare complex diseases in adults and children. Working with collaborators in the scientific and medical communities literally worldwide, TGen makes a substantial contribution to help our patients through efficiency and effectiveness of the translational process. For more information, visit: www.tgen.org.



FOLLOW THE CROWD

In Support of Alzheimer's Research

The knowledge gained from this test could help determine what triggers Alzheimer's disease – and possibly – other brain disorders.

Each day, countless people experience periodic bouts of memory loss. This occasional lapse in one's recall ability – often referred to as a “senior moment” – occurs more frequently as we age.

Where did I place the car keys? Where are my sunglasses? How did I forget the quart of milk on my mental grocery list?

A slight decline in one's memory performance is expected as we age. But when the senior moments occur frequently enough to impair one's ability to function on a daily basis, they could be the early warning signs of Alzheimer's. The nexus between the senior moment and progressive memory loss due to Alzheimer's disease is an area of research that intrigues and drives TGen's Dr. Matt Huentelman.

For Huentelman, an Associate Professor in TGen's Neurogenomics Division, and one of TGen's leading experts in Alzheimer's research, advances in genomic sequencing, brain imaging and other biomedical technologies have significantly aided his research into the underlying biology of memory and his studies into the genetic underpinnings of Alzheimer's.

“It's a big question,” Dr. Huentelman said. “We're definitely on the path toward the answers, but we're still far from a complete understanding of the disease. In addition to the genetic factors involved in Alzheimer's, we still need to understand the environmental risk factors, exactly how the

disease progresses, and how it can be halted or even prevented.”

Today's technology helps by allowing Dr. Huentelman and his research team to identify many of the genetic risk factors associated with Alzheimer's, and by providing a much-improved blueprint for selecting drug development targets. The hope is that these genomics-informed targets will eventually lead to better therapies and greater patient benefit.

Certainly the ability to search the entire human genome is a great start, but Dr. Huentelman knows it will take more than technology. With more than 5 million Americans living with Alzheimer's, it also will take the right type of data to inform his studies – and that is largely driven by the right collection of research volunteers.

Going Social

To help drive the research, Dr. Huentelman and his colleagues created an online memory test they're promoting through a TGen crowdsourcing website: mindcrowd.org. With a targeted sample size of 1 million people, this will provide a broad sampling of the human population across the entire aging continuum.

Since its launch in April, more than 23,000 people have completed the MindCrowd test. But to reach the goal of 1 million, researchers will need many more volunteers.



“We’ve already had participants from more than 100 nations and every state in the U.S.,” Dr. Huentelman said. “I can’t help but feel that we need just a little luck to make it go viral and reach the 1 million mark.”

TGen, in collaboration with the University of Arizona and the Alzheimer’s Prevention Initiative, will use the MindCrowd test results to learn about the role of genetics in the memory test performance of healthy individuals.

“Understanding brain performance in healthy people provides a glimpse of the natural spectrum of variation associated with aging, and that new knowledge could help us show what goes wrong in Alzheimer’s disease and possibly other brain disorders,” Dr. Huentelman said.

Researchers now recognize that social networking and crowd sourcing can significantly power specific types of research projects. In many respects, they have demonstrable benefits over traditional volunteer recruiting approaches.

“What makes MindCrowd unique is the large number of participants we plan to reach, and the eventual tie to genomic testing,” Dr. Huentelman said.

Dr. Huentelman is quick to note, however, that the anonymous, 10-minute test is neither a diagnostic tool for Alzheimer’s disease nor an indicator of future risk. It tests a very specific portion of the brain to see how it works. His hope is that this first MindCrowd test engages participants and gets them excited about being part of what could lead to a better understanding of Alzheimer’s disease. It also shows that science can be accessible. Not everyone needs a Ph.D. to participate.

Those who complete the MindCrowd test can see their results within seconds, and there’s a feature that allows them to compare their score with others by age, gender, education level and other groupings.

“We encourage participants to challenge their friends, families, and co-workers,” Dr. Huentelman said. “Bottom line, it’s fun, and each completed test is potentially of great benefit to the millions of people who have, or are at risk of getting, Alzheimer’s. Each person who takes the test is making a significant contribution to our study and, we hope, to the eventual solution of Alzheimer’s disease prevention.”

Be Part of the Solution

TAKE THE TEST  **10 MIN**

The MindCrowd test consists of a series of word pairs. Participants review a list of pairs and then receive a word cue to recall the word with which it was originally paired. This simple word association tests a specific portion of the brain to see how it works.

Education Level	Score (%)
Less than High School	32%
High School	44%
Some College	55%
1-2 years	59%
3-4 years	65%
5-6 years	79%
College Degree	76%
Master's Degree	71%
Professional Degree (PhD, MD, etc.)	70%

Once you have completed the test, you can see your results within seconds. There is also a feature that allows you to compare your score –by a number of categories, including age, gender, and handedness– against others who have taken the test. You can also share your results with family and friends and encourage others to take the test by sharing the MindCrowd link of www.mindcrowd.org



TGen CANCER RESEARCH GETS BOOST FROM APS, WHO HONORS A NATIVE SON



Don Robinson was a man known for his leadership, integrity and kindness.

As President and Chief Operating Officer of Arizona Public Service Co. [APS] at the time of his passing, and one of Arizona's leading citizens over the past three decades, he leaves behind a legacy that touched the lives of thousands. And in a gesture synonymous with his life's values, APS leadership furthered Robinson's legacy with a gift supporting cancer research at TGen.

Robinson passed away in early April after a long battle with cancer. In his honor, APS on June 19 dedicated its Phoenix customer care offices in his name: now called the Don Robinson Building. As part of that dedication ceremony, an emotional APS Chairman and CEO Don Brandt presented TGen with a donation in Robinson's name on behalf of the APS Foundation, APS's Board of Directors and the company's 6,000 employees.

On hand to accept the gift were TGen President and Research Director Dr. Jeffrey Trent, TGen Physician-In-Chief Dr. Daniel Von Hoff, and former APS Chairman and CEO and current TGen Board Chairman Bill Post. TGen – specifically Dr. Von Hoff – was instrumental in managing Robinson's care during his fight with cancer.

"TGen played a tremendous role in helping Don through his illness. I can't thank Dr. Von Hoff enough for his kindness and compassion. It was a great comfort to my husband," said Robinson's wife, Chloe. "I am also moved by APS's commitment in Don's memory to bettering the lives of individuals dealing with

cancer by supporting the research at TGen."

Upon presenting the donation, Brandt remarked that by supporting the Institute, "TGen can continue to do the great work and provide the same level of hope and comfort to patients in the future that you gave to Don."

An Arizona native, Robinson, 59, was a beloved and widely respected figure throughout APS and Arizona.

"Don was a true gentleman and a real friend. There have been few – maybe none – who have known our business and our state like Don," said Brandt. "One could accurately describe Don as brilliant, an exceptional leader and a visionary, and still not touch upon his best qualities – his faith, his humanity, his generosity and his kindness."

Robinson served on the boards of the Arizona Chamber of Commerce and Industry, the Herberger Theater, the Fellowship of Christian Athletes, the Fellowship for Senior Living and the Phoenix Police Reserve Foundation. His community efforts earned him several honors, including Scottsdale Leadership's Corporate Leadership Award, and the Arizona Chamber of Commerce's Transformational Leader Award.

Since Don Robinson's passing, tributes have poured in from across Arizona from community leaders, industry representatives and employees, expressing appreciation for this special man, including Arizona Governor Jan Brewer, who said, "Arizona has lost one of its true leaders of business and community."

The Gift of *Family*

A nephew honored with the naming of a laboratory to fight rare childhood disorders

For Abby and David Harbour, nothing is more important than family. Hunter Brown, 15, who has lived with a debilitating rare disorder his entire life, is one of three sons of David's sister and brother-in-law, Trisha and Jim Brown.

To honor their family's fight, Abby and David have made a generous donation to name the Abby and David Harbour Laboratory in Honor of Hunter Brown inside TGen's Center for Rare Childhood Disorders.

"Hunter has opened our eyes to the struggle of parents who have a child with an undiagnosed rare disease," David Harbour said. "His courage, and my sister and brother-in-law's courage, and their family – and what they go through on a daily basis – it's so difficult that we want to do whatever we can to try to bring choices, if not a cure, for people who are in the same circumstances."

Along with Valley philanthropist Jacquie Dorrance, David co-chairs the Center's National Advisory Committee.

"My wife Abby and I have a passion for children who don't have the same opportunities as others," said David Harbour of Scottsdale. "We've been lucky and blessed in our life – we have a daughter – so anything we can do to help, that's our goal."

Dr. Vinodh Narayanan, Medical Director of the Center, said the Harbour's gift will help TGen scientists to substantially advance the Center's goal of providing answers for children and their families who have otherwise run out of hope.

"Funding this Center will advance critical aspects of our mission: Supporting the advancement of genomic methods that



allow us to accurately diagnose and counsel our patients and their families; supporting cutting-edge research into the biology of these disorders; and discovering novel treatment approaches – the ultimate goal of personalized genomic medicine," Dr. Narayanan said.

The Harbour's joined forces with TGen after David Harbour met TGen Foundation President Michael Bassoff and became aware of the institute's life-changing research.

"Through their extraordinary contribution, Abby and David Harbour are enabling TGen to bring hope and answers to those children and their parents, who so desperately need help," Bassoff said. "We are extremely grateful for their leadership and generosity."



HOPE IN ACTION

TGen's Center for Rare Childhood Disorders provides renewed hope for children and families

"TGen has been such a gift for our family, it's allowed us to take their medical care to another level."

A few hundred feet from where the rooftop ceremony was taking place, the medical suite housing TGen's Center for Rare Childhood Disorders waited its moment in the sun. Soon, the gathering of dignitaries and supporters would tour the new facility and learn first-hand how TGen faculty and clinicians have leveraged the power of genomics into a powerful new tool for medicine, and a beacon of hope for countless children suffering under the weight of an undiagnosed disease or disorder.

"This clinic opens up a whole new frontier of science," said Dr. Richard Carmona, the 17th Surgeon General of the United States who served as keynote speaker for the Center's October 15 ribbon cutting.

Dr. Carmona, now the President of the non-profit Canyon Ranch Institute and a professor at the University of Arizona and The Ohio

State University, praised TGen's state-of-the-art biomedical science, its ability to seek out the genetic origins of disease, and provide a diagnosis for young patients whose parents have often gone years wondering what was wrong with their child.

"TGen represents the future of medicine," said Dr. Carmona, who served as U.S. Surgeon General from 2002-06. "This is very, very powerful science. And this is just the tip of the iceberg. Eventually, this work is going to lead to other areas of medicine."

Dr. Carmona also praised the vision of TGen President and Research Director Dr. Jeffrey Trent and the TGen staff and faculty, recalling as unimaginable a decade ago the science practiced by TGen today.

"It's an extraordinary place that we have in this community," Dr. Carmona said. "Jeff and

SPOKEN FROM THE HEART

his team are dealing with medical challenges that nobody else in the world is dealing with.”

Drawing inspiration from British poet and scholar, Peter Levi, Dr. Trent captured the Clinic’s promise through the Levi quote, “Hope in every sphere of life is a privilege that attaches to action. No action, no hope.” The clinic, he said, is hope in action.

Dr. Trent went on to thank Dr. Carmona, Center supporters and government dignitaries for their unwavering commitment to TGen, including Speaker of the Arizona House of Representatives Andy Tobin, Governor Brewer’s Chief of Staff Scott Smith, and Phoenix Mayor Greg Stanton, who said TGen “represents the very best of this community.”

Dr. Trent emphasized how the Center provides patients and families with answers, noting what a joy it was to see a number of patients the Clinic has helped.

Shelby Valint, a 13-year-old Phoenix girl who before TGen sequenced her genome spent most of her life in a wheelchair, said, “It changes your whole life. It helps so much.”

Newell Belnap, whose four children are all vulnerable for a form of mitochondrial disease – which affects the powerhouse of the body’s cells – credited the Center’s Medical Director, Dr. Vinodh Narayanan, with saving the life of his and wife Becky’s youngest son, Seth.

Using genomic sequencing, the Center’s Co-Directors – Drs. David Craig and Matt Huentelman – worked with Dr. Narayanan to end the Belnap’s diagnostic odyssey by providing them with the molecular based information they needed to best understand how to treat their children.

“TGen has been such a gift for our family,” said Belnap, thankful that Seth and the Belnap’s other children – Sydney, Spencer and Sierra – all have a diagnosis. “It’s allowed us to take their medical care to another level.”

Master of Ceremonies, KTAR Radio personality Karie Dozer, who also Chairs the Center’s Parents Advisory Committee, asked Dr. Narayanan what makes TGen unique?

“What we have here is the ability to do something that is not possible most places in the world,” he said.

Jennifer Smestad wasn’t always the poised, well-spoken young woman who earlier this year won the Miss Arizona competition.

As a child growing up in Gilbert, Arizona, Jennifer was hobbled by an unknown disorder that left her hurt and frustrated, and at times unable to function.

Her head would twitch violently, causing neck pains. She would occasionally strike herself unconsciously. Sometimes she would make “weird, high-pitched noises.”

An associated obsessive-compulsive disorder made it difficult to walk up stairs, since each step had to be perfect. And she found it difficult to write, repeatedly erasing and starting over again.

Her mother relentlessly researched what might be wrong with her, seemingly online 24/7 and flying to distant cities to try to find a cure.

“I had extreme anxiety, ending up at the hospital at times,” Jennifer recalled. “I was constantly sore, and sometimes I just wanted to just stay in bed all day.”

After years of uncertainty, at age 10 she was diagnosed with Tourette Syndrome, which causes involuntary movements and vocalizations. Following years of counseling, medication and finally acupuncture, by age 15 Jennifer was free of symptoms.

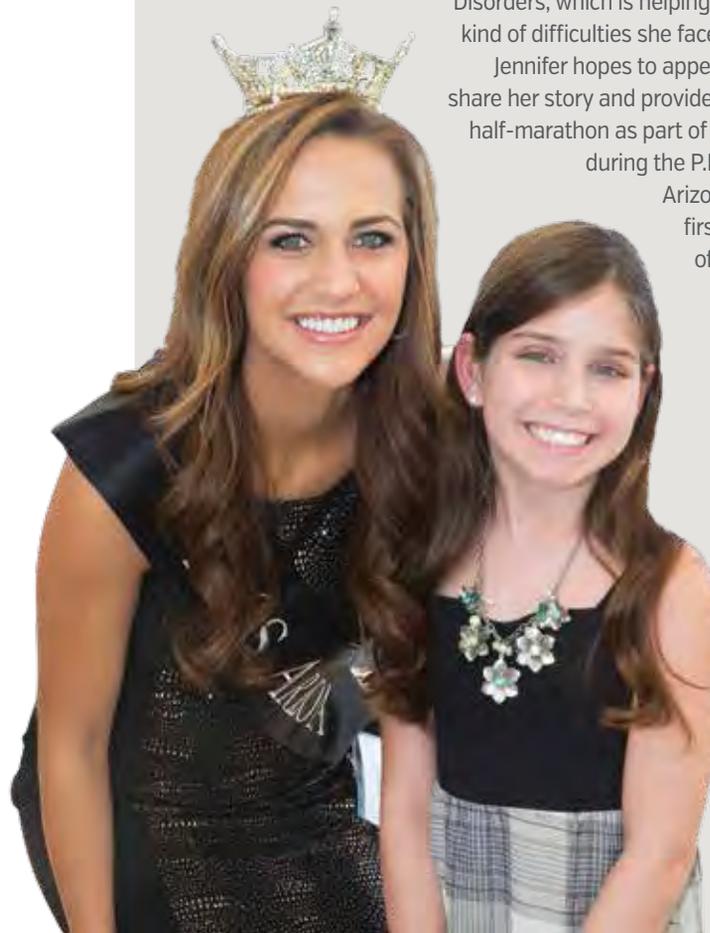
“It was such a relief when I was diagnosed,” said Jennifer, who plans to continue her college education, specializing in communications and nutrition in hopes of someday landing a media position, specializing in health and fitness.

Jennifer has tremendous empathy for the children and parents of young patients seeking help from TGen for their own undiagnosed conditions. As a contestant in Miss Arizona and Miss America, Jennifer has championed the cause of childhood neurological disorders.

Now, she is supporting TGen’s Center for Rare Childhood Disorders, which is helping other children overcome the kind of difficulties she faced as a child.

Jennifer hopes to appear at TGen functions to share her story and provide hope for others, including a half-marathon as part of TGen’s “Run for Kids” Jan. 19 during the P.F. Chang’s Rock ‘n’ Roll

Arizona Marathon, which for the first time includes TGen as an official charity.



Miss Arizona Jennifer Smestad (left) has something in common with TGen patient Shelby Valint (right) – they both have successfully battled rare childhood disorders.

GRIDIR



“The team will attempt to identify biomarkers associated with documented concussion and sub-clinical concussion.”

RON GENOMICS

Study Tackles Biomarkers Associated With Football Concussions

With football season underway, the focus on concussions sustained from high-impact hits is at an all time high. Concussion is the most common form of mild traumatic brain injury (mTBI). Currently, there is limited data on the genomic and molecular changes associated with mTBI or the effect of repeated head impact exposure to the brain that does not result in a diagnosed concussion.

TGen, Riddell Sports and the Arizona State University (ASU) football program hope to change all that.

In early May, TGen partnered with Riddell, an Easton-Bell Sports brand, to embark on a study to advance athlete concussion detection and treatment.

Expanding upon TGen's work in the area of head trauma, the investigative team led by Drs. Kendall Van Keuren-Jensen and Matt Huentleman will attempt to identify biomarkers associated with documented concussion and sub-clinical concussion.

In late September, ASU and its Sun Devil football program joined TGen and Riddell in the study. Riddell equipped Sun Devil players with specially designed wireless helmet sensors to collect impact data. The information gathered from the system will be combined with molecular information from Sun Devil players that experience concussion, with the objective of helping physicians diagnose concussion and better identify when a player might be expected to recover and return to the field.

"There's no question that identifying genomic biomarkers will revolutionize what, up to now, have been relatively imprecise methods of detecting when an athlete is too hurt to play," said Dr. Jeffrey Trent, TGen President and Research Director. "By their nature, many

sports carry inherent risks of head trauma. Our research could minimize the long-term damage that sometimes results from such injuries."

Often, head injuries present no physical changes that can be viewed using conventional imaging techniques.

However, symptoms experienced by concussed athletes (headaches, loss of memory, temporary unconsciousness, confusion, drowsiness) indicate there are functional changes that can last several days. These symptoms possibly result from structural brain damage – only detectable at the molecular level – including torn axons and synaptic connections that prevent transmission of the brain's electrical impulses.

At the beginning of the training season, TGen collected biological sample from players to establish baseline data. During the season, biologic samples are collected prior to game day, immediately following game day, and on the second day following each game.

Biological information from a player's genome is merged with real-time helmet-sensor information provided by Riddell's Sideline Response System. This SRS system provides researchers, athletic staff and players with information about the frequency and severity of head impacts during games and practices. This information will be compared with players' biological samples.

TGen is measuring changes in RNA (DNA's complimentary nucleic acid), associated with head impacts through samples of blood, saliva and urine. By using RNA as a sensitive indicator of changing conditions underlying brain injuries, this data could improve the ability to detect at-risk patients for future neurological, cognitive and behavioral complications.

Continued ▶

This SRS system provides researchers, athletic staff and players with information about the frequency and severity of head impacts during games and practices.

TGen researchers April Allen and Khalouk Shahbauder monitor helmet impacts by ASU football players at Sun Devil Stadium



“We believe this study will have the unique ability to provide a molecular ‘risk’ and ‘recovery’ score, enabling physicians to better identify when a player might be expected to recover from the effects of the concussion and get back on the field,” said Dr. Van Keuren-Jensen, a TGen Assistant Professor, whose technique for studying molecular information at a micro level will drive the research.

As part of the study, TGen will work with the Barrow Neurological Institute, whose B.R.A.I.N.S. [Barrow Resource for Acquired Injury to the Nervous System] project treats patients age 15 and older who have sustained a traumatic brain or spinal cord injury.

“Combining our neurological expertise, and the information from our B.R.A.I.N.S. program, with TGen’s genomic knowledge and Riddell’s helmet technology, will provide great insight into how we measure concussions and how they affect the human brain,” said Dr. Javier Cárdenas, a neurologist and brain injury

expert with Barrow Neurological Institute.

“The genomic data could aid in the treatment process and will greatly add to the growing body of knowledge we’re acquiring about head injury patients.”

Joining with Barrow are athletic trainers from A.T. Still University and SAFE Football, which teaches alternative game-play techniques that reduce head impacts while increasing competitiveness.

Desert Testing is collecting bio samples and data.

“Our partnerships with Barrow Neurological Institute, A.T. Still University, and Safe Football provide a multifaceted approach to identifying athletes in need of medical attention, to educating athletes on concussion and brain injury, to reducing the risk of injury through development of better techniques, and to improving treatment outcomes,” said Dr. Huentelman, TGen Associate Professor and a co-investigator on the study.



Dr. Javier Cárdenas leads clinical studies

Dr. Javier Cárdenas, a concussion specialist at Barrow Neurological Institute, is a key player in TGen’s ASU-Riddell study of football brain injuries.

Dr. Cárdenas leads the Barrow Concussion Network, which is the first of its kind in the nation and offers comprehensive, compassionate, cutting-edge treatment and rehabilitation to victims of concussion and other brain injuries.

The Barrow Concussion Network provides baseline testing, a statewide concussion registry, and concussion education through a program called Barrow Brainbook. Barrow Brainbook has educated more than 180,000 Arizona high school athletes, provided thousands of computerized concussion baseline tests for high school athletes, and created a culture of safety in sports.

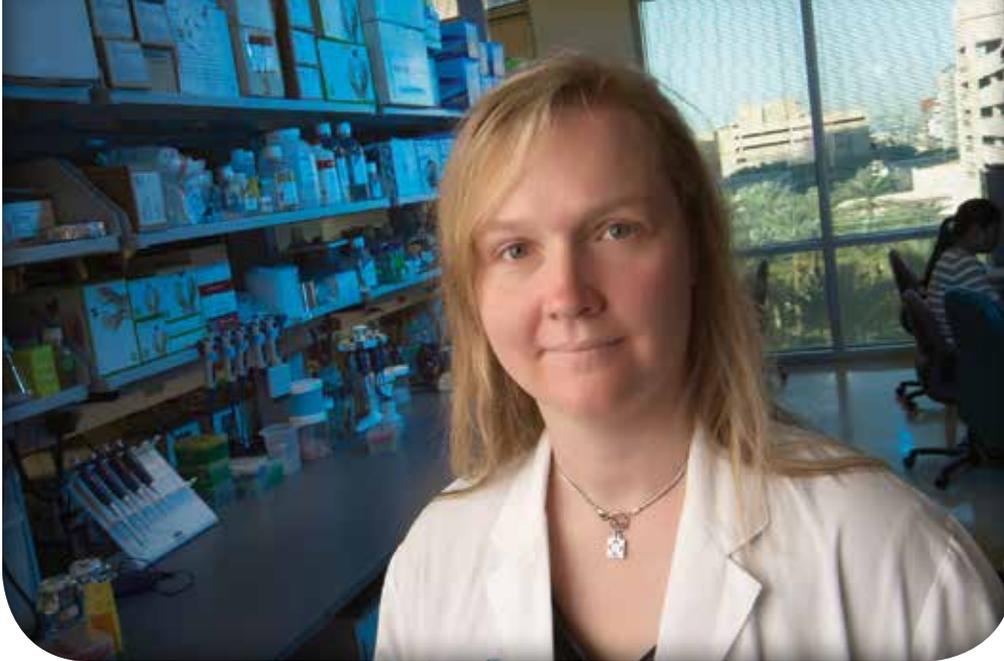
Among the goals of the Barrow Concussion

Network is to investigate the epidemiology of sports concussion, identify risk factors, establish a network of care, and create a research platform for better understanding concussion.

Dr. Cárdenas also has created a video game app to help players avoid injury called Barrow Brainball: <http://bit.ly/19FshR3>.

“Working with TGen is key to solving the concussion riddle,” said Dr. Cárdenas.

Dr. Cárdenas graduated ASU with highest honors and a Bachelor’s degree in Education. He earned his medical degree in Neurology with honors from the University of Arizona College of Medicine. His awards include: Pediatric Intern of the Year; The Walt Vikram Troester Memorial Scholarship, for Exemplary Compassion in the Care of Neonates; and Outstanding Resident Teacher of the Year.



Dr. Kendall Van Keuren-Jensen, the study's senior author.

A SCIENTIFIC FIRST

TGen researchers profile microRNA in cerebrospinal fluid using state-of-the-art sequencing technology

In what TGen researchers believe to be a scientific first, microRNAs that could identify and diagnose patients with neurological disorders have been profiled in cerebrospinal fluid (CSF) by using next-generation sequencing technology.

These small RNAs, also called miRNAs or microRNAs, are involved in post-translational regulation of gene expression. In addition to residing inside the cell, these small RNAs are thought to be exported from the cell in microvesicles and in association with RNA binding proteins where they can be isolated and examined as extracellular RNA (exRNA). Because these exRNAs can potentially travel into CSF, or even into peripheral blood, they hold promise as diagnostics for disease and injury of the central nervous system.

The miRNAs identified in this study were isolated and profiled using next-generation sequencing, which spells out the individual chemical bases in the exact order in which they occur.

"The purpose of this study was to maximize RNA isolation from RNA-limited samples and apply these methods to profile the miRNA in human CSF by small RNA deep sequencing," said Dr. Kendall Van Keuren-Jensen, the study's senior author.

The study, *Identification of extracellular miRNA in human cerebrospinal fluid by next-generation sequencing*, was published in March in the scientific journal *RNA*, a peer-reviewed publication of the RNA Society.

Isolation of miRNA in CSF has presented a challenge to researchers. Blood plasma, serum, and CSF contain low amounts of total RNA, of which miRNAs – which were first characterized in the 1990s – make up only a tiny fraction.

"We systematically tested RNA isolation efficiency using commercially available kits and compared their performance on human blood plasma samples and then applied these techniques to the even smaller amounts of RNA isolated from CSF," said Dr. Kasandra Lovette Burgos, formerly of TGen and now an account executive at NuGen Technologies, the study's first author.

"We found that the miRNA expression profile of CSF, as expected, is substantially different from that of plasma or serum from blood," Dr. Van Keuren-Jensen said. "To our knowledge, this is the first time that the small RNA fraction from CSF has been profiled using next-generation sequencing."



COPING WITH CANCER

TGen CLINICAL TRIALS PROVIDE IMMEDIATE PATIENT BENEFIT

TGen's laboratory research is immediately translated into innovative cancer treatments that provide patient benefit – today. TGen is conducting more than 40 clinical trials at the Virginia G. Piper Cancer Center Clinical Trials, through our partnership with Scottsdale Hospital. One of those TGen-supervised clinical trials, an international study of 861 patients, resulted Sept. 6 in the U.S. Food and Drug Administration approval of Abraxane for patients with advanced pancreatic cancer.

Two of those pancreatic cancer patients are Pam Ryan and Lynne Jacoby. Along with patient Kendall Baynes, who has adrenocortical cancer, they all credit TGen with helping them cope with their disease. Here are their stories.

A SECOND OPINION THAT SAVED A LIFE

*Pam Ryan
sought a
second opinion
from TGen's
clinical team*



Pam Ryan of Phoenix thought at first she was suffering from strained muscles in her legs.

But when she visited her doctor it was discovered she had blood clots in her legs, and her lungs.

A subsequent CT scan discovered a tumor on her pancreas – Stage IV pancreatic cancer.

Her family was told she might only have weeks to live.

“The first day I found out about this – as I'm reeling in shock – I meet the oncologist who takes me out in the hallway and says,

essentially, she's going to die, and you need to be prepared for that,” said Jim Ryan, Pam's husband of more than 40 years.

Pam sought a second opinion from TGen's clinical team, headed by TGen Physician-In-Chief Dr. Daniel Von Hoff.

“Dr. Von Hoff, and TGen, I really think have saved my life,” Pam said. “I'm so thankful for TGen and their clinical trial, and especially for the hope that it offers future patients. I truly believe in my heart that it's going to change the percentages of survival. It's all because of TGen and their research.”

“What Dr. Von Hoff and TGen are doing is making a quantum leap forward in the ability of modern medicine to cure what had previously been essentially a death sentence,” added Jim. “I can't tell you how exhilarating it is to go from no hope to ‘Dr. Von Hope’ [Dr. Von Hoff]. Total hope.”

Besides her husband, Pam's family includes two children and four grandchildren. “They're all the love of my life, and they're my inspiration to keep me going, and staying positive, and fighting for life here with them.”



WORTH OUR INVESTMENT

Lynne Jacoby of Phoenix had gone from healthcare professional to cancer patient to healthcare advocate – one of the most outspoken proponents of TGen’s clinical trials.

In April 2012, Lynne received a diagnosis of pancreatic cancer, the nation’s fourth leading cause of cancer death.

Because no early detection test exists for this relentlessly aggressive cancer, Lynne’s cancer – like that of many pancreatic cancer patients – had already advanced to Stage IV. In Lynne’s case, the cancer had spread to her liver. Coupled with the knowledge that three-in-four patients live less than a year and less than 6 percent live five years (the lowest survival rate of any cancer), Lynne’s doctor’s offered her little hope.

“I was told my life would be measured in weeks,” she said.

While Lynne accepted the diagnosis, she refused to accept the prognosis. After joining a clinical trial at the Virginia G. Piper Cancer Center Clinical Trials, a partnership between TGen and Scottsdale Healthcare, Lynne’s fate took a turn for the better.

Clinical trials provide patients the benefit of otherwise unavailable treatments. In Lynne’s trial, she received a combination of standard chemotherapy plus an added drug called Abraxane, which contains albumin; a protein that pancreatic tumors like to eat. The drug acts like a Trojan horse: once inside the tumor, the nano-sized albumin quickly and easily enters the bloodstream and the tumor, and releases a drug that eats the cancer from the inside out.

In Lynne’s case, it worked. A year later, tests showed she was tumor free: “I feel great and enjoy every day I get to be alive. I have outlived my own shock at hearing the news, the sad and terrified looks of friends and family, and yes, even the expectations of my doctors,” she said at the time. “I am living proof that it works, and every day, I meet others in my situation, for whom clinical trials and new treatment regimens are the best or only hope,” she said.

In recent months, Lynne’s cancer returned. But, because of continuous monitoring, it was caught



Clinical trials provide patients like Lynne Jacoby the benefit of otherwise unavailable treatments.

early, and Lynne remained hopeful. But despite all efforts, she passed away in early October at her north Phoenix home, surrounded by family and so much love.

Lynne spoke in Chicago earlier this year at a special event coinciding with the annual meeting of the American Society of Clinical Oncologists (ASCO). She started writing a blog (strikeoutcancer.blogspot.com). And she advanced in every way she could the importance of continued federally-funded research and the need – and economy – of clinical trials.

“I work in the healthcare industry and I know, humanitarian issues aside, keeping a patient alive and healthy is the most cost-effective care,” she said at the time. “It’s what I call a ‘virtuous circle’ because the best financial outcome is that I survive and I continue to pay my insurance premiums, and as I return to health, I use fewer medical resources, easing the burden on the healthcare system. It’s a virtuous circle because what’s best for the patient is best for the healthcare system – providers and payers – and best for society as our productivity continues.”

Lynne maintained that clinical trials are pointing doctors in new directions, refining treatments, and making progress through medical innovation.

“Is that worth our investment? Does that merit our support? Let me answer this way,” Lynne said. “In the end, I would say everyone’s precious life is measured in weeks. None of us knows how much time we have left. Our job is to make all of our lives as long, as comfortable and as worthwhile as possible. We can’t afford not to.”

See related story on following pages ▶

TGen GIVES HOPE TO TEENAGER WITH RARE ACC TUMORS

“It seems so selfish now, but losing my hair was the one thing I was upset about most. Not that my disease was spreading or that I was about to enter the ultimate test of strength.”

Kendall Bayne is a 17-year-old high school student from Roanoke, Virginia, who once lived what she calls “the normal teenage life.”

Others might say she’s exceptional.

Kendall was an A-plus student and homecoming queen who excelled daily in competitive cheerleading.

But in October 2010, during cheer practice, she began having pains on her right side, which got worse when she ran.

“I went to the doctor numerous times but continued to get misdiagnosed,” she said.

In February 2011, Kendall took a hard fall while on a family skiing trip. The pain was extreme.

“The very next day, Valentines Day, I went to the emergency room where a CT scan revealed that I had an 11-centimeter-long tumor sitting on my right adrenal gland,” Kendall said. The skiing mishap had caused the tumor to shift, causing severe pain.

Following surgical removal of the tumor, Kendall learned that the overwhelming majority of adrenal tumors are benign. For Kendall, however, the look on her doctor’s face said it all: she had cancer.

“My life changed forever at that moment,” Kendall said.

She learned she had Adrenocortical Carcinoma (ACC), an aggressive cancer of the adrenal glands, above the kidneys. It is so rare it affects only 1 or 2 people in a million.

Initial scans following surgery showed her tumor free. But 6 months later, a scan showed her lungs contained eight tumors, which also required surgical removal.

Since then more tumors have appeared, and Kendall has undergone extensive hospitalization and numerous rounds of painful and debilitating chemotherapy.

“It seems so selfish now, but losing my hair was the one thing I was upset about most. Not that my disease was spreading or that I was about to enter the ultimate test of strength,” she said. “I became totally dependent on those



around me. I would go without eating for days and was even too sick to open my eyes. I just laid there.”

Finally, her body couldn’t take the chemotherapy anymore. She had pneumonia, requiring another extended hospital stay that included four blood transfusions.

In February 2013, two years after being diagnosed, another scan showed two new tumors on her kidney, which required three weeks of radiation.

“My dad has always told me this isn’t a sprint; cancer is a marathon,” she said. “And he is so right.”

Kendall and her family consulted some of the top cancer centers in the nation, including TGen, which is conducting some of the world’s



Left: Kendall Bayne celebrates life on her kayak.
Below: Kendall sporting shorter hair from treatment.



most innovative studies of ACC through the work of Dr. Michael Demeure. Kendall now is receiving a new experimental drug.

“It is our hope that this new therapy will give me and patients like myself a chance to live and be healthy again,” Kendall said. “The research that TGen performs gives patients a huge dose of hope and a reason to believe cancer will be cured, or at the least become a chronic disease.”

She dismisses her many tumors, now scattered throughout her body.

“I’m the happiest person you could ever meet. I don’t have time to be sad and miserable. I may be sick, but I try to do everything I would before my diagnosis,” said Kendall, who in May felt well enough to attend her Junior Prom, and in August returned to school for her senior year.

“I have so much to offer to this world and so many things I want to accomplish and experience. I am forever grateful and blessed that TGen is helping me beat cancer.”

Vice President Dan Quayle elected to TGen Foundation Board



At its October meeting, the TGen Foundation Board of Directors elected former U.S. Vice President Dan Quayle, who served under President George H.W. Bush from 1989-93, to the Board. Vice President Quayle attended grade school and high school in Phoenix and

Scottsdale and he and his wife, Marilyn, are now residents of Paradise Valley. He brings to the TGen Foundation his vast career experience in politics and financial investment.

"It is my honor to be selected to be a part of TGen and the phenomenal work this biomedical institute is doing to find better treatments for the most serious diseases affecting humanity," said Mr. Quayle, who also is a former U.S. representative and senator from Indiana, and who today is chairman of Cerberus Global Investments, a private equity company with \$25 billion under management.

TGen Foundation Board Chairman Bennett Dorrance welcomed Mr. Quayle, noting that he is instantly one of the best known among a cadre of top-flight Arizonans who serve on the non-profit panel.

"Today we welcome Vice President Dan Quayle to our TGen family with high expectations and confidence that he will further enhance our philanthropic reach across the nation and help fuel TGen's genomic research of the world's most pressing diseases," Dorrance said. "We welcome his involvement, his extraordinary relationships and his business acumen."

Dr. Jeffrey Trent, TGen President and Research Director, also welcomed Quayle, whose term as Vice President (1989-1993) coincided with Dr. Trent serving as Scientific Director of the National Human Genome Research Institute at the National Institutes of Health (NIH) in Bethesda, Maryland.

"In 1990, the NIH and the Department of Energy joined with international partners in a quest to sequence all 3 billion letters in the human genome. Vice President Quayle is acutely aware of the importance of this public effort, and remains an advocate for genomic research and what it means for our patients," Dr. Trent said.

TGen Foundation President Michael Bassoff said that the addition of Quayle to the TGen Foundation Board of Directors would undoubtedly be of huge importance to the future of the institute.

Mr. Quayle graduated from DePauw University in 1969, and received his law degree from Indiana University in 1974.

He was first elected to the U.S. House of Representatives in 1976 at age 29; to the U.S. Senate in 1980 at age 33; and Vice President of the United States in 1988 at age 41, during which he made official visits to 47 nations and served as chairman of the National Space Council.

Dr. DiStefano selected for NIH grant review panel



In July, the National Institutes of Health (NIH) appointed Dr. Johanna DiStefano, Director of TGen's Diabetes, Cardiovascular & Metabolic Diseases Division, to a four-year term as a member of the Kidney, Nutrition, Obesity and Diabetes Study Section in the NIH's Center for Scientific Review.

In that capacity, Dr. DiStefano helps review grant applications, make recommendations, and helps assure the quality of the NIH peer review process. She was selected based on her competence, judgment, objectivity, scientific achievement, and peer-reviewed publications in scientific journals.

Dr. Von Hoff selected Fellow of AACR Academy



Dr. Daniel D. Von Hoff, TGen Physician-In-Chief, was among the first class selected in March by the American Association for Cancer Research for its newly formed Fellows of the AACR Academy.

AACR created the Academy to recognize and honor distinguished scientists whose major scientific contributions have propelled significant innovation and progress against cancer. AACR selected fellows through a rigorous peer review process that evaluated individuals on the basis of their stellar scientific achievements in cancer research, and only individuals who have made exceptional contributions to cancer and/or cancer-related biomedical science are eligible for election.

Dr. Price appointed to federal advisory panel on food safety



Dr. Lance Price, Director of the Center for Food Microbiology and Environmental Health at TGen's Pathogen Genomics Division, has been appointed to the National Advisory Committee on Microbiological Criteria for Foods [NACMCF].

As a member of the NACMCF, Dr. Price counsels the Secretaries of Agriculture and of Health and Human Services on food-safety issues. Specifically, the 30-member panel assesses the microorganisms that indicate whether foods have been properly processed.

Models, a few drinks and a night out: what guy could ask for more?

Toss in the fact that it's for a good cause, and you have *Guys Night Out*, the latest addition to Saks Fifth Avenue's Key to the Cure fundraising weekend that supports TGen cancer research. The unique event centered on auctioning off designer shirts worn by female models.

If the initial success of attracting more than 100 of Phoenix's leading men is any indication, *Guys Night Out* should be around for years to come.

Not all fun and games, however, the night also featured talks about prostate cancer by TGen President Dr. Jeffrey Trent, Deputy Director Dr. John Carpten, TGen Foundation Board Chairman Bennett Dorrance, and urologist and cancer researcher Dr. Gil Brito.

It was an engaging opportunity for some of Arizona's finest to learn more about TGen and its research from those who are passionate about what they do. Proceeds from the event will support a joint prostate cancer research project between Dr. Carpten and Dr. Brito.

The following day, as part of Saks Fifth Avenue's 15th annual Key To The Cure campaign, they held their signature fashion show, organized around their October 17-20 Friends & Family Shopping Weekend, in which Saks Phoenix donated 2 percent of sales to support breast and ovarian cancer research at TGen.

GUYS NIGHT OUT

Organized by co-chairs Katie Mueller, Jacquie Dorrance, Robyn DeBell and Penny Gunning – along with their dedicated committee – the event celebrated another successful year.

"TGen is very fortunate to have Saks as a partner in supporting TGen's cancer research that benefits our patients, and the leadership and commitment of our outstanding Co-Chairs and team," said Erin Massey, Vice President of Development for Cancer Programs. "Key to the Cure and *Guys Night Out* provide funding that allows TGen scientists the flexibility to pursue new and innovative research into breast, ovarian – and now – prostate cancer."





MindCrowd Superhero

Lynda Carter advocates TGen's Alzheimer's study; urges everyone to take the test

During a visit to TGen, actress-singer Lynda Carter, best known for her iconic role as TV's *Wonder Woman*, announced that she would support TGen's Alzheimer's disease investigations, especially by advocating TGen's MindCrowd study (learn more about MindCrowd on pg. 2).

"My mom died of Alzheimer's disease on February 18, 2013. Will you all take this 10-minute memory test to help us?" she urged her followers in a Sept. 12 tweet from @RealLyndaCarter.

Take the MindCrowd test by visiting mindcrowd.org.

Carter visited TGen in conjunction with her induction, along with TGen President Dr. Jeffrey Trent, as the inaugural members of the Scottsdale Unified School District Foundation's Hall of Excellence. Both are graduates of Arcadia High School, and both were honored Sept. 7 at the SUSDF *Quest for the Best Gala* in Scottsdale.

The Hall of Excellence was created to showcase the academic, athletic, scientific and

artistic achievements of SUSD and its alumni. It honors graduates who have excelled in their respective fields and whose achievements reflect admirably upon the school district.

"We are very pleased to be recognizing Lynda Carter and Dr. Trent," said SUSD Foundation Chair, Price Nosky. "By honoring individuals from different fields, we will accentuate the diverse paths to greatness that can emerge from the educational and extra-curricular activities that make the SUSD a destination school district."



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