

Translational Genomics Research Institute

TGEN TODAY

- 02 **Nathalie Meurice**
research profile
- 04 **Logistics Meets Research:**
The Thurston Project
- 08 **TGen's Bodour Salhia**
visits Egypt as Komen delegate
- 14 **Making Miracles: Troy**
Richards' Quest for a Cure

MINING THE GENOME

**NEXT-GENERATION SEQUENCING
USED TO SPEED RESEARCH PAGE 6**

FALL 2009

 TGEN
A Non-Profit Medical
Research Institute



Supporting TGen

Rimsza leads TGen Foundation “Legacy Society”

Former Phoenix Mayor Skip Rimsza, who helped attract TGen to Arizona, will lead an effort by the TGen Foundation aimed at providing long-term funding for TGen’s research programs.

The TGen Foundation’s Board of Directors named Rimsza the Chairman of the Foundation’s Legacy Society.

In this new role, Rimsza is expected to engage the many individuals whose past support has made TGen a major international biomedical research institute.

Rimsza will develop a broad range of special opportunities and activities for members of the Legacy Society.

Rimsza emphasized that TGen is unique

within the sphere of Valley non-profit organizations.

“TGen is so special because every day they are making scientific advancements and changing the course of healthcare, not only locally, but around the world,” he said.

Rimsza played a leadership role in the 2002 effort that established TGen in Arizona, and led the way in building TGen’s state-of-the-art headquarters at the center of Phoenix’s downtown Biomedical Campus.

For more information about TGen and the Legacy Society, please contact TGen Foundation Associate Vice President Denise A. McClintic, JD, LLM, at 602-343-8611.

Translational Genomics Research Institute

TGEN TODAY

- Page **2** — Fulfilling a Lifelong Dream: *Research Profile*
 Page **4** — Logistics Meets Research: *The Thurston Project*
 Page **6** — Speed and Substance: *Next-Gen Sequencing*
 Page **8** — City of 10,000 Walkers
 Page **14** — Making Miracles: *Troy Richards' Quest for a Cure*



- 10** H1N1 Swine Flu Test **11** TGen ROI Study **12** TGen In-Brief
16 Stepping Up for StepNOOut **17** TGen Foundation News Brief
 Back Cover Seena Magowitz Golf Classic

About TGen

The Translational Genomics Research Institute (TGen) is a non-profit organization dedicated to conducting groundbreaking research with life changing results. Research at TGen is focused on helping patients with diseases such as cancer, neurological disorders and diabetes.

TGen is on the cutting edge of translational research where investigators are able to unravel the genetic components of common and complex diseases. Working with collaborators in the scientific and medical communities, TGen believes it can make a substantial contribution to the efficiency and effectiveness of the translational process. For more information, visit: www.tgen.org



FULFILLING A LIFELONG DREAM

Dr. Nathalie Meurice helps guide TGen-UA Pharmacy
\$7.5 Million Translational Medicinal Chemistry Program



A Collaborative Effort

Dr. Meurice will lead the Southwest Comprehensive Center for Drug Discovery and Development's computational chemistry efforts, while Co-PI's Dr. Christopher Hulme (top left), Associate Professor at the UA College of Pharmacy will lead the center's medicinal chemistry efforts and TGen Sr. Investigator Dr. Spyro Mousseis (bottom left), will lead the high throughput screening efforts. The investigators each have expertise in critical sectors of the drug discovery pipeline, forming a collective team with complementary educational backgrounds and experiences.

TGen Research Profile

More than anything, Nathalie Meurice always wanted to tend to those with medical needs.

And today at TGen, where colleagues know her as Dr. Meurice, she does — though not in the way she once envisioned.

“For a long time, I wanted to be a nurse so I could help patients,” Dr. Meurice said without hesitation when asked what set her along the path of her current career.

Born and raised in Soignies, a small town southwest of Brussels in French-speaking Belgium — near where Napoleon met his Waterloo and the modern-day military headquarters of NATO — Meurice’s foray into science and medicine came courtesy of a backhanded compliment.

As Dr. Meurice recalls, she was devastated when a teacher told her she was too talented to be a nurse and that she needed to set her sights higher. Luckily, a high school teacher helped her fall in love with Chemistry.

“Chemistry is everywhere in our lives,” said Dr. Meurice. “When I found a connection between chemistry and the life sciences it became a theme throughout my education.”

Soon after, the woman who once dreamed of becoming a nurse was well on her way to obtaining her doctorate degree at the University of Namur. A city rooted in the Middle Ages, Namur lies at the confluence of the Meuse and Sambre rivers. It is a place of quiet contemplation, where pedestrians rule the academic city center. There, she spent a decade under the research tutelage of Professor Daniel Vercauteren, who Dr. Meurice credits with significantly contributing to her

development by instilling scientific rigor and high standards.

Dr. Meurice also discovered that, while she loved working in the laboratory with organic chemistry, the chemicals gave her headaches. Fortunately, an explosion of computer speed and memory provided new opportunities in the newly emerging field of computational chemistry and drug discovery.

Like many successful scientists, Dr. Meurice found a mentor — Dr. Gerald Maggiora— whom she would

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ultimately shadow from Belgium to Michigan to Tucson, and eventually, Phoenix and TGen.

The two first met at a three-day college symposium on computer-aided discovery. Maggiora, who at the time directed computational chemistry for U.S. drug-maker Upjohn, invited Meurice to visit Upjohn’s operations in Kalamazoo, Michigan. There, she worked as a visiting student for a semester, learning how the pharmaceutical industry used computational

chemistry in its drug discovery efforts. She also learned valuable lessons in project management.

“From my earliest interactions with Dr. Meurice at Pharmacia and Upjohn, where she was a visiting student, to my continuing collaborations with her today, she has been an inspiration and a joy to work with,” Dr. Maggiora said. “Dr. Meurice is not afraid of new ideas and will charge fearlessly into new fields if that is what’s needed to further her research. Her breadth of knowledge is impressive and includes subjects as diverse as quantum mechanics and biochemistry. This puts her in a good position to drive drug research in today’s highly interdisciplinary environment.”

Like many student-mentor relationships, Meurice’s career followed Maggiora’s, who today is Adjunct Professor of Pharmaceutical Sciences at the University of Arizona’s Department of Pharmacology and Toxicology in the College of Pharmacy and a TGen Adjunct Senior Investigator.

“There is a strong connection there. He’s the link. We always stayed in contact,” said Dr. Meurice, who joined TGen in 2006 as an Adjunct Faculty member, eventually transitioning in 2007 to Associate Investigator.

At TGen, Dr. Meurice’s work focuses on alleviating bottlenecks that exist between the laboratory-based discovery of promising therapeutic targets and the ultimate goal of delivering new, safe and effective drugs to address unmet medical needs of the patient. After nearly 18 months of strategic planning, she recently helped launch the Southwest Comprehensive Center for Drug Discovery and Development (SCD4D), a joint venture announced in October 2008...



“IF TGEN CAN CONTINUE TO REDUCE TIME AND COST, IT WILL GIVE THEM A STRATEGIC ADVANTAGE IN OBTAINING FUNDING, ACQUIRING SAMPLES, AND CONDUCTING CLINICAL TRIALS — ALL OF WHICH WILL MORE QUICKLY PROVIDE HELP FOR PATIENTS.”

Time is money. Money is time. These two common phrases carry considerable consequence for non-profits. Ray Thurston's contributions to TGen provide added value in both contexts.

Thurston, the founder of Sonic Air, is fascinated with quickly getting from one place to another, whether that means people, packages or ideas.

“It became our culture of constant quality improvement,” Thurston said of the Scottsdale-based specialty nationwide air-courier business he ran for nearly two decades.

Sonic Air's success didn't go unnoticed. In 1995, package delivery giant United Parcel Services purchased Sonic Air, and retained Thurston for a time to instill that same operational efficiency as CEO of the UPS Logistics Group.

Today, TGen benefits from Thurston's penchant for operational efficiency.

In 2006, Thurston committed \$3 million over three years to a trio of breast cancer research projects. The results produced \$5 million worth of research and saved time in the process. And with another commitment this year of an additional \$3 million over 3 years, TGen will apply Thurston's techniques to its many bioinformatics and operational functions.

“Our bioinformatics capacity is constantly increasing as the technologies grow more powerful. It's amazing how much information is processed,” said Tess Burleson, TGen's Chief Operating Officer.

Dubbed the “Thurston Project,” this latest endeavor is as much an intellectual as a capital endowment that, long-term, will impact standardized operating procedures by influencing research methodology as well as training and career development.

“At TGen, Ray's name is synonymous with reducing costs while increasing efficiency in all that we do,” Burleson

said. “He has funded a project to help embed that thinking into our culture at TGen, not just for informatics, but operationally. How do we become more operationally efficient, so we can focus most of our dollars on science.”

Thurston’s relationship with TGen began in 2003 after hearing Dr. Jeffrey Trent, TGen’s President and Research Director, speak about the importance of shrinking the amount of time needed to conduct research and drug testing so new therapies could be applied as

a diagnostic tool robust enough to help predict therapeutic response.

Thurston used a Gantt chart to map the process of scientific research and prescribed target times for each, including: collaborating with hospitals, acquiring tissue samples, extracting genetic material, performing tumor-profiling experiments, and exchanging data with bio-statisticians to get biologically relevant results for interpretation and validation. He identified bottlenecks and suggested how to resolve them.

the identification of two molecular signatures consistent with hormone-independent forms of breast cancer. The published results from the studies appeared in *Frontiers in Bioscience* and *Molecular Cancer Research*.

While the third study ran nine months over due to unexpected delays in acquiring samples, it nonetheless remains a promising and ambitious study to prospectively identify a molecular signature that would accurately diagnose every new breast

LOGISTICS MEETS RESEARCH

Thurston Project Influences Operational and Research Methodology

quickly as possible to patients.

Thurston, following a trend in recent years by philanthropists seeking greater influence over the direction their charitable dollars take, offered TGen a sizeable donation if they were willing to listen to his ideas about becoming more efficient. TGen leadership embraced the concept, going so far as to invite Thurston to work with the researchers to establish a series of accelerated deadlines.

Adding Better Processes to inquiries

“I found it extremely rewarding to work with Ray. He didn’t at all dictate my research. He focused on the infrastructure and logistics to make the research go faster – and therefore save significant dollars,” said Dr. Heather Cunliffe, who headed three inter-related breast cancer research projects funded by Thurston’s initial donation.

Two studies – one on hereditary breast cancer and another on hormone receptor-negative breast cancer – focused on deciphering why tumors occur and why they often become aggressive and resistant to treatment. The third study centered on developing

Thurston, a member of the TGen Foundation’s Board of Directors, even donned a lab coat and jumped into the research.

“I wanted to go through every process so I could understand it and make recommendations on anything I saw that would cut down the time,” he said.

After laying out the steps Thurston felt would save time and increase efficiency, he met quarterly with Cunliffe to discuss progress and review deadlines – altering the process as needed. In the end, he showed Cunliffe how the time and money saved in the process could fund additional research.

“Many of these components can be lengthy processes,” Dr. Cunliffe said. “Ray was able to get us to list every single step and challenge us to come up with a faster process.”

How did the studies fare?

The first study, completed in half the time initially projected, successfully identified a molecular signature consistent with hereditary breast cancer. The results may indicate new events that play a role in the initiation of disease, and could play a role in early cancer detection and improved patient management.

The second study shaved one-third off the anticipated time, and resulted in

tumor and predict optimal treatments for each patient; an important goal of personalized medicine. Once the samples were procured the study took less than 12 months to complete.

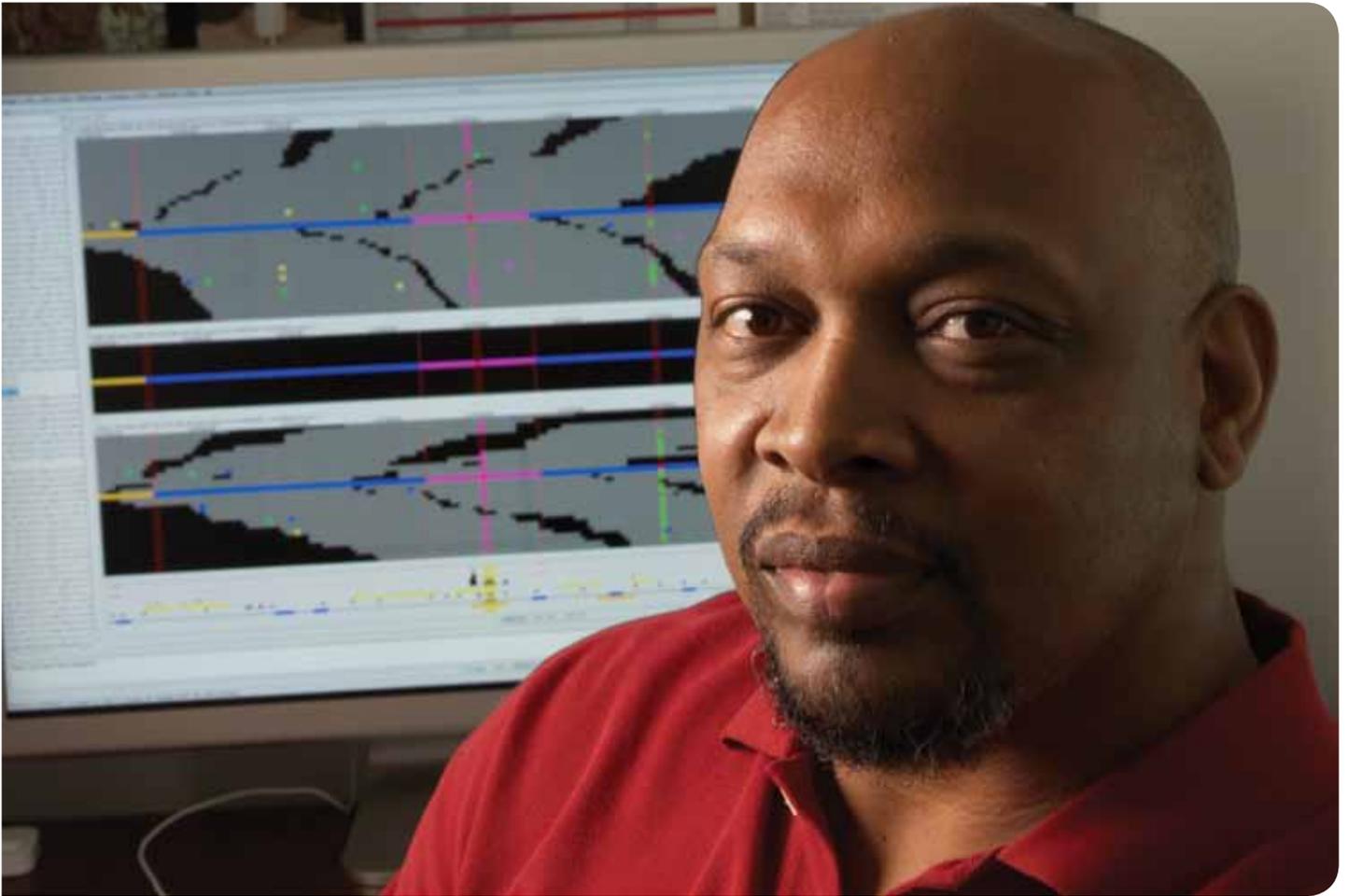
Processes, Milestones Help Drive Success

“We have adopted the process-driven approach, including establishing milestones. It helps to be streamlined and efficient; it keeps us on-target so we don’t get sidetracked on tangential scientific issues,” Dr. Cunliffe said.

Dr. Trent, noting the significant timelines involved in turning a laboratory discovery into something to benefit patients, praised the efficiency efforts. “Ray Thurston has helped us across a spectrum of areas to move with a greater sense of urgency.”

Thurston himself points to what might be the most important gain.

“If TGen can continue to reduce time and cost, it will give them a strategic advantage with everything from obtaining grant funding to acquiring samples to conducting more clinical trials with drug companies — all of which will more quickly provide help for patients.”



Speed and Substance

Next-Generation Sequencing Transforms Today's Biomedical Research

For more than three decades, the “Sanger” method dominated genetic sequencing – the spelling out of the A’s, G’s, C’s and T’s in a molecule of DNA in search of the variations that cause human disease.

Named for Dr. Frederick Sanger, an English biochemist and two-time Nobel laureate in chemistry, the Sanger method provided science in the late 1970s an advanced tool for automating DNA sequencing, eventually leading to the deciphering of whole genes, and in 2003, an entire human genome.

While significantly faster, and with

reduced handling of toxic chemicals and radioisotopes than previous laboratory experiments, Sanger’s method still required hundreds of DNA capillary sequencers and dozens of employees in huge factory-like sequencing centers.

In recent years, a new technology has eclipsed the Sanger system: next-generation or “next-gen” sequencing, systems housed in freezer-sized devices run by a single operator.

“Next-gen sequencing allows us to dig deeper into the genome than ever before by providing more information

and increasing our probability of identifying something significant.” said Dr. John Carpten, Director of TGen’s Integrated Cancer Genomics Division. “The long-term hope is that doctors will leverage this information to inform decisions about patient care.”

The holy grail of sequencing is the ability to spell out the entire 3 billion bases of an individual human genome for \$1,000 or less, allowing more people to be tested for disease causing genetic lesions and matched to better treatments. But it may be a while before people walk around with their

own genome on a memory stick.

Still, next generation sequencing is quicker, costs less, produces more data and holds the promise of advancing biomedical science at a faster rate than ever before. The prospect of a \$1,000 genome would allow researchers to scale up their investigations, providing more data at less cost.

"I think we have a long way to go before realizing the power of these technologies from a consumer-genetics standpoint," said Dr. Carpten, who has worked at the cutting edge of genomic science for more than 20 years. "I believe that one of the most immediate uses of these technologies for clinical practice, from my point of view, lies in the area of genomics-guided therapeutics for cancer."

Sequencing can help researchers find the answers to many pressing questions: Are there mutations associated with the initiation of cancer? Are there mutations associated with drug-resistance in cancer? Are there mutations associated with progression of cancer? According to Dr. Carpten, 15 years ago he could examine at most 5 genes at a time: 5 years ago, maybe 50 genes.

Next-gen Benefits TGen Research

"Now I can look at the entire set (more than 21,000) of annotated genes across the genome in a relatively efficient and cost effective manner. As the technology continues to improve – as throughput and resolution improve – it will allow us to search more panoramically across the genome, rather than having to focus on a specific region, based on *a priori* knowledge of the biological relevance of a given gene. This will allow for more global interrogation the genomic landscape of tumors. To me, nothing could more exciting."

So, can we sequence the full genome of a tumor and identify targets for treatments?

"We are there," said Dr. Carpten.

"We're hoping to perform a demonstration study to fully sequence

the genome (DNA) and transcriptomes (messenger RNA) for a series of patients with late-stage cancer in hopes of informing the best and most appropriate target for treatment for each patient's specific tumor. To perform and complete a study of that type to me would be fulfilling my purpose in life. It would be a dream come true. To be honest, this is the reason I came to TGen."

Although Dr. Carpten is not yet ready to release details, he hopes that the study will start sometime in 2010.

TGen's Team Effort

The increased information generated by next-gen sequencing requires a

team of computational experts to sift through the billions of data points in search of relevance and order. On this front, Dr. Carpten is quick to praise the efforts of TGen colleagues – Dr. David Craig, John Pearson and Dr. Ed Suh – in working towards overcoming these bioinformatic and computational challenges.

And to remain an elite institute, TGen must continue to be associated with the world's best technology, he said. "It is important for TGen, if we are going to remain competitive, to engage with the providers, acquire the equipment and optimize the assays."

TGen's Neurogenomics Division had acquired an Illumina next-gen platform in 2007. After some consideration, Dr. Carpten decided to look into a new platform offered by Applied Biosystems, now a division of Life Technologies Corp. He based the decision on his long-standing relationship with the

company. "Since my post-doc days, Applied Biosystems had always treated me like a partner rather than just another customer," he said.

Dr. Carpten and his lab team of Christiane Robbins and Tracy Moses successfully tested TGen's first Applied Biosystems SOLiD device in 2008. According to Carpten, "you need to have great laboratory staff to bring up these types of technologies and TGen's Research Associates are second to none." Through a partnership with Life Technologies, TGen this year acquired additional SOLiD devices to meet demand, as a growing number of TGen investigators take advantage of the technology. According to

"I BELIEVE THAT ONE OF THE MOST IMMEDIATE USES OF THESE TECHNOLOGIES, FROM MY POINT OF VIEW, LIES IN THE AREA OF GENOMICS-GUIDED THERAPEUTICS FOR CANCER."

Carpten, several TGen investigators are funded to incorporate next-gen sequencing technologies in their research, including Drs. Jeffrey Trent, Paul Keim, David Duggan, Matthew Huentelman and Kevin Brown. Others are quickly following suit.

"Our scientific vision, clinical motivation, strong informatics and computational infrastructure, puts us in a fairly elite category as an institute, and it shouldn't be taken for granted," said Dr. Carpten, who ticks off Boston's Broad Institute, Seattle's Fred Hutchinson Cancer Research Institute, and Washington University in St. Louis as a few examples.

"I just don't know if the general public realizes how incredible this place really is," Dr. Carpten said. "We're playing in Yankee Stadium. This is Major League. Now its time to step up to the plate and try to knock a few of these diseases out of the park!"

Dr. Bodour Salhia (inset), a TGen cancer researcher, traveled to Egypt in October as a U.S. delegate with the Susan G. Komen for the Cure organization in a highly successful effort to raise awareness about breast cancer.

On Oct. 23, the eve of Cairo's first Komen race, pink spotlights bathed The Great Pyramid of Giza.

The next day, Dr. Salhia joined nearly 10,000 people, most in pink attire, running among the pyramids in the first Komen event in the Land of the Nile; a monumentally historic experience, which she said deeply impacted participants and could eventually benefit cancer patients worldwide.

The U.S. delegation consisted of 42 individuals from across America – all with different stories, but with the common goal of a world without breast cancer. Among the Komen attendees were: Nancy G. Brinker, Founding Chair of Susan G. Komen for the Cure; Hala Moddelmog, former President and CEO of Komen; and Annetta Hewko, Vice President of Komen's Global Strategies and Programs.

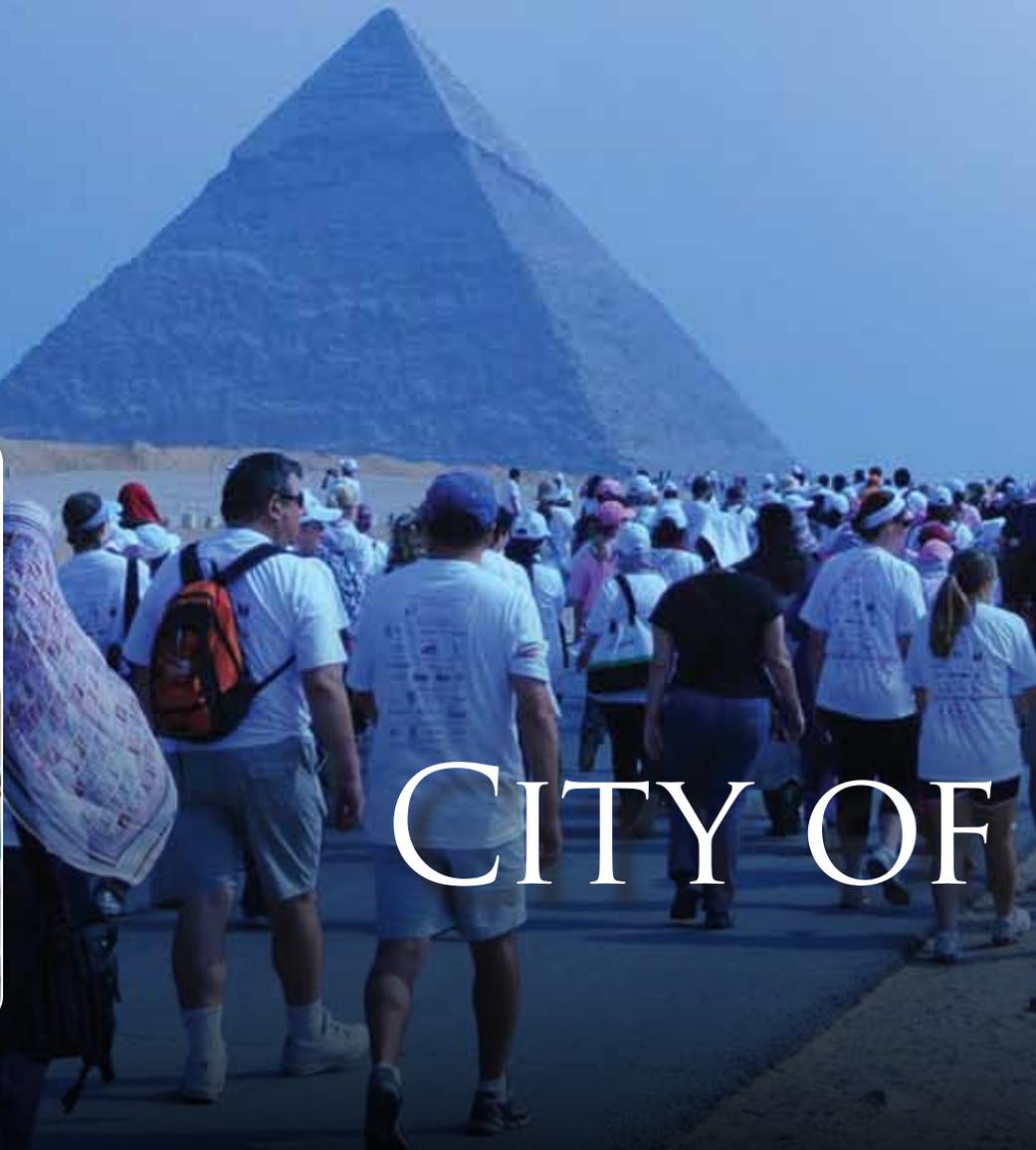
Dr. Salhia met with more than 20 cancer research advocates from 10 Mid East countries, listening to dignitaries and learning about the efforts of the Breast Cancer Foundation of Egypt and the Suzanne Mubarak Regional

Center for Women's Health and Development.

"In a country and region where breast cancer efforts continue to be riddled by a lack of awareness, misguided stigma and a shortage of medical resources," Dr. Salhia said, "I was amazed and encouraged to see the powerful emergence of hope and change, as well as the growing number of international partnerships needed for progress."

As a breast cancer researcher at TGen, Dr. Salhia said the trip perfectly aligned with her long-held vision and passion, as well as her Egyptian heritage.

As part of her post-doctoral fellowship in the lab of Dr. John



CITY OF

Carpten, Director of TGen's Integrated Cancer Genomics Division, part of Dr. Salhia's research includes a study of breast cancer in Egypt.

The study involves acquiring more than 300 breast cancer specimens from Egyptian pathologists Drs. Elia Ishak and Salwa Gaber; a collaboration with Dr. James Resau, Deputy Director for Special Programs at the Van Andel Research Institute, who helped construct a tissue microarray of samples and assisted in a molecular phenotypic analysis; and insights about breast cancer and molecular pathology by Dr. Coya Tapia of the Institute for Pathology at the University of Basel, Switzerland, and by Dr. Galen Hostetter, an

Associate Investigator in TGen's Integrated Cancer Genomics Division.

"I believe that this type of international scientific team is critical in making progress against health disparities among underserved populations," said Dr. Salhia, whose visit to Egypt was funded in part by a \$15,000 grant from cancer research advocate Sylvia Chase. Other breast cancer research by Dr. Salhia has been funded through a \$180,000, three-year grant from the Komen foundation.

The World Health Organization ranks breast cancer as the most common cancer type worldwide among women, having affected

an estimated 25 million people. It represents 35 percent of cancer cases in Egypt.

"Our primary goal for this study is to determine the prevalence of intrinsic breast cancer subtype as a preliminary measure of the molecular uniqueness of breast cancer in Egypt. For example, we know that the prevalence of the basal subtype, which is associated with poor prognosis, is higher in African American women," Dr. Salhia said. "This study is intended to aid clinicians in making better treatment and prognostic decisions, based on the molecular characteristics of breast cancer in Egypt."

10,000 WALKERS

TGen researcher is U.S. delegate at first Komen event in Egypt

TGEN SEEKS EMERGENCY FDA APPROVAL OF NEW SWINE FLU TEST

H1N1



TGen and a business collaborator have submitted a request to the U.S. Food and Drug Administration for emergency use of a new test to diagnose the 2009 H1N1 swine flu virus.

TGen's David Engelthaler presented test details November 1 at the 47th annual meeting of the Infectious Diseases Society of America (IDSA) in Philadelphia.

The test, developed within TGen North's (Flagstaff) Pathogen Genomics Division, can not only detect influenza — as some tests do now — but also can quickly determine strain type and whether it is resistant to Tamiflu®, the primary H1N1 anti-viral drug on the market today.

As with other influenza strains, H1N1 can be expected to develop resistance to current medications, and new treatments will be needed to respond to this and future pandemics.

"The problem with influenza is that it is becoming resistant to the antiviral drugs available," said Dr. Paul Keim, a Professor of Biology at Northern Arizona University and Director of TGen North.

Engelthaler, Director of Programs and Operations for TGen North, said this would be the only resistance test available that uses a standard molecular technique that rapidly makes exact copies of specific components of H1N1's genetic material.

"So far, it looks like this assay is very effective with strains in the U.S., and we expect it to have the same accuracy with strains around the world," said Engelthaler, a former State Epidemiologist for Arizona and former State of Arizona Biodefense Coordinator.

TGen and PathoGene LLC, a partnership that includes a group of Flagstaff business people as well as Engelthaler

and Keim, developed the assay, or test, for H1N1 flu.

PathoGene and TGen officials hope to secure emergency FDA approval for the test as soon as possible.

Currently, only the U.S. Centers for Disease Control and Prevention and a few select labs can test for resistance, using cumbersome and time intensive technology, Engelthaler said.

A readily available test for H1N1 does not exist at most doctors' offices. Currently, a state or federal health agency conducts testing, and most often only for those patients with a chronic disease or who require hospitalization and appear at high risk due to a suppressed immune system.

"Our test gives control to the clinician, who then determines if current therapies will work or not, and this is important moving forward. When the H1N1 outbreak first

started (in April), everything was 100 percent sensitive to Tamiflu. But now, we're starting to see isolated cases of resistance pop up," Engelthaler said.

The World Health Organization has, to date, identified 75 instances of resistance to Tamiflu in the H1N1 swine flu virus.

"The novelty in our study is the use of increasingly common laboratory tools to rapidly and accurately detect resistance to anti-influenza drugs," Engelthaler said.

In addition to Keim and Engelthaler, TGen's Flu Team includes Research Coordinator Elizabeth Driebe and Research Associates Erin Kelley, Sarah Mancini, and recently Kelly Sheff. The Flu Team, under Driebe's coordination, has been assisting with new drug development and disease surveillance in Arizona for nearly three years.

FULFILLING A LIFELONG DREAM ...continued from page 3

...between TGen and the UA College of Pharmacy, funded by a \$7.5 million federal economic recovery grant.

Drs. Meurice, UA's Chris Hulme and TGen's Spryo Mousses and colleagues at the SCCDDD plan to assemble a translational medicinal chemistry team capable of designing and selecting likely drug candidates for rapid response to a host of diseases, including neoplastic, metabolic, cardiovascular, immunological and neurological disorders.

"We will evaluate drug-like compounds for particular targets and

determine which compounds have the desired activity," Dr. Meurice said. "What is really unique is that we are taking an industrialized approach to medicinal chemistry that is more likely to have a significant impact on healthcare, and implementing it in academia."

Advanced computer analysis synergizing with medicinal chemistry, and validation through laboratory experiments, will facilitate and guide much of the work along the drug discovery value chain.

The SCCDDD will get up and

running over the next two years during a build phase, while researchers develop a "portfolio of targets" and produce more than 20,000 potentially beneficial drug-like compounds. The five-year goal is to assemble an Arizona compound collection of about 100,000 small molecules that have promising biological properties.

"The biologists and chemists will work toward a common goal of making a difference for the patients," she said.

For Dr. Meurice, that fulfills the same goal as her childhood dream of becoming a nurse.

TGEN'S ECONOMIC ENGINE

New Study Shows TGen provides Arizona with \$77 million in annual economic impact; \$321 million predicted by 2025

TGen is playing a major role in helping Arizona develop a knowledge-based economy, and just seven years after TGen's formation, its economic impact is substantial.

According to an independent analysis, TGen's total annual economic impact is \$77.4 million, and that impact is predicted to grow to more than \$321 annually by 2025.

"As we make important and significant contributions to the local economy, TGen is helping place Arizona on the world biosciences map through our cutting-edge discoveries in cancer, neurological, cardiovascular and infectious-disease research," said Dr. Jeffrey Trent, TGen's President and Research Director.

TGen has outpaced all previous performance marks and projections, according to an economic impact report by the economic research team of Tripp Umbach.

The report shows that TGen in 2008

more than doubled the results recorded just two years ago in its return on investment, jobs, taxes paid and total economic impact, which included spin-off businesses and commercialization of TGen-led research.

When the impact of TGen-generated business spin-offs and commercialization are included, the study shows, TGen in 2008 produced \$14.07 for every \$1 invested by the state, \$5.7 million in taxes and \$77.4 million in total annual economic impact.

"TGen has certainly kept its promise to the State of Arizona to be a strong economic engine," said Paul Umbach, the President of Pittsburgh-based Tripp Umbach. "Our updated analysis shows dramatic increases in economic, employment, and government revenue impacts on Arizona's economy."

Including projected business spin-offs and commercialization, the report said, TGen in 2025 would return \$58.42 for every \$1 invested by the state, create

4,116 jobs, generate \$27.4 million in taxes, and produce a total annual economic impact of \$321.3 million.

"The analysis clearly illustrates that commercial spin-off activities from TGen are rapidly having a positive economic impact on the Arizona economy at a time when adding jobs is important," said Jim Harris, Vice President of TGen Business Development.

Tripp Umbach, a national leader in economic forecasting, also concludes in its 2009 report that — to continue TGen's progress and accelerate commercial development — state support for TGen can create even greater economic impact in future years.

"In order to continue to accelerate TGen's growth and the growth of Arizona's bioscience/biomedical sector, TGen would benefit from continued support from the State of Arizona," the report said.



TGen ROI by the Numbers

In 2008, **there was a stronger return** on the State's \$5.5 million non-general fund investment than in 2006. Return on investment of TGen's operations increased from \$3.95 for every \$1.00 invested to \$8.09 for every \$1.00 invested in 2008.

TGen's economic impact on the State of Arizona has more than doubled from \$21.7 million in 2006 to \$44.5 million in 2008 and is projected to **generate substantial future growth** both operationally and commercially.

Combining both operational and commercial activities in 2008, TGen generated more than \$77.4 million in the state's economy. This represents **an increase of 357 percent** in total economic impact since 2006.

TGen's presence in Arizona generates a significant opportunity for nationally competitive, knowledge-based employment. In 2008 TGen generated full-time employment (directly and indirectly) for 461 residents of the State of Arizona. TGen has **doubled its employment impact** in only two years from 220 total full-time jobs in 2006.

TGen's operations and commercial activities in Arizona **generate significant state tax revenue**. In 2008 TGen generated \$5.7 million in state taxes (directly and indirectly). TGen has more than doubled its generation of state taxes in only two years from \$1.9 million in 2006.



Jennifer Griego

Award Targets Brain Tumor Research

SAIC-Frederick Inc., under its prime contract with the National Cancer Institute, has named TGen as one of five national centers selected to conduct cancer

comprehensive genomic data involving 40 brain tumor models and 20 proven types of targeted therapies to create treatment programs for brain-tumor patients.

TGen President receives Breath of Life Award

On October 25, the Arizona Chapter of the Cystic Fibrosis Foundation recognized Dr. Jeffrey Trent, TGen President and Research Director, as the 2009 Distinguished Honoree at their 2nd annual Breath of Life Gala. The Gala honors those in the local community who have

antibiotic resistance at their earliest time-points.

CF is an inherited disease that affects the lungs and digestive system. Symptoms include frequent lung infections, chronic coughing, poor growth and shortness of breath. 1,000 new cases of CF occur annually, with more than 70 percent of patients diagnosed by age 2. In the 1950s, few children with cystic fibrosis lived to attend elementary school. Today, advances in research and medical treatments have enhanced and extended life. Children and adults with CF can now expect to live into their 40s and beyond, according to the foundation.

with advanced skin cancer," said lead investigator Daniel D. Von Hoff, MD, TGen's Physician-in-Chief. "By strategically initiating what we call "precision oncology", or using the right drug for each cancer, this study offers great potential against basal cell carcinoma and other cancers."

The trial results demonstrated that GDC-0449, a Hedgehog Pathway Inhibitor, appears to shrink tumors in locally advanced and metastatic BCC. Known as the "Hedgehog" trial, the clinicians observed a durable clinical benefit — defined as tumor shrinkage visible on X-ray or other physical exam or improvement in symptoms without tumor growth — in 1

TGEN IN BRIEF

experiments using advanced computer simulations.

The \$691,930 award establishes the "In Silico Research Centers of Excellence" and includes two 12-month option periods that if executed amount to an additional \$1,373,582 for a total of \$2,065,512 over three years. The Center of Excellence will use part of the NCI Cancer Biomedical Informatics Grid (caBIG®), which is a data-sharing network for researchers, physicians and patients. The caBIG® program is designed to accelerate methods for detecting, diagnosing, treating and preventing cancer.

"We will use this unique opportunity to focus with our collaborators on new ways to quickly and more effectively treat patients with brain cancer," said John Pearson, the project's Principal Investigator and Head of TGen's Bioinformatics Research Lab.

TGen researchers will use *in silico* research in a program called "Test to Best", that uses

made outstanding contributions to fighting and finding a cure for cystic fibrosis (CF).

TGen North researchers in Flagstaff are hard at work applying their cutting edge molecular tools to analyzing respiratory samples from CF patients in hopes of helping individuals like 8-year-old Jennifer Griego (pictured left) and others with CF. They are capitalizing on previous research knowledge to dive deeper into understanding the microbial dynamics in these samples to a greater extent than ever before. With today's powerful genomic tools, the TGen North researchers are able to look at the highly complex communities of bacteria and fungi in the respiratory tract of CF patients and provide a greater understanding of changes in these communities, especially in response to different therapies.

Other areas of interest include developing tools to not only quickly identify all respiratory microbes but to detect antibiotic resistance and potential for

Clinical trial signals advances in skin cancer

Analyses of clinical trial results published September 11 in the *New England Journal of Medicine* (NEJM) shows a potential new investigational therapy for advanced and metastatic basal cell skin cancer.

The study, conducted at TGen Clinical Research Service (TCRS) at Scottsdale Healthcare and two other sites appears to demonstrate tumor shrinkage and limited side effects. TCRS is a strategic alliance between TGen and Scottsdale Healthcare.

These findings are significant because no proven therapy exists for advanced basal cell carcinoma (BCC). BCC is the most common cancer in the United States with about one million new cases diagnosed each year. Arizona has one of the highest incidences of skin cancer in the world.

"Until now, no treatment existed that effectively slowed tumor growth in those patients



Dr. Daniel Von Hoff

of 33 patients evaluated. Others had stable disease for prolonged periods of time. Only 4 patients had progression of disease.

Patients seeking additional information about clinical trials may contact patient care coordinator Joyce Ingold, RN, at 480-323-1339, toll free at 1-877-273-3713 or at jingold@shc.org.

TGen and Biodesign Institute win innovation award

Arizona Governor Jan Brewer presented a top award for economic development August 28 to TGen and the Biodesign Institute at Arizona State University,

TGen and ASU's Partnership for Personalized Medicine won the 2009 Excellence in Economic Development award in the category of Innovative Economic Development. Governor Brewer presented the award at the 2009 Governor's Regional and Rural Development Conference.

The award recognizes partnerships, organizations, associations, service clubs, and companies, which have successfully created and implemented community and economic development strategies in the past year.

The Partnership for Personalized Medicine is a venture by TGen, ASU's Biodesign Institute and Seattle's Fred Hutchinson Cancer Research Center in partnership with the Government of Luxembourg to speed new personalized healthcare treatments to patients, reduce costs, create a European clinical research center, and bring national and international investment to Arizona.



Dr. Ramesh Ramanathan

New drug aims to 'seek and destroy' many types of cancer

In October, TGen Clinical Research Services (TCRS) at Scottsdale Healthcare began testing a drug designed to "seek and destroy" common cancers such as breast, prostate, endometrial, pancreatic, ovarian,

skin and testicular cancers. The Phase 1 clinical trial will help determine if EP-100 is safe and effective for use among patients with solid cancer tumors, with fewer side effects than chemotherapy or radiation treatment.

Dr. Ramesh K. Ramanathan, M.D., principal investigator for the trial in Scottsdale, said the drug is a membrane-disrupting peptide (tMDP) designed to "seek and destroy" cancer cells by targeting those with excessive luteinizing hormone releasing hormone (LHRH) receptors.

Excessive LHRH receptors are found in a wide range of cancers, including breast, prostate, endometrial, pancreatic, ovarian, skin and testicular cancers.

The study is designed to evaluate the safety of EP100 and will enroll as many as 36 adult patients with solid tumors whose tumor biopsies indicate that they have excessive LHRH receptors.

TD2 establishes European footprint for cancer research

TGen Drug Development (TD2) and the Institut Paoli-Calmettes (IPC) have forged a strategic alliance focused on cancer.

The partnership between TD2, a subsidiary of TGen, and Marseille, France-based IPC's comprehensive cancer center enables both non-profit institutes to speed research discoveries to patients with cancer, by expanding their clinical research network to evaluate new therapies in the U.S. and Europe in an effort to more quickly introduce new drugs into clinical trials.

TD2 and IPC will focus their efforts on discovering molecular alterations within cancers and finding biomarkers that will help

identify new therapeutic targets for developing therapeutic treatments for individual patients. IPC and TD2 will collaborate on a number of primary tumor and metastasis in selected cancers, as well as initiate an exchange program for medical oncologists between the two institutions.

"Aligning with IPC represents a significant opportunity for TD2 and TGen to further expand our research affiliations into Europe," said Dr. Daniel Von Hoff, TGen's Physician-In-Chief.

Professor Patrice Viens, a medical oncologist and General Director of IPC, said the alliance with TD2 will enable IPC to bridge new international relationships: "This alliance with TD2 translates to our continuing efforts to expand our collaborations in basic research and medical activities beyond Europe."

IPC is one of the largest university-affiliated comprehensive cancer centers in France, involved in the management of nearly 6,000 new cases of cancer each year. IPC established a Biological Resource Center (BRC) in oncology that has 70,000 tumor and biological fluid samples, mostly of breast, pancreatic and blood cancers. IPC had more than 600 patients in clinical trials during 2008.

TGen DNA discovery will be used to solve crimes

High-tech forensics firm, Casework Genetics, is applying new technology developed by TGen and University of California, Los Angeles, to help enable law enforcement labs to solve crimes.

Casework Genetics licensed the TGen-UCLA technology and



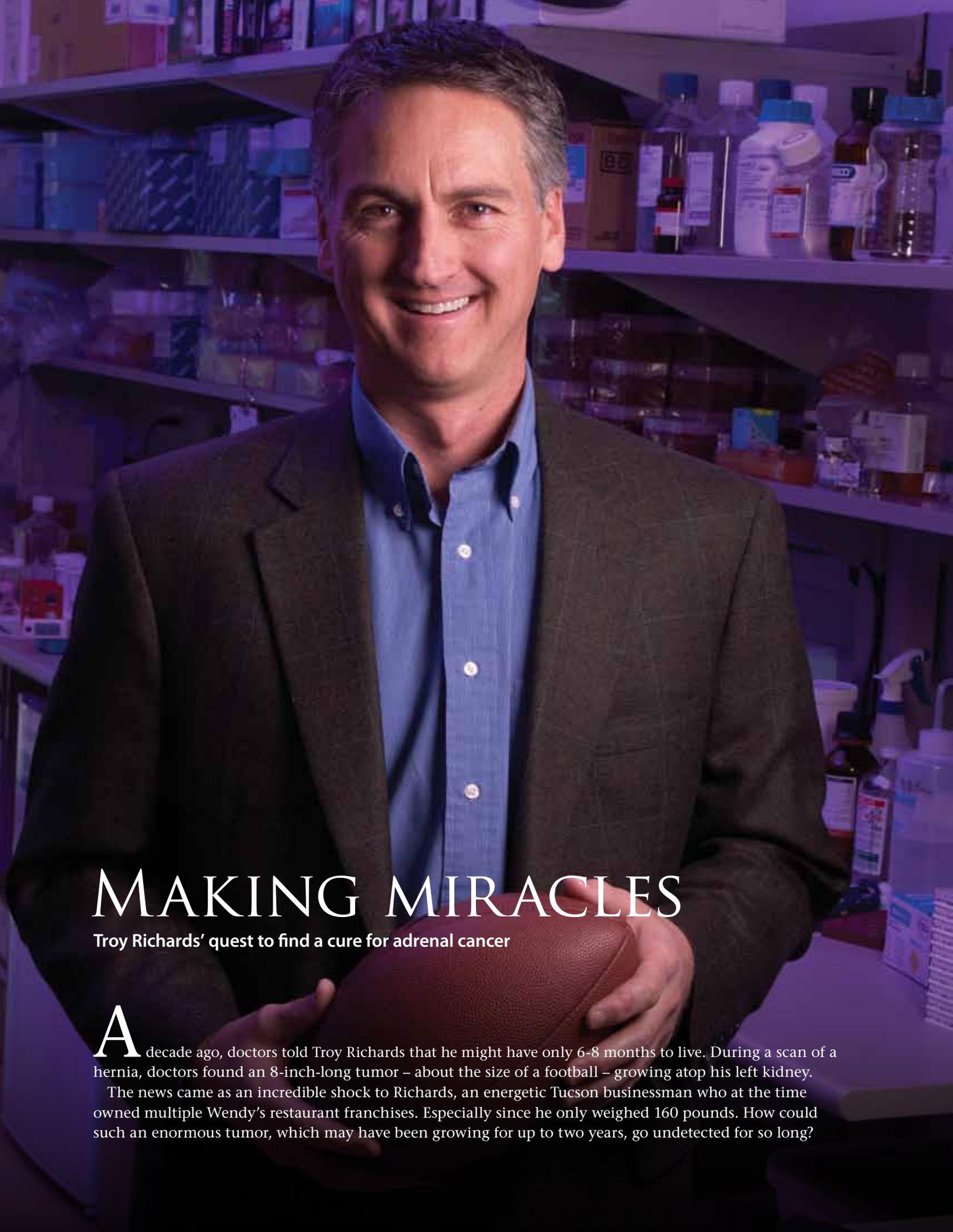
Dr. David Craig

paired it with other patents it developed allowing the Virginia-based firm to identify the DNA of individuals in complex mixtures, with an unprecedented degree of detail, even when mixed with the DNA of as many as 100 other persons.

There are nearly 20 million arrests in the U.S. annually, and police now require DNA evidence in the overwhelming majority of cases, which places increased demands on local, state and federal law enforcement labs. Casework Genetics offers a viable solution that enables police agencies to solve many more crimes.

Dr. David Craig, a co-discoverer of the technology and Associate Director of TGen's Neurogenomics Division, said Casework Genetics has the ability to significantly impact the field of forensic identification. Working with collaborators at UCLA, Craig first published the genomic techniques employed by Casework Genetics in a scientific paper published last year in PLOs Genetics.

Casework Genetics is the first of several companies assisted by the Phoenix-based Catapult Bio, a non-profit organization established this year to accelerate new scientific ideas, transforming them into commercial products and viable business ventures.

A man with short, graying hair, wearing a blue button-down shirt and a dark suit jacket, is smiling warmly at the camera. He is holding a brown leather football with both hands in front of his chest. The background is a laboratory or pharmacy setting with shelves filled with various bottles, containers, and boxes. The lighting is soft and focused on the man.

MAKING MIRACLES

Troy Richards' quest to find a cure for adrenal cancer

A decade ago, doctors told Troy Richards that he might have only 6-8 months to live. During a scan of a hernia, doctors found an 8-inch-long tumor – about the size of a football – growing atop his left kidney.

The news came as an incredible shock to Richards, an energetic Tucson businessman who at the time owned multiple Wendy's restaurant franchises. Especially since he only weighed 160 pounds. How could such an enormous tumor, which may have been growing for up to two years, go undetected for so long?

TGen Foundation News

Such is the nature of adrenocortical carcinoma (ACC), a rare cancer of the adrenal glands that usually displays no symptoms or pain, and simply displaces organs as it grows inside the body cavity, often going undetected until its late stages.

ACC occurs in as few as 1-in-1.7 million Americans annually. The disease develops in the adrenal cortex, the outside layer of the adrenal gland. There are two adrenal glands, one above each kidney in the back of the upper abdomen. The adrenal glands are part of the endocrine system, which produces hormones that regulate bodily functions.

Surgeons removed Richards' tumor, along with one of his kidneys. But four and one half years later, the cancer returned, this time as a spot on his left lung. Doctors monitored that tumor for a while, and when they saw it growing, surgeons also removed that tumor, and part of his lung, too.

"Multiple diagnoses and multiple surgeries persuaded me to start looking into research," said Richards, whose Tucson oncologist, Dr. Richard Rosenburg, contacted a colleague at the Arizona Cancer Center, Dr. Daniel Von Hoff, TGen's Physician-In-Chief.

A few days later, Richards received a call from Dr. Von Hoff, and they talked for 90 minutes about setting up an ACC research program at TGen. Two weeks later, in May 2005, Richards arrived at TGen for a meeting with Von Hoff and Dr. Michael Demeure, a surgeon who had published a scientific paper about ACC. That day, Richards and Drs. Von Hoff and Demeure began putting together a plan for what would become TGen's ACC Research Program.

During the planning process, Richards developed a tumor in his liver. Surgeons removed the tumor and part of his liver. But this time the tumor underwent genomic profiling, which revealed a genetic marker that his physicians believed showed Richards' ACC could be treated with Velcade, a drug usually used to treat multiple myeloma.

"This is where the power of profiling and teamwork comes in," said Richards, who received the targeted chemotherapy for four months. And except for a spot of cancer on his right lung, removed in May 2008, Richards remains cancer free, and he attributes his remarkable health to the scientific research at TGen.

"It was not looking real good. I can only say there is a good chance that molecular profiling saved my life. You could say I am living proof that it works," said Richards.

Soon after, Richards developed a website adrenalcancersupport.org and co-founded what is now the largest ACC support group on the Web. He often receives

calls from patients throughout the world, whom he encourages to participate in clinical trials.

Today, Richards, now an active member of the TGen Foundation Board, brims with hope and enthusiasm about what is happening through TGen's ACC program under the clinical leadership of Drs. Von Hoff and Demure and Dr. Kimberly Bussey, a TGen Associate Investigator and lead scientist for TGen's ACC Research Program.

The ACC program conducts research and clinical studies courtesy of Richards and others through Richards' Advancing Treatments for Adrenocortical Carcinoma (ATAC) Fund.

In early October, their efforts culminated in a clinical trial at TGen Clinical Research Services at Scottsdale Healthcare (TCRS), which focuses on patients with inoperable tumors who have relapsed or failed to respond to conventional therapies. OSI-906 is the first ACC drug to reach Phase 3 trial, and could potentially become the first drug in nearly half a century approved by the FDA to treat ACC. TCRS was the first of 41 clinical trial sites planned worldwide.

"Troy brings a sense of urgency and a connection to the ACC patient community that made this trial possible. This is a huge accomplishment for the ACC Research Program at TGen and a great testament to what patient-advocated research can accomplish in a short period of time," said Dr. Bussey.

Meanwhile, Dr. Bussey remains active with a pilot project focused on a gene called SIRT-1, which is under expressed in ACC. Bussey and her colleagues are looking into ways to make SIRT-1 more active and, combined with other compounds, find a more effective and less toxic way to address ACC.

Plans are also underway to sequence the full genome of 12 cancerous and 12 benign ACC tumors – essentially spelling out their DNA codes. This should provide researchers with information about mutations and otherwise act as a springboard for additional research and therapeutic development. Richards said this program will produce a wealth of new data that should draw young researchers around the world into this field of study.

Though ACC is rare, discoveries into its causes may apply to other types of cancer, too, said Richards, who is constantly amazed at the innovative research and powerful technology employed by TGen.

"If there is a cure for cancer, I have no doubt a number of the answers will come from the efforts of TGen scientists and clinicians," Richards said. "And while we want a cure, right now, more than anything, we want to be able to provide treatments that are much better than what is out there now. I think that's the first step."

Stepping up for StepNOut

Record participation helps raise more than \$137,000 for pancreatic cancer research



The TGen Foundation's 4TH annual StepNOut for Pancreatic Cancer was especially memorable this year for two families.

For the Cadwell family, the run, walk and dash on Nov. 1 at Tempe's Kiwanis Community Park was a time to remember JoAnn and Frank Cadwell, a couple who both passed away from pancreatic cancer within weeks of each other in 2008.

Their daughter, Stephanie, and son, Ron, established a memorial for their parents through the TGen Foundation. In addition, they brought more than 100 employees of the family's CWIE Holding Company to participate in the walk. The Cadwell Memorial was a presenting sponsor of the event, along with the Arizona Diamondbacks.

"Because pancreatic cancer is the worst of all cancers and affects so many people, it's important for us to help raise awareness," said Stephanie Cadwell. "My brother, Ron, and I both hope that in the near future, researchers will develop an early detection test or better still, find a cure. That's our hope."

The business family from the law firm of Lewis and Roca remembered their colleague, Rick Halloran, at this year's walk. Rick, who worked 18 years at the law firm, passed away in October of pancreatic cancer. Lewis and Roca brought more than 125 participants as part of "Team Rick" to StepNOut.

"When Rick died, so many of us felt helpless. We were unable

to do anything to move forward except grieve privately," said Randy Papetti, one of Rick's partners at Lewis and Roca. "The walk — and all it involved — gave us a small but meaningful opportunity to collectively do something to help fight the disease and to begin to move past the tragedy together. We are very grateful for that opportunity."

Mark Curtis, co-anchor for KPNX-TV's 12 News, once again served as the honorary chair and master of ceremonies. Curtis lost his mother, Judy Stein, to pancreatic cancer in 2008.

This year's event drew more than 900 participants and raised more than \$137,000 — a 64 percent increase over the \$88,000 raised at last year's event. StepNOut helps fund TGen's pancreatic cancer research, headed by world-renowned expert Dr. Daniel Von Hoff, TGen's Physician-in-Chief and Director of TGen's Clinical Translational Research Division.

Rosanna Robinson Norman, who lost her husband, Michael, to pancreatic cancer, chaired this year's StepNOut event for walk organizers, the TGen Foundation's National Pancreatic Cancer Committee.

The National Cancer Institute estimates that in 2009 pancreatic cancer will take the lives of more than 35,000 of the 42,000 Americans annually diagnosed with this devastating disease. More than 75 percent of patients succumb to pancreatic cancer within the first year of diagnosis.



Celebrity chef Eddie Matney shares a light moment with Trina Ypsilanti and Al Gula. The event raised \$30,000 in support of TGen breast cancer research.

GULA'S GALA!

The inaugural Marilyn B. Gula Mountains of Hope Foundation Sight, Sound & Taste for a Cure, held Oct. 23 at the LMC Home Entertainment Ltd. showroom in Scottsdale, raised \$30,000 for TGen's advanced breast cancer research.

Allen J. Gula Jr's wife Marilyn lost her battle with breast cancer in 2006, organized the unique event in conjunction with Breast Cancer Awareness month.



Garagiola and Dr. Heather Cunliffe

More than 200 guests mingled through home theater and media rooms while dining on culinary delights prepared by Eddie Matney, celebrated Valley chef and owner of Eddie's House restaurant in Scottsdale.

Special guests included legendary baseball player and announcer Joe Garagiola who graciously posed for pictures and signed baseballs and copies of his book Just Play Ball, with all proceeds donated to the TGen Foundation.

Golf tournaments raise funds, awareness

The 10th annual Bernice E. Holland Golf Tournament, held June 7-8 at the Country Club of Colorado in Colorado Springs, attracted 120 golfers and resulted in \$85,000 for TGen's colon cancer research from the Bernice E. Holland Foundation.

The foundation, established in 1999 by Rick Holland in memory of his mother, Bernice, is committed to raising funds for research and colon cancer awareness.

To date, he has raised nearly \$500,000 in support of TGen research.

The 3rd annual Terri Link Memorial Fund Golf Tournament, held Oct. 17 at the Georgia Club in Statham, Georgia, raised \$26,540 for TGen's adrenocortical cancer (ACC) research program.

Drew Link, whose wife Terri passed away from ACC in 2006, organized the event which attracted 29 sponsors and 82 golfers despite cold and rainy conditions.

mark your calendars Upcoming Foundation Events



Alana's Champs 5K
Benefits brain cancer research
December 13
Kiwanis Community Park
Tempe, Arizona

Tea for TEAL
Benefits ovarian cancer research
February 2, 2010
Sheraton Phoenix
Downtown Hotel
Phoenix, Arizona

**Students Supporting
Brain Tumor
Research Walk-a-thon**
Benefits brain cancer research
February 27, 2010
Arizona State University
Tempe, Arizona



unTEAL a Cure
Benefits ovarian cancer research
March 7, 2010
Kiwanis Community Park
Tempe, Arizona

Stride for Life Arizona
Benefits lung cancer research
April 11, 2010
Tempe Arts Park
Tempe, Arizona

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

Seena Magowitz Celebrity Golf Classic raises money for pancreatic cancer research

Jai Pausch (pictured below at microphone), who lost her husband Dr. Randy Pausch in 2008 to pancreatic cancer, is the honorary chair of the 7th Annual Seena Magowitz Celebrity Golf Classic.

Randy was the Carnegie Mellon University computer science professor

who became famous for *The Last Lecture*, a speech that has been turned into a book and film about the importance of achieving childhood dreams.

Jai Pausch will join Roger Magowitz, who co-founded the event along with his friend Ray Bojanowski, in honor of Roger's mother, Seena, who passed away from pancreatic cancer.

This star-studded event at the Westin Kierland Resort & Spa has raised \$1.3 million since its debut in 2003, and organizers hope to generate \$500,000 this year. The golf event competition, with 216 golfers, is sold out.

An awards luncheon on December 5 will include a presentation by Dr. Daniel Von Hoff, TGen's Physician-In-Chief and a world-renowned authority on pancreatic cancer. Dr. Von Hoff will discuss the progress being made to improve the quality of life for patients suffering from pancreatic cancer.

Pancreatic cancer, the nation's fourth leading cause of cancer death, is the most lethal type of cancer, with a five-year mortality rate of 95 percent. Less than 2 percent of the National Cancer Institute's federal

research funding is dedicated to pancreatic cancer research.

To help raise funds, this year's event includes some big prizes:

— A 2010 Volkswagen Golf, valued at \$17,000, donated by Jason Kuhn of Kuhn Volkswagen, will be among the items auctioned Dec. 5.

— A 1.01-carat princess cut diamond appraised at \$5,500, donated by Roger and Jeanne Magowitz of Mattress Discounters. The diamond will be in one of 100 glasses of champagne that will be sold for \$100 per glass during the December 4 casino night party.

"These prizes and special events offer unique ways for the home furnishings industry to support the fight against pancreatic cancer," said Roger Magowitz.

Sponsors of the event include: Tempur-Pedic, Protect-A-Bed, Symbol, Sealy and International Bedding and Mattress Firm.

Events for non-golfers include a private tour of Frank Lloyd Wright's Taliesin West complex, and a behind-the-scenes tour of the Arizona Diamondbacks operation at Chase Field.

The event also helps fund the El Segundo, Calif.-based Pancreatic Cancer Action Network.

For more information: Please visit www.helptgen.org and click on the events calendar, or contact Erin Massey at 602-343-8470.

