PETER MICHAEL FOUNDATION 2016 YEAR IN REVIEW





In looking back over the past year, both the Peter Michael Winery and the Peter Michael Foundation have provided us with much to feel proud and excited about. While the specific accomplishments and new opportunities differ for each, it's what they share—our unwavering passion and commitment—that fuels them both.

Over the past year, we have seen and heard firsthand how the foundation has made a difference in prostate cancer treatment. We've seen these differences measured in terms of advancements in research and development as well as in the ways in which they've impacted patient's individual lives.

It is enormously rewarding to know that we are not only helping prostate cancer patients by providing information and referrals, but that we are helping both men and women with other cancers as well through referrals. I want to personally thank Dr. Hedvig Hricak for her incredible responsiveness in accepting and facilitating treatments at Memorial Sloan-Kettering for so many patients, with a diversity of conditions, who have come to the foundation for help.

The foundation has been a pioneer in supporting the leaders in immunotherapy at University of California San Francisco for the past seven years and we were honoured to be featured on the back cover of the UCSF Medicine magazine (shared here and on our website).

Peter Michael Foundation was also honoured by Memorial Sloan-Kettering Cancer Center in New York for its commitment to prostate cancer research and the advancement of post-doctoral fellows in the field. This honour speaks directly to the foundation's ability to find and fund the best-of-class clinician scientists at an early stage and stay with them.

This accomplishment, and all our other achievements this past year, would not be possible without the enduring and generous support we receive from our friends. We look forward to the year ahead with tremendous optimism and, as always, eternal gratitude for your support and inspiration.

Yours sincerely

Emily Michael, Founder



I to r: Walter Menzel, Dr. Hedvig Hricak, Emily and Paul Michael at the Memorial Sloan-Kettering Honors Wall in Manhattan.



The work we do at the Peter Michael Foundation, and the achievements we report on at the year's end, are never the result of one person. It's all of you—friends, supporters, investors, directors, advisors, scientists, physicians, chefs, auctioneers, volunteers and valued colleagues—who make what we do possible. And, while the scope of our work is often of grand proportions, the ways in which it impacts people can be felt on the most personal level. This year, I experienced that firsthand.

On my recent birthday I learned that my PSA score had increased. While still a relatively low absolute number, it had doubled in nine months, which was cause for concern. While the work we do at the foundation has always been driven by personal passion, in the back of my mind I was pleased to have the learning that might benefit me personally someday.

This was reflected in my decision to have an MRI scan instead of immediately leaping to a biopsy or other invasive procedure. The results of the initial radiology report indicated that I didn't need to undergo a biopsy, but had that not been the case, I would have, again, benefitted from what I've learned through the foundation-supported research, and I would have undergone an image-guided biopsy instead of the standard 12-core biopsy.

The important work of advancing the diagnostic and treatment options available to those who face prostate cancer has always been core to the foundation's mission, as has the foundation's focus on understanding how its work impacts people personally. My experience this past year, being one of those people possibly facing cancer, didn't alter my understanding of what we do or why it's so important. But it did remind me, in the most fundamental of ways, the impact our work has to not just change the outcome of a person's diagnosis but to impact the way in which a person feels when faced with the diagnosis itself.

On behalf of all of us at the Peter Michael Foundation, I want to express our deepest appreciation—and my personal, heartfelt gratitude—for your enduring support, involvement and friendship.

Thank you all!

Walter &. Menzel

Walter B. Menzel, Executive Director



Friends of the Foundation



Ray and Laura Pirrello; Chicago, Illinois with Chef Daniel Boulud, Stars New York 2017

Many years ago, Ray and I attended an informal dinner at a friend's home and were served our first glass of Peter Michael Chardonnay. Ray realized from the first sip this was a unique tasting experience and what happened over the course of many years to follow was a blessing in disguise.

Peter Michael became our favorite celebratory wine shared with family and friends during special occasions. But at some point, we transitioned from enjoying PM wine on special occasions to a regular basis often inviting our neighbors, Dan and Deb Marszalek and Chuck and Linda Colander to join us.

On Ray's milestone 50th, I scheduled a Peter Michael Winery tour and tasting and the three couples headed to Sonoma to celebrate. There we met Jeff Ehrlich, a fellow Chicagoan who gave us a memorable tour of the property. While there, Ray noticed a book on the coffee table commissioned by Sir Peter Michael entitled *Hands and Hearts* | *Dedicated to the Fight Against Cancer*. The book's content and photography were impressive, and knowing it was produced to raise money for cancer research and patient care was most intriguing.

Jeff told us about the Peter Michael Foundation and how the book came together. He then shared details of the Stars event at the winery and Ray vowed we would return the next year to experience the wines and culinary creativity. And so it was there on that sunny day at Peter Michael, another friendship was made. That winery experience was one of many which would change our lives forever.

We attended our first Stars event in 2011 with six of our friends. We met many dedicated PM wine

lovers and supporters of the Foundation. We toasted, cheered and generously supported the foundation that night - which included Ray's purchase of a stay at the Peter Michael Guest House. It was also the first time we met Sir Peter, Lady Michael, Paul and Emily Michael, Jenny Koehler and Walter Menzel.

In August 2014, we returned to Côte Deux Mille with the Colanders and Marszaleks to celebrate the Foundation's 10th anniversary. We had a fantastic time and left with two special auction items... another winery stay and a Peter Michael wine-paired dinner in Manhattan personally prepared by acclaimed Chef Michael Richard!

A week following our return from Stars, we received devastating news. Chuck was diagnosed with advanced pancreatic cancer that spread to his liver. Upon hearing the news, we hurried to the Colander's home to comfort and support them. With everyone gathered around, Chuck opened a bottle of Peter Michael wine and toasted to all the good times, good friendships, and to love and support going forward.

Ray and I decided to reach out to the PM Foundation because we knew Walter worked with top cancer specialists and hospitals. Walter called his contacts and their responses were quickly shared with Chuck and Linda.

Chuck soon followed an aggressive Chemotherapy schedule. He and Linda created a calendar indicating treatments days, recovery days and the days he began to bounce back from treatment. They looked ahead and predicted Chuck's good days for travel. Walter and Jenny at the Foundation were extremely helpful and supportive when we contacted them to accelerate the two trips we purchased at the Stars Auction given Chuck's drastic diagnosis.

The Peter Michael Guest House was the trip Chuck wanted to make first. Jenny and Walter worked around his treatments to make that happen and Jeff was flexible with his schedule in case Chuck wasn't strong enough to move about for the tour. Jeff afforded us time after the tour to reminisce about previous PM trips, the wine and the history of our friendship. Chuck seemed happy. The weekend there rejuvenated him and he was feeling good!

The trip to New York was also planned around Chuck's treatments. It was enjoyed by us, our children, the Colanders and the Marszaleks a few days before Thanksgiving.

In January 2016, Chuck Colander passed away. I notified both Walter and Jeff as Chuck had been fond of both men since his very first winery tour and Stars event. Both sent heartfelt condolences and their support to Linda and us.

We enthusiastically support the Foundation knowing their support is available to us and our friends.

Laura Pirrello

Comment

Chuck Colander's life and spirit will be honored and live on in a memorial book to be installed at Peter Michael Winery and a display at the Peter Michael Foundation.



Dr. Hedvig Hricak

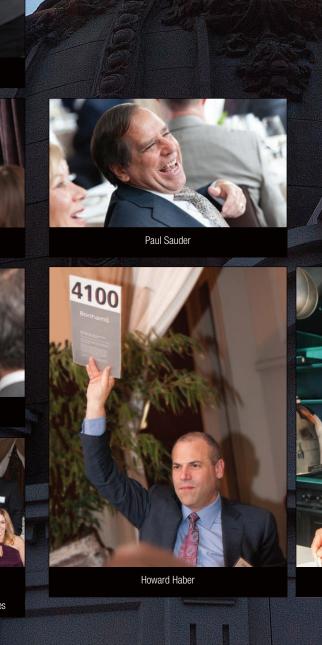
Dan Donnelly



Mark Rubin

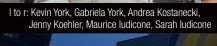














standing: Bob Hay, Howard and Joia Haber, John Henriques seated: Cynthia Stepien, Ian Blum, Melissa Haber, Lana Henriques



Kevin York, Gabriela York



Chef Christopher Kostow, Sir Peter Michael



Peter Stoneberg, Sue Hoeschler



standing: Michele Grasso-Dennis, Richard Crowell, Art Tuverson seated: Cynthia Tuverson, Joe Carroll, Leah Carroll, Dean Dennis



Dr. Sanjiv S. Gambhir



Mark Evans, Tracy Evans



Doug Lee, Rebecca Enders, & Nariman Manoochehri



Julia Massa, Sir Peter Michael, Aaron Gershenberg



Gabriela York, Cristina Zamorano





STARS

KNIGHTS VALLEY

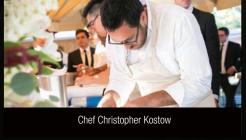
Li Zhang, Aaron Gershenberg



Laura Pirrello



Don Listwin, Jenny Beeler, Charles Beeler





Roland Boney, Missy Boney



Joe Carroll, Leah Carroll



Emily Michael, Walter Menzel



Brandon Behle, Elizabeth Behle



Paul Michael, Pamela Kramlich, Dick Kramlich



l to r: Fred Jones, Anne Mayfield, Mark Maier, Walter Menzel, Charlotte Fink, Fred Fink



o r: Walter Menzel, Chef Jason Hall, Jenny Koehle Chef Tyler Rodde, Jeff Ehrlich



I to r: Steele Dewey, Molly Dewey, Chris Glasgow, Wilson Glasgow



l to r: Dorian Gunter, Peggy Gunter, Colin Shaw, Steve Earle, Cynthia Earle, Robert Balsley, Perrin Dargan, Lisa Dargan



r: Dan Elmore, Jr., TK Wetherell, Virginia Wetherell, Dan George, Beverly Elmore

SOUTHERN STARS





Seared Duck Breast paired with 2011 L'Esprit des Pavots Estate Cabernet Blend

STARS:

Intimate, multi-course dinners in stunning locations

Award-winning Peter Michael wines thoughtfully paired with each course

Bonhams live auction of unique experiences, rare wines, and wine-paired dinners

Meet the physician-scientists funded by the PMF Fellowship Grants

Net proceeds benefit innovative prostate cancer research



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Please notify us of any errors, omissions or misspellings for us to correct.

Comprehensive Cancer Center



UCSF Department of Medicine

FRONTIERS OF MEDICINE



Oncologist Lawrence Fong, MD (center), who co-leads the UCSF Cancer Immunotherapy Clinic, consults with Gabriel N. Mannis, MD (left),

Cancer Immunotherapy

FRONTIERS OF MEDICINE



Sir Peter Michael (left), an entrepreneur, philanthropist and founder of the Peter Michael Winery, supports cancer immunotherapy research at UCSF through the Peter Michael Foundation, which hosts dinner auctions across the country to raise funds for prostate cancer research. Paul and Emily Michael (above), Sir Michael's son and daughter-in-law, help run the winery and foundation.

Donor Profile: Peter Michael Foundation Raising a Glass for Research

With expertise in everything from technology to wine, Sir Peter Michael is a Renaissance man. The engineer and entrepreneur's accomplishments include founding several technology companies, including Quantel, which transformed television graphics. He later co-founded Classic FM, the first commercial radio station in the United Kingdom, and established a luxury hotel and restaurant in England. He was knighted by Queen Elizabeth II in 1989.

While working in Silicon Valley in the 1970s, he fell in love with Northern California. Michael bought a ranch in Calistoga and established the Peter Michael Winery, which he runs with his son and daughter-in-law, Paul and Emily Michael. His vineyards produce some of the world's top wines — a Peter Michael Cabernet Sauvignon Napa Valley Au Paradis 2012 was chosen as Wine Spectator's 2015 Wine of the Year.

He also established a philanthropic foundation to support innovative treatments for prostate cancer. The Peter Michael Foundation hosts dinner

auctions across the United States, with exquisite meals prepared by famed chefs like Thomas Keller. "People come from all across the country for the food and wine," said Walter B. Menzel, the foundation's chief executive officer and executive director. "They come as guests, and leave as friends." The proceeds from these events support cuttingedge prostate cancer research at four top cancer centers across the country, including UCSF.

Even before its potential became widely known, the Peter Michael Foundation began supporting cancer immunotherapy. For the past six years, the Foundation has funded a postdoctoral research fellow in the lab of Lawrence Fong, MD. Efim Guzik Distinguished Professor in Cancer Biology, who directs the UCSF Cancer Immunotherapy Clinic and co-leads the Cancer Immunotherapy Program of the UCSF Helen Diller Family Comprehensive Cancer Center. "The resources from the Peter Michael Foundation have made a big impact on our research program," said Fong. "They provided consistent support year after year at a time when cancer

immunotherapy was not the high-visibility field that it is now. This allowed us to make continued progress positioning our program for even greater successes."

These research projects have included identifying biomarkers that may help determine which patients are most likely to respond to immunotherapy, and studying whether combining immunotherapy treatments could lead to more robust clinical responses.

"We fund really smart people who are working on innovative, highrisk projects," said Menzel. "Immunotherapy has great promise. We've all read about 'superresponders'—people who are right in the sweet spot, and the cancer is completely gone [after receiving immunotherapy]. But those people are few and far between. What was it in that patient and that treatment protocol that connected so effectively, and can you replicate that at scale?"

The Peter Michael Foundation (petermichaelfoundation.org) hopes their support will improve the efficacy of immunotherapy for more patients.









Mentor: Hedvig Hricak, M.D., Ph.D., Dr. h.c. Chairman, Department of Radiology

Fellows: Dr. Andreas Wibmer and Dr. Kristin Granlund

The value of prostate MRI for predicting clinical outcomes

Dr. Hedvig Hricak was one of the earliest pioneers of MRI of the prostate and has been a leading expert in the field for more than 30 years. The growing interest in and use of prostate MRI now being witnessed around the world is due in no small part to the large body of work produced by her research team. With support from the Peter Michael Foundation, Dr. Hricak's team continues to identify and refine novel applications of MRI to improve the diagnosis and management of prostate cancer.

One major focus of the team's research has been the need to better differentiate low-risk disease that can be safely monitored from higher-risk disease that requires immediate treatment. Dr. Andreas Wibmer, a PMF-funded Fellow at MSKCC, is involved in two studies that address this need. One is a large-scale assessment of the value of prostate MRI for predicting clinical outcomes. In this study, the preoperative MRI scans of 2100 patients obtained between 2001 and 2006 are being re-interpreted by 7 sub-specialized genitourinary oncologic radiologists according to the most recent MRI interpretation guidelines. Unlike those of prior studies, the size of this study's population and the length of the follow-up period (up to 15 years) allow for correlation of imaging data with actual cancer-specific survival rather than with surrogate endpoints, such as pathologic tumor grade. The other study investigates specifically how prostate MRI could be efficiently used to identify patients with localized low-risk prostate cancer, for whom active surveillance might be a safe management option. It aims to produce a nomogram—or statistical tool—that incorporates clinical, histopathologic, and MRI variables to help clinicians and patients make fact-based, safe management decisions.

Taking advantage of their interdisciplinary team of scientists and clinicians, MSKCC has also begun the first clinical studies utilizing hyperpolarized MRI. In this new and potentially

transformative imaging approach, a novel device called a hyperpolarizer is used to change the nuclear spin of a chemical agent, so that after it is injected into the body, its metabolic transformation can be visualized with MRI. With the help of PMF fellow Kristin Granlund, a Stanford University trained Electrical Engineer, MSKCC's team is not only establishing the ability of hyperpolarized MRI to image patients (Figure 1AB), they are also assessing the technique's reproducibility and comparing the imaging findings to the extent and grade of disease in patients undergoing prostatectomy (Figure 1C). In the first 17 patients imaged, metabolism of the injected agent to hyperpolarized lactate was higher in regions of Gleason grade 4/5 cancer than in areas of lower-grade disease. These exciting results directly link the biology of prostate cancer to the results of hyperpolarized MRI. Moving forward, the investigators will aim to integrate this new, non-invasive metabolic imaging technique into ongoing clinical trials to assess prostate cancer treatment response.

Figure 1. (A)

Schematic for the conversion of hyperpolarized pyruvate to its metabolic products in vivo. Generation of lactate via the enzyme flux through lactate dehydrogenase (LDH) is highlighted as this is the route we anticipate will be elevated in prostate patients.

▲ Conversion of Hyperpolarized Pyruvate in vivo

Figure 1. (B)

Representative hyperpolarized pyruvate dynamics with accompanied T2-weighted anatomic imaging demostrates localized and time resolved metabolism in the human prostate.

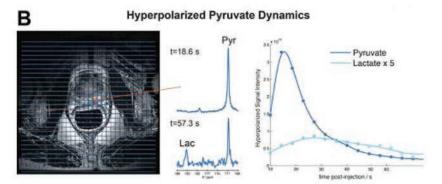
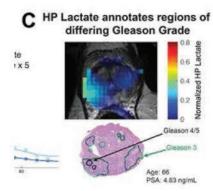


Figure 1. (C)

Regions of heterogeneous metabolism are shown in the prostate of a representative patient as compared to step section histopathology of the same gland after surgical removal. Levels of elevated metabolism are seen in both regions, with significantly higher HP Lactate observed in the regions of higher grade.



To increase awareness of this research and of the potential of hyperpolarized MRI, Dr. Granlund presented recent findings at the annual meeting of the International Society for Magnetic Resonance in Medicine.

The MSKCC team is deeply grateful for the support of the Peter Michael Foundation and looks forward to further exploiting the potential of MRI to enable more effective, less invasive diagnosis and treatment of prostate cancer.



Stanford University Medical Center





Mentor: Sanjiv Sam Gambhir, MD, PhD Fellow: Idan Steinberg, PhD

Progress on Dual Modality Transrectal Ultrasound and Photoacoustic Imaging of Prostate:

In recent years we have developed and bench-to-bedside translated an integrated transrectal ultrasound and photoacoustic device that synergizes the strengths of transrectal ultrasound and photoacoutic imaging. The device uses a miniaturized capacitive micromachined ultrasonic transducer array, for simultaneous imaging of both anatomical and molecular optical contrasts (intrinsic: hemoglobin; extrinsic: intravenously injected Indocyanine green (ICG)) of the human prostate. During the past two years we have conducted a pilot clinical study on 20 patients in the Stanford hospital.

Results from the first 10 patients were used for assessing the device performances and ability to measure intrinsic contrast. The later 10 patients were administered FDA approved ICG while imaging (from 2.5 mg up to 75 mg total). Imaging the *in vivo* Hemoglobin absorption enabled mapping of the vascular structures of the prostate and surroundings as identified on US images, such as seminal vesicles, neurovascular bundles, and dorsal vascular complex (shown in figure 1a and 1b). Intravenous administration of the ICG absorption enhanced the photoacoustic contrast of the prostate. The plots of ICG time activity showed an average peak ICG arrival time of 3 minutes and a wash-out of 7 minutes post injection (shown in figure 1c). In the future, a photoacoustic specific agent targeting the gastrin-releasing peptide receptor (Bombasin) will be our agent of choice. However, as it was not yet approved for administration in humans, the non-specific ICG allowed us to assess the capabilities of the current device.

To conclude, our current device was able to image the prostate vascularity as well as the arrival of external contrast agent into the prostate. Thus, we were able to overcome the existing limitations of standard TRUS and offer new diagnostic and prognostic insights into the prostate cancer screening and management. These results were submitted for the journal of Nature Communications.

Future directions:

While the current device allowed us to image ICG *in vivo*, the current technology should be further improved in order to allow us imaging of trace amounts of imaging agent (the current doses are quite high) and quantitative estimation of the chromophore concentration. Thus, we are in the process of revamping our entire system:

We've rewritten our entire imaging software to allow us more robust and precise reconstruction algorithms on both the ultrasound and especially the photoacoustic aspects. Those algorithms will also be used to reanalyze past measurements and improve imaging quality there as well. Initial performance of our algorithm are shown in figure 2 and compared to the commonly used universal back-projection algorithm.

We are in the process of designing a second generation device based on our experience so far. We will use a much broader ultrasound array with multiple frequency bands to considerably improve sensitivity and image quality. This will be achieved without changing the transducer size to allow patient comfort.

We've already upgraded our acquisition system and laser source to allow better performance and smaller footprint. This will allow us to use the system intra-operatively. To support the continuation of this research we will image another 24 prostate cancer patients with ICG administration.

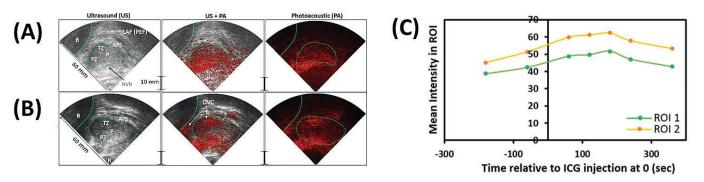


Figure 1: In vivo structural and functional imaging of human prostate using ultrasound and photoacoustics (A) and (B) are two separate TRUSPA frames, each frame consisting of ultrasound (US), photoacoustic (PA), and co-registered US+PA image captured in real time. Ultrasound images clearly provided the sagittal anatomical information such as transitional zone (TZ) and peripheral zone (PZ) of prostate (P), partial bladder (B), seminal vesicles (SV), rectum (R), and anterior fibromuscular stroma (AFS) with respect to the position of the rectum (R). (A) Shows strong photoacoustic contrast from the neurovascular bundle (NVB) in the posterior peripheral region. (B) Shows photoacoustic contrast from dorsal vascular complex (DVC) that spans AFS and interface of posterior prostate and bladder regions and also from the region proximal to seminal vesicle. (C) Time measured relative to ICG injection vs. mean PA signal measured in two regions of interest around the prostate area. The systemic buildup and wash out of the external ICG contrast is clearly shown.

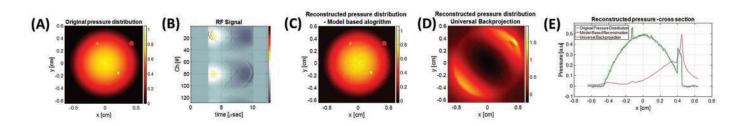


Figure 2: New Model-based reconstruction algorithm (A) Initial photoacoustic pressure distribution showing both smoothly varying background as well as four discrete features on top of it. (B) The time signals (RF signals) in each of a 128 detectors surrounding the sample as due to the photoacoustic pressure. A 2% noise was added to the simulation. (D) Reconstructed pressure distribution using our model based algorithm. (D) Reconstruction of the pressure distribution using the commonly used Universal back-projection algorithm which emphasizes boundaries. (E) A cross section of the reconstructed pressure showing the model based reconstruction responding to both slowly varying and abrupt features of the initial pressure as opposed to the universal back-projection that ignores the slowly varying background. This leads to non-quantitative imaging.







Daniel George, MD.
Professor of Medicine and Surgery, Divisions of Medical Oncology and Urology in the Duke University School of Medicine

Tian Zhang, MD
Fellow in hematology and medical oncology at Duke University

Using Copper to Sensitize Prostate Cancers to a "New" Treatment

In advanced stages of prostate cancer, the androgen receptor is overexpressed and drives cells to absorb copper in high concentrations. Therefore, we sought to screen for drugs that killed prostate cancer cells only in the presence of copper. We identified disulfiram (DSF), which is an approved drug for treatment of alcohol abuse. In the absence of alcohol it is well tolerated with only minor side effects. In our prostate cancer models, DSF blocked the growth of cells and caused them to die when copper was present. When we took copper away, the drug no longer worked. Not surprisingly then, when DSF was given to prostate cancer patients without additional copper, the drug didn't do much.

We have studied the copper-DSF activity extensively in the laboratory and have shown that the antitumor effect is increased, not reversed, by adding excess copper and occurs with far lower doses of DSF than previously thought were needed to kill cells. All together, these results suggest that DSF may be far more effective against prostate cancer if we can increase the copper concentrations within tumors of patients with widespread disease. To test our theory we have initated a Phase I study to look at the treatment effects and side effects of DSF in advanced prostate cancer patients using increasing doses of intravenous copper combined with oral copper and DSF tablets.

The first goal of our study will be to show the safety, tolerability, and best dose of intravenous copper followed by DSF. We will perform a positron emission tomography (or PET) scan that follows a tiny dose of radioactive copper when injected intravenously in patients to measure how much copper the tumors take up. When possible, we will also measure copper levels and the androgen receptor activity in patients who agree to undergo a tumor biopsy. We will use these tests along

with blood levels of copper to determine the best dose for further testing. Of course, our other goal is to describe any positive treatment effects in patients to the combination of intravenous copper and oral DSF. We will be specifically studying patients who have progressed on standard hormonal therapies as well as a group of patients with liver metastases (where we know DSF can penetrate) as well as a group of patients with neuroendocrine prostate cancer (who have no effective standard treatments).

Tian Zhang, MD, is a fellow in hematology and medical oncology at Duke University. She graduated magna cum laude with a B.A. in Biochemistry from Columbia University in the City of New York in 2005 and earned her M.D. from the Health Sciences and Technology program at Harvard Medical School-MIT in 2009. She completed residency training in internal medicine at Duke University Hospital and will complete fellowship training in hematology/medical oncology in June 2015. She will become faculty in medical oncology in July 2015. Her research interests include the development of novel therapeutics and biomarkers/companion diagnostics for targeted therapies in genitourinary malignancies.

Daniel George, MD is a Professor of Medicine and Surgery, Divisions of Medical Oncology and Urology in the Duke University School of Medicine. He also has appointments in the Duke Clinical Research Institute and the Duke Cancer Institute where he is the Director of Genitourinary (GU) Oncology. He is an internationally recognized clinical researcher and thought leader in GU malignancies, with over 150 peer-reviewed publications. His areas of research include new drug development and biomarkers of GU cancers with an emphasis on signal transduction pathways and angiogenesis.

UPDATE:

African American men exhibit 2 times higher incidence and 3 times higher mortality rates from prostate cancer compared to Caucasian American men. Much of this disparity remains after controlling for factors related to access to care. Our team has focused on understanding the genetic factors that drive the more aggressive prostate cancer in African American men could lead to treatment strategies for all patients with aggressive disease. Based on preliminary work supported by the PMF in 2013-14 we were awarded an NCI RO-1 grant to study specific genetic targets identified through prior screening efforts for possible therapeutic intervention. This grant scored within the top 10% reviewed and will begin funding in the fall of 2017.



Appreciation and Acknowledgement

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