



# Sidney Kimmel Cancer Center

AT



## Thomas Jefferson University



Pioneers and Heroes

# at a glance

- We have collaborative efforts spanning five continents including North America, South America, Europe, Asia and Australia
- More than **1,000** physicians, scientists and staff from **50** countries treat nearly **250,000** cancer patients at **30** Sidney Kimmel Cancer Network member organizations
- More than **\$60 million** in cancer research grants
- A **\$6.7 million** five-year Promise Grant from Susan G. Komen for the Cure
- **\$20+ million**  
Donor support during the past three years to help our researchers move quickly in finding new treatments for cancer
- **\$1.5 million**  
Funds raised by the Philadelphia Eagles to support Jefferson's breast cancer research
- **40,000**  
Breast imaging exams done annually at the Jefferson – Philadelphia Eagles Breast Health facility. It is the busiest center in the region.

## Sidney Kimmel Cancer Center Partnerships Worldwide

- **Centro Di Riferimento Oncologico Di Aviano**  
(Aviano, Italy)
- **Fortune Link & Champion Medical Advancement Associates (CMAA)**  
(Beijing, China)
- **Kazan Federal University**  
(Kazan, Russia)
- **Lankenau Institute for Medical Research & Drexel University**  
(Philadelphia, PA)
- **Melbourne University**  
(Sydney, Australia)
- **M.M. Shemyakin and YU.A. Ovchinnikov Institute of Bioorganic Chemistry and Russian Academy of Sciences**  
(Moscow, Russia)
- **Research Centre for Natural Sciences Hungarian Academy of Sciences**  
(Budapest, Hungary)
- **Universita' Degli Studi Di Napoli Federico II**  
(Naples, Italy)
- **University of Debrecen**  
(Debrecen, Hungary)



Karen E. Knudsen, PhD

Director,  
Sidney Kimmel Cancer Center  
at Thomas Jefferson University

Chair,  
Department of Cancer Biology

## Pioneers & Heroes

Cancer has affected each of us in some way. We've fought and survived cancer, and we've lost loved ones. At the Sidney Kimmel Cancer Center (SKCC) at Thomas Jefferson University, we believe that every day is one day closer to a cure, with help from hundreds of pioneers at our Center and member Network, and through our heroes, the donors, who refuse to let cancer win.

Each day brings us closer to a cure because we face it with some of the best and brightest in the world – distinguished researchers, radiation oncologists, medical oncologists, surgeons, neurosurgeons, urologists, gastroenterologists and cancer specialists – many of whom are recognized on prestigious lists like Best Doctors in America®.

As a National Cancer Institute (NCI)-designated cancer center – one of only 68 in the nation – we are committed to the continued improvement of outcomes for our patients. We share this commitment with our consortium partners at Drexel University and the Lankenau Institute for Medical Research, and the vast opportunities we collectively have for future discoveries in cancer prevention, diagnosis and treatment. We do what we do, every day, in tandem with 30 members of the Sidney Kimmel Cancer Network. Through our combined efforts we touch the lives of more than 250,000 cancer patients annually, with the opportunity for thousands to participate in breakthrough clinical trials.

We are proud that SKCC is recognized as a *Blue Distinction Center for Complex and Rare Cancers* by the Blue Cross and Blue Shield Association, and that our physicians practice at Thomas Jefferson University Hospitals – ranked by *U.S. News & World Report* among the nation's Best Hospitals for cancer treatment.

And because cancer has no borders, we share our expertise nationally and internationally. Recently, the Worldwide Innovative Networking (WIN) Consortium, an international genomic medicine collaborative devoted to accelerating the delivery of personalized medicine, announced SKCC as one of its six new members – the only one in the tri-state area.

For us, it's local. It's global. It's personal. From the generous gift made to our Center by philanthropist Sidney Kimmel, to our pioneering physicians and everyday heroes (our donors), you will see through their eyes, in the pages that follow, how each day...is one day closer to a cure for cancer.

Karen E. Knudsen, PhD

# Sidney Kimmel

## Investing in the Institution, Cause and City He Loves



In June 2014, Thomas Jefferson University announced the fifth-largest naming gift in American academic medicine history, given by philanthropist Sidney Kimmel to Jefferson Medical College, now known as the Sidney Kimmel Medical College at Thomas Jefferson University, in recognition of this extraordinary gift.

"This \$110 million gift from the Sidney Kimmel Foundation is transformational," remarked President and CEO Stephen K. Klasko, MD, MBA, during the announcement. "It will markedly improve our teaching and learning technologies, provide student scholarship and research support, and position the Sidney Kimmel Medical College at Thomas Jefferson University as a premier and innovative center for medical training and research."

"Mr. Kimmel is investing in our institution and believes in Jefferson enough to put his name on our medical college. His recent and past philanthropic efforts send an amazing signal to others that we're the place they should invest in, too. Our commitment is to make sure that his gifts to Jefferson are the *best* investments he'll ever make."

### A Commitment That Began at Jefferson

Mr. Kimmel's relationship with Jefferson dates back to 1996, when he generously donated \$10 million toward cancer research at Thomas Jefferson University – then the largest individual gift Jefferson had ever received. With this remarkable commitment to supporting cancer research, he began his journey to becoming one of the nation's leading individual donors in this area. In honor of his gift to Jefferson, the University renamed its world-renowned National Cancer Institute (NCI)-designated cancer center the Kimmel Cancer Center at Jefferson and more recently amended to become the Sidney Kimmel Cancer Center at Thomas Jefferson University.

### Philly Heart and Soul

Mr. Kimmel became an immensely successful entrepreneur, as founder and chair of the Jones Apparel Group, a leading women's clothing manufacturer. More recently, based in Southern California, he has been a prolific film producer of such box-office hits as *Moneyball*, *The Lincoln Lawyer* and *The Kite Runner*.

Through all of his success and travels, Mr. Kimmel has maintained strong ties with his Philadelphia roots. He has given tens of millions of dollars to such Philadelphia institutions as the National Constitution Center, the National Museum of American Jewish History, the Kimmel Center for the Performing Arts and Jefferson.

"I'm a Philadelphian. My heart has always been here, even though I don't live here now," Mr. Kimmel says. "And I believe that Jefferson is the soul of this city – particularly now, because I sense a new burst of energy with Steve Klasko who is revitalizing this institution."

"It is no secret that we live in a world of change. It is rapid and dramatic. Nowhere is that more so than in health care. I'm delighted to join Jefferson on its transformational ride to the forefront in the delivery of medical education and health care, and to the center of Philadelphia's economic wellbeing. My wife, Caroline, and I are so happy to have our name linked to Jefferson and to be able to make a difference once again in the city that made so much of an impact on me."

*We extend our sincerest thanks to Mr. Kimmel for his generosity and his unwavering commitment to Jefferson that span nearly two decades.*



# 'Charting' New Course for Breast Cancer Treatment

Hallgeir Rui, MD, PhD, spends a lot of time in the lab, but his thoughts are never far from the bedsides of the countless patients he helps through his research in breast cancer.

A team led by Dr. Rui, Scientific Director of the Jefferson Breast Care Center, and Edith Mitchell, MD, FACP, Clinical Professor of Medicine and Clinical Oncology at the Sidney Kimmel Cancer Center, is in the final year of a five-year collaborative classification program to identify 250 therapy-relevant protein markers in breast cancer tumors. The study will create an invaluable tool to aid future research, leading to more effective and precisely targeted drug treatments and, hopefully, better outcomes for patients with breast cancer.

## Following His Heart

Helping people is what initially attracted Dr. Rui, also Professor of Cancer Biology, Medical Oncology and Pathology, to the medical profession as a young man in his native Oslo, Norway. He entered medical school when he was 18, but soon received discouraging news from an upperclassman: In the time it would take him to complete six years of medical school, there would be a glut of physicians in Norway – and a scarcity of places to work.

"That was pretty depressing," recalls Dr. Rui, deciding at the time to pursue a PhD and an MD. It wasn't long before he was captivated by the possibilities of a career in research. "My thought was that I can help patients by doing research equally as much, or maybe more so, than I can in the clinic."

Following stints at the National Cancer Institute and Georgetown University Medical Center, Dr. Rui was recruited to Jefferson in 2006 to assemble and lead a matrixed team of multidisciplinary investigators and staff, eventually helping secure, along with Dr. Mitchell, a Susan G. Komen for the Cure Promise Grant of \$6.7 million for five years for continued breast cancer research.

The classification program, which involves tissue analysis of 5,000 breast cancer tumors, has been part one of the Komen project. The study should lead to the development of a classification map for different breast cancer tumor types based on therapy-relevant marker combinations. Each sample will be classified and predictions can be

made for tumors with similar profiles for likely response to particular drug therapies. Future researchers and pharmaceutical companies will then be able to consult the classification map to frame clinical trials of novel drugs or drug combinations by selecting appropriate patients. The idea, Dr. Rui said, is to "enrich clinical trials for the most likely responders."

The second part is an adaptive clinical trial, which offers a more customized and personalized approach to the treatment of triple-negative breast cancer. The trial, with lead investigators Tiffany Avery, MD, in the Department of Medical Oncology, and Adam Berger, MD, in the Department of Surgery, offers chemotherapy paired with a supplemental medication called a "Parp Inhibitor" which interferes with DNA repair, and is designed to target the breast cancer cells to increase response to treatment and decrease the risk of recurrence.

## Collaboration is King

It's the first investigator-initiated adaptive clinical trial ever at Jefferson and represents a new method for modifying trials so that patients receive the most benefit possible. "Patients are randomized at an import juncture in the trial where there is a higher chance of success," says Dr. Rui. "This is a more effective trial strategy that can reduce the number of patients needed to get statistical significance. That's a major benefit."

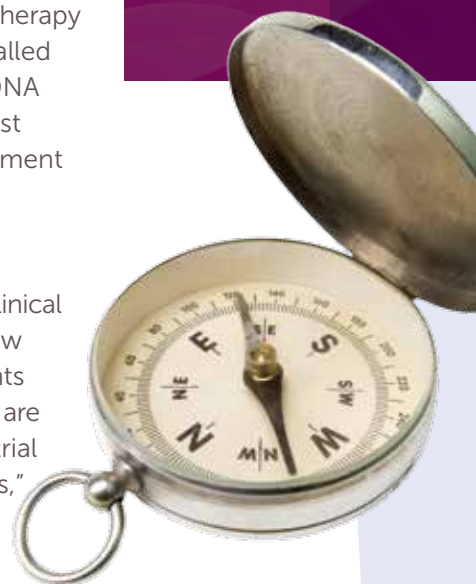
The Komen Promise Grant is significant in that it is one of only a few programmatic grants intended to support collaborative, multidisciplinary research programs. Programs funded through this grant are expected to achieve results that would not otherwise be attainable by investigators working independently. They should have significant potential to reduce breast cancer incidence and/or mortality within the decade.

"The ability to work with clinicians and pathologists has been a tremendous benefit at Jefferson," Dr. Rui says. "You can do more translational research," he adds, referring to the "bench-to-bedside" model of harnessing knowledge to produce new drugs, devices and treatment options for patients. "It's really ideal."

As was Dr. Rui's decision to pursue a career in research.



Hallgeir Rui, MD, PhD



# Every Cancer Case is Personal

Massimo Cristofanilli, MD, sees part of himself – and his father – in each of the cancer patients he treats. It's what enables him to provide the level of care he wishes his father had received over the four years that followed his diagnosis for bladder cancer.

Dr. Cristofanilli was just 22 and living in Italy, when his father died. He was by his side throughout the journey, during which he witnessed the many deficiencies of the Italian healthcare system, where surgeons and oncologists would not treat patients in a multidisciplinary fashion. It's why he decided to become an oncologist.

**“The most pleasant part of my job is to interact with patients and help them. I always try to understand their problems and listen to their concerns. I imagine myself as the young man standing by his father in the exam room, unable to ask but willing to listen. Every case is very personal to me.”**

**— Massimo Cristofanilli, MD**

“I remember listening to a conversation between a radiation therapist and a medical oncologist about the possibility not to use an additional palliative treatment for my father, and the risks and costs of the treatment and inpatient stay. This was just one month before his death. He was never given a choice. I did not know if and what to ask.”

It's an experience that Dr. Cristofanilli, Director of the Jefferson Breast Care Center at the Sidney Kimmel Cancer Center, never wants to see recreated. A renowned medical oncologist and researcher in breast cancer, with a particular interest in inflammatory breast cancer (IBC), Dr. Cristofanilli, who also serves as the Deputy Director of Translational Research, spearheads Jefferson's efforts to fight the disease by applying innovative research and novel diagnostic

methods to the clinical care of patients.

IBC is the most aggressive and deadly form of breast cancer and one that is still commonly missed by women and some physicians. Although it accounts for between two and five percent of all breast cancers in the U.S. – and 13 percent of breast cancers globally – it is responsible for a disproportionate number of deaths from breast cancer.

IBC tends to strike younger women, is more common in African Americans and isn't usually associated with lumps. The most common symptoms are pain in the breast or arm and a warm or swollen breast. It can often be confused with mastitis. This type of breast cancer disease is resistant to most types of therapy available. Women receiving this diagnosis face incredibly difficult decisions about their treatment and their lives as they navigate what is for most a terminal illness at a young age.

Dr. Cristofanilli and his team are currently working on a number of clinical trials for IBC and metastatic breast cancer. One of those involves circulating tumor cells (CTCs), and examining whether levels of CTCs can predict survival in metastatic breast cancer. In a separate trial, a drug currently used to treat a type of lymphoma has shown surprising benefit in preclinical studies of IBC. The finding, published in the October 2013 issue of the *Journal of Experimental Therapeutics and Oncology*, has led to development of a phase 1/2 clinical trial at the Sidney Kimmel Cancer Center to test the agent, romidepsin, in combination with nab-paclitaxel chemotherapy for advanced IBC. Researchers hope this new combination of anticancer agents will lead to better outcomes for patients with IBC.

Despite this encouraging news, Dr. Cristofanilli stresses that there is a dire need for further research. The problem, he says, is that IBC is considered a rare disease, and grants funding rare diseases are difficult to secure. “It's not felt that inflammatory breast cancer deserves that type of attention.”

Regardless, he'll continue to push on – always with compassion in mind.



Donors Carole and Jules Lieberman and Massimo Cristofanilli, MD, (center) recently dedicated a plaque in the Jefferson-Philadelphia Eagles Breast Health Center to memorialize Jamie Brooke Lieberman who lost her battle with inflammatory breast cancer at 35.

## A Million-Watt Smile *Her smile.*

When people reflect on Jamie Brooke Lieberman, the first thing they inevitably think of is her smile. "She called herself a party in a person," says her mother, Carole Lieberman. "She had a million-watt smile."

Family and friends are still saddened by the light that went out in their lives when Jamie lost her battle to inflammatory breast cancer, at 35, on June 6, 2012, less than two years after being diagnosed. She will forever be remembered for devoting her days – from the time that she was diagnosed – to raising awareness of both the needs of younger survivors and the rare but aggressive form of the disease that took her life in its prime. Spearheaded by her parents, Carole and Jules, her loved ones continue working on the causes she so passionately championed.

"I knew I was left a mission," says Carole. "I knew I wanted to carry on Jamie's work and leave a legacy for her. But mostly, for my daughter and for the need to spread awareness and get the word out there about inflammatory breast cancer."

**"I knew I was left a mission. I knew I wanted to carry on Jamie's work and leave a legacy for her."**

In establishing the Jamie Lieberman Cancer Research Memorial Fund, the Liebermans have raised thousands of dollars – much of it through the sale of colorful crafted bracelets – for cancer research. The handmade "Jamie Brooke" bracelets sell for \$40, all of which goes to the Memorial Fund.

The Liebermans recently presented a \$125,000 gift to the Sidney Kimmel Cancer Center in memory of their daughter and to support research being conducted by Dr. Cristofanilli. A plaque in Jamie's memory, inscribed with the words "May Her Zest for Life Inspire Others," was recently dedicated at the Jefferson-Philadelphia Eagles Breast Health Center.

Says Carole, "she taught so many people, me above all, about the power of being positive, and the power of making a difference."

*The "Jamie Brooke" Bracelets can be ordered by emailing Carole Lieberman at [cjl1200@aol.com](mailto:cjl1200@aol.com).*





Nicole Simone, MD

## Starve a Cell, Feed a Future

For Nicole Simone, MD, Director of Breast Radiation Oncology, the notion of telling women with breast cancer to reduce their daily calories seemed illogical and counterintuitive... at first. But the more she studied the connection between lower caloric intake and a reduction in breast tumor size with radiation therapy, the less convincing she needed.

After several years of researching her hypothesis in the lab, Dr. Simone established a link in her published studies showing that by restricting calories she could potentially improve the effectiveness of radiation therapy in breast cancer cells. In addition, her research also indicated that tumors in highly metastatic models of triple negative breast cancer (which does not respond to hormonal therapy) actually shrunk in size when radiation was combined with calorie restriction.

"The pre-clinical information really showed us that there is significant potential for calorie restriction to actually change the biology of tumors and enhance the opportunity for clinical benefit," says Dr. Simone. "When we decreased calories by about 20 percent, we could begin to see the increase in the tumor's response to radiation. Tumors got significantly smaller when radiation and caloric restriction were added."

She found that by combining a healthy diet with standard therapies such as radiation or chemotherapy, she could improve breast cancer outcomes; the combination caused greater tumor shrinkage and a decrease in metastases in the laboratory.

### Counting Calories

With evidence in hand, Dr. Simone is now leading the first-of-its-kind clinical trial to evaluate the impact of calorie reduction on radiation therapy for women with breast cancer.

Recent studies have shown that too much weight makes standard treatments for breast cancer less effective, and patients who gain weight during treatment are shown to have worse cancer outcomes. When treating women with breast cancer, evaluating their metabolism is very important.

"Breast cancer patients are often treated with hormonal therapy to block tumor growth and

are given steroids to counteract the side effects of chemotherapy," notes Dr. Simone. "Both treatments can alter a patient's metabolism, which can lead to weight gain. In fact, women gain an average of 10 pounds in their first year after treatment for breast cancer."

Dr. Simone's research, dubbed the CaReFOR trial (Caloric Restriction for Oncology Research), hinges on a multidisciplinary approach to treatment. Patients enrolled in the clinical trial also work with Daniel Monti, MD, Executive and Medical Director, Myrna Brind Center of Integrative Medicine at Jefferson. He and his team work with patients to determine how to safely reduce their caloric intake by 25 percent. Patients keep an online diet journal to help stay on track for 10 weeks while they undergo radiation. If findings indicate that reducing calories improves their outcomes, it's possible that dieting could become a standard – and affordable – part of treatment.

Dr. Simone is also excited about early, unpublished results examining caloric restriction in combination with chemotherapy. While a large percentage of patients with breast cancer, as much as 70 percent, undergo radiation therapy, a smaller percentage chooses to undergo mastectomy, often followed by rounds of chemotherapy.

### Minimizing the Effects

Can caloric restriction improve the effectiveness of chemotherapy? Early results are promising. "We've looked at two clinically well-established chemotherapy drugs and we've seen the same basic effect," Dr. Simone says.

"Not only did caloric restriction produce a better response, there appeared to be decreased normal tissue toxicity, as well. That's kind of exciting," she said, "since we cause side effects among patients using our standard cancer treatments."

Dr. Simone sees a movement to limit toxicity in cancer therapy within the next several years. "With methods like calorie restriction, we're learning that we can turn off molecules associated with cancer in a nontoxic way, and I hope we can ultimately use this to safely enhance treatment with minimal side effects."

Less is more – Dr. Simone is convinced.





Mary Louise Leuters

Maureen Pomifeacz (left) and Delores Harter, volunteers with the 'Ladies of Port Richmond,' have helped the group raise nearly \$500,000 in their community in support of the fight against breast cancer...one delicious cupcake at a time.

## Our Fundraising Guardian Angels

At a time of decline in research funding from external sources, including a decrease in grants from the National Cancer Institute, the Sidney Kimmel Cancer Center at Thomas Jefferson University is thankful for its fundraising guardian angels in Port Richmond.

Started by Mary Louise Leuters, a two-time breast cancer survivor, the Ladies of Port Richmond have raised more than \$430,000 for breast cancer research over the last 10 years – all from such grassroots efforts as bake sales, church breakfasts and an annual walk through their Port Richmond neighborhood. The group's efforts have championed over \$304,000 in dedicated funds to Jefferson and their support has been vital in providing seed money that has allowed our faculty to conduct preliminary research that has helped secure National Cancer Institute grants.

Mary Lou and the Ladies of Port Richmond have created the framework of what can be replicated by other individuals and organizations in our community to replace diminished government funding of critical cancer research. She has provided supreme leadership and education to fellow volunteers who have in turn increased funding that has helped to advance and accelerate clinical and investigative breakthroughs.

She started her relationship with the Sidney Kimmel Cancer Center by volunteering – making copies and sitting with people during chemotherapy – after she beat breast cancer the second time. But that wasn't enough. Mary Lou decided to start the Ladies of Port Richmond – a group whose members are generally in their 70s. After watching television coverage of the Susan G. Komen Breast Cancer Walk at the Philadelphia Museum of Art on Mother's Day, she called friends to her kitchen table and asked, "Why can't we do that in our neighborhood?"

There have been ten annual neighborhood walks since, numerous activities like comedy night at the Cannstatter Club in Northeast Philadelphia, casino bus trips, breakfasts and more.

Before stepping down from her 10th consecutive year as president, Mary Lou has a goal to accomplish – to exceed raising \$500,000 for local breast programs. No one would dare bet against her.

**The Ladies of Port Richmond have created a grassroots organization that has helped to fund and accelerate clinical and investigative breakthroughs in cancer research.**



## With a 'Cup of Joe,' Team Science Heats Up

It's the afternoon before the 2nd Annual Baltimore-Philadelphia Prostate Cancer "Amtrak Alliance" Summit, and Karen Knudsen, PhD, Director for the Sidney Kimmel Cancer Center at Thomas Jefferson University, is understandably excited. There are some last-minute details to tend to, such as who can take a few photos to capture the unique event.

The cheekily named "Amtrak Alliance" is just the latest example of the spirit of collaboration – this one with prostate cancer researchers just a train ride away at Johns Hopkins – of which Dr. Knudsen, also Chair for the Department of Cancer Biology, the Hilary Koprowski Endowed Professor of Cancer Biology, Urology and Radiation Oncology, and leader of the Sidney Kimmel Cancer Center Prostate Program, is a huge proponent. Notably, Dr. Knudsen leads one of only eight National Cancer Center-designated Prostate Cancer Programs in the U.S.

"I think our motto should be 'we play nice with others,'" says Dr. Knudsen. "And it's been good for all of us. Patients and donors don't want to hear, 'Oh, we can only do this research for Jefferson.' They want to hear that you're willing to do whatever it takes to improve care and save lives. The 'Amtrak Alliance' is our testament to the fact that we completely believe in that."

### 'Group Think'

That's just one testament. The Greater Philadelphia Prostate Cancer Working Group, also a brainchild of Dr. Knudsen, is another. She formed the group in 2008, seeing a need for collaboration among institutions throughout Philadelphia in order to achieve better outcomes. This multi-institutional think tank comprises senior basic scientists, translational researchers and clinicians from Jefferson, Drexel University College of Medicine, University of Pennsylvania School of Medicine, Lankenau Institute for Medical Research, Wistar Institute, Fox Chase Cancer Center, University of Delaware and Sheba Medical Center. The group is dedicated to the prevention, diagnosis, management and cure of prostate cancer.

"I'm a big believer in team science, both within Jefferson and beyond," Dr. Knudsen says. "Any deficit you have within your own program you can invariably make up for by teaming up with a group within the city. I think it's come down to the point where there's no expertise I can't find within the working group we now have."

Indeed. Active members have expertise in all aspects of prostate cancer, including hormone signaling, detection/diagnosis, imaging, tumor progression and clinical management. The group meets monthly to critique grant proposals, review clinical trials and develop strategies to prevent, detect and treat prostate cancer. Collaborations within the group have resulted in new advances in understanding disease progression, acquisition of external funds necessary for project development and commencement of preclinical studies designed to improve therapeutic outcomes.

"This has advanced the pace of the science for everybody involved," says Dr. Knudsen, who was recruited to Jefferson in 2007 after a successful career at the University of Cincinnati College of Medicine.

Dr. Knudsen's research interests focus on the mechanisms by which androgen governs prostate cancer growth, pathways that deregulate this process in disease progression and the influence of both environmental and genetic factors on therapeutic response.







A multidisciplinary 'blend' of oncology experts, including Karen Knudsen, PhD, Leonard G. Gomella, MD, Adam P. Dicker, MD, PhD, and Wm. Kevin Kelly, DO, meet weekly over a cup of joe to exchange ideas about new prostate clinical trials and more.

What's really intriguing about prostate cancer, she says, is testosterone. "Testosterone is the bad guy. It's the thing that tells prostate cancer cells to go and grow, and that's how you treat patients. Destroying testosterone is the treatment for metastatic prostate cancer."

Taking her "team science" approach further, Dr. Knudsen recently initiated a weekly Prostate Cancer Program Leader's "coffee klatch" with Jefferson colleagues Leonard G. Gomella, MD, Chair of Urology and co-lead of the Prostate Cancer Program; Wm. Kevin Kelly, DO, Director of Solid Tumor Oncology; Adam P. Dicker, MD, PhD, Chair of Radiation Oncology; and Drexel's Alessandro Fatatis, MD, PhD. The Prostate Coffee Club, a multidisciplinary blend of oncology expertise, meets at 7:30 every Tuesday morning at

the Starbucks® near Jefferson. As Dr. Knudsen puts it, "ideas germinate there and priority items percolate out." In fact, the "Amtrak Alliance" took shape there, perhaps over a caramel macchiato or two.

Meetings last no more than an hour and feature quick exchanges. Clinical trial ideas are often hatched.

"I don't know why, but that environment is great," Dr. Knudsen says. "There's something about it being first thing in the morning. Maybe there's magic because it's not on any one person's turf – it's not my meeting, it's not the urologist's meeting, it's the meeting."



# Fighting Prostate Cancer on Two Continents

It seems especially fitting that Kosj Yamoah, MD, PhD, was among the 2014 recipients of the *Young Investigator Awards*, presented by the Prostate Cancer Foundation (PCF). Dr. Yamoah, Chief Resident, Department of Radiation Oncology at Jefferson, has been a young investigator nearly all his life. At the age of 7, he became the youngest person ever to enter high school in Ghana. He began college at 13, and by the time he was 17, was pursuing a career in medicine at the University of Ghana Medical School.

"I had a unique academic trajectory," Dr. Yamoah, the 2014 J. Eustace Wolfington PCF Young Investigator, says modestly. "I've always had an interest in medical research, and that's what brought me to the United States."

## About That DNA...

Receiving the *Young Investigator Award* from an organization like PCF, which funds the best and brightest prostate cancer researchers in the country, is testament to the significance of Dr. Yamoah's research that shows that African-American men are one population that may be harmed by new guidelines that favor observation over treatment of early-stage prostate cancer. Prostate cancer is notoriously variable, but recent research has identified significant differences in the frequency and expression of various genes and biomarkers that may be racially based.

As the majority of genetic analyses have focused on prostate cancer in men of European

descent, Dr. Yamoah aims to identify DNA-based biomarkers of aggressive disease in men of African descent. His work will provide critical insight into the factors contributing to increased mortality rates among African-American patients with cancer.

But Dr. Yamoah believes his research can help identify people at risk in wider populations as well. Such was the case in 1994, when the link between BRCA1 and BRCA2 mutations and breast and ovarian cancer was discovered. Later, additional studies with DNA samples, originally donated for Tay-Sachs disease research, revealed that people of Ashkenazi-Jewish heritage are more likely to have mutations in these genes than members of the general population. A woman's risk of developing breast and/or ovarian cancer is greatly increased if she inherits a harmful mutation in the BRCA1 gene or the BRCA2 gene.

Dr. Yamoah hopes his research will "help identify a pathway where a biomarker signature will not only help find African Americans who are at high risk for prostate cancer, but will also translate to other races at high risk. So even though we're using race as a surrogate risk factor, the biology will help us understand aggressive disease in a broader scheme."

Such information is critical for the development of successful treatment plans, because individual tumor biology can indicate potential for disease progression and metastasis.

## Study Abroad

After two years of medical school in Ghana, Dr. Yamoah came to New York, attending the Icahn School of Medicine at Mount Sinai. There, he pursued the MD/PhD program and specialized in molecular biology with a research focus on the protein degradation that leads to cancer. He then completed a one-year internship at Morristown Medical Center in New Jersey. He published numerous papers along the way, established himself in the field of radiation oncology, and eventually became a U.S. citizen via the National Interest Waiver.

"So now, being a true African American," he laughs, "and seeing these disparities, is almost what propelled me to this area of work."





The Prostate Cancer Foundation Young Investigator Awards fund the best and brightest prostate cancer researchers in the country. Between 2013-14 Jefferson was honored to have four recipients: Matthew Schiewer, PhD, Nicole Simone, MD, Robert Den, MD, and Kosj Yamoah, MD, PhD.

Dr. Yamoah credits many mentors along the way, including Adam P. Dicker, MD, PhD, Chair of Jefferson's Department of Radiation Oncology, and Timothy Rebbeck, PhD, at the University of Pennsylvania.

His research has led Dr. Yamoah back to Ghana, where he now hopes to improve prostate cancer outcomes there. A recent study led by Dr. Yamoah examined prostate cancer diagnoses and treatment delivery in black men living in the West African region, with the hope of devising research strategies to help improve health outcomes. The research team plans to develop

treatment regimens tailored to the needs of Ghanaian men, which may differ from guidelines currently utilized in the U.S. and Europe to better address the disease burden and reduce mortality rates in Ghana.

"Prostate cancer is the second leading cause of mortality in Ghana," he said. "The connection with Ghana puts Jefferson in a strong position to not only impact that country in terms of cancer control, but also help us understand some things that will better the African-American community here. So it's a win-win partnership."



# A Game Changer



This past year, Jefferson and the Philadelphia Eagles celebrated 10 years of teaming up to Tackle Breast Cancer. This partnership has been a game changer—contributing significantly to Jefferson’s efforts to beat breast cancer.

The milestone was celebrated at the outset of the Eagles 2014 season, with a dinner gala at Lincoln Financial Field. “For 10 years, the Philadelphia Eagles and their fans have teamed up with Jefferson to Tackle Breast Cancer,” noted Stephen K. Klasko, MD, MBA, President and CEO, Thomas Jefferson University and Jefferson Health. “The organization has been extraordinarily generous in giving to Jefferson to support our work to care for patients with cancer and to develop better cancer treatments.”

Dr. Klasko presented Eagles President Don Smolenski with the *Spirit of Commitment and Leadership Award* to recognize all the organization has done and continues to do to fight breast cancer. The Eagles have raised over \$1.5 million for breast cancer research.

The Philadelphia Eagles have been exemplary citizens of our community and longtime partners of the Sidney Kimmel Cancer Center at Thomas Jefferson University. Their commitment to giving back to Philadelphia – by supporting our Cancer Center and many other charitable and civic initiatives – is an inspiration to the whole community.

Each year, to kick off breast cancer awareness month, more than 100 Jefferson volunteers attend an Eagles game to sell pink Eagles hats to raise money for breast cancer care and research, and hand out pink rally towels to fans. The team’s support of Breast Cancer Awareness Month and of the Jefferson-Philadelphia Eagles Breast Health Center has enabled us to perform more than 40,000 breast-imaging exams annually – making Jefferson the busiest center in the region, and optimistically, the busiest one in helping to save lives.



Ted Popp, Jr., Uveal Melanoma Patient Advocate,  
Connie Popp, Swoop, Stephanie Bonham, Ted Popp, Sr.

Eagles Tribute Dinner Co-Chairs,  
Joseph Weiss, Sharon Pinkenson and  
Antony and Jamie Joffe





# TACKLE CANCER with Jefferson

About one in eight American women will develop breast cancer in her lifetime. It's the toughest, most personal battle you may ever face – but you don't have to face it alone. Jefferson's comprehensive approach to breast care will reinforce your personal strength and determination with the highest levels of expert quality care. Our services include the most advanced imaging and screening techniques, genetic testing, medical and radiation oncology, breast surgery, follow-up care and more. To tackle breast cancer, choose Jefferson for your team.

**Jefferson.edu/Breast      1-800-JEFF-NOW**  
Center City Philadelphia and South Philadelphia



**Sidney Kimmel  
Cancer Center™**  
at Thomas Jefferson University  
NCI-designated



*Tackling Breast Cancer*



Jefferson volunteers selling Tackling Breast Cancer hats and T-shirts at Lincoln Financial Field



Stephanie Stahl, Reporter for CBS 3/CW Philly 57, Stephen K. Klasko, MD, MBA President and CEO, Thomas Jefferson University and Jefferson Health, Don Smolenski, President, Philadelphia Eagles, and Richard G. Pestell, MD, PhD, MBBS, FRACP, Professor, Department of Cancer Biology



Michael Fischette, Charis Gehret Fischette, Swoop, Devyn Gehret (Chair, SKCC Next Generation Committee) and Charles Gehret



Edith Mitchell, MD, FACP

## Facing the Enemy

For those facing an uneven battle against cancer, there is one determined Jefferson physician who has relentlessly taken up the cause. And as a former U.S. Air Force Brigadier General (the first female physician to be named as such), Edith Mitchell, MD, FACP, is up to the task of fighting for underserved populations facing the disease. In 2012, she led researchers and clinicians at the Sidney Kimmel Cancer Center to establish the Center to Eliminate Cancer Disparities.

As the Center's Director and Clinical Professor of Medicine and Medical Oncology at Sidney Kimmel Medical College, Dr. Mitchell leads research on a range of cancers, waging combat on behalf of those special groups within Jefferson's nearby urban and suburban communities that are at highest risk of developing the disease.

### Serving the Underserved

Whether it's the local Asian-American community, young people, African Americans, women or other diverse groups, Dr. Mitchell and her fellow researchers at the Center delve deeply to identify the health needs and disease prevalence of diverse populations – and then zero in on how those needs can be met. Currently, the Center is focusing its research on three types of cancer and supporting a project that enables women who are financially challenged to more easily access screenings for two cancers found to be treatable, if detected early.

Here are the major areas of research:

- For women afflicted with the deadliest form of breast cancer – triple-negative breast cancer – the current treatment is chemotherapy, which has a lower percentage of success than with other variants of the breast disease. With highly involved lab procedures under investigation, the Center is at work developing other possible treatments and ways to better evaluate tumors to determine other targets.
- The Center's Healthy Women's Project reaches out to women at a financial disadvantage, giving them access to free screenings for breast and cervical cancer – two cancers for which screenings have been found by the National Cancer Institute to significantly offset death rates.
- With the knowledge of a disturbing trend – the increase in colon cancer in younger people

by two percent annually for the last 10 years – research at Jefferson is underway to determine if age-related molecular, biological and clinical factors could play a part in treatment – and if a different course of treatment is needed than that given to older patients (traditionally the average age of the population contracting the disease is 69).

- Prostate cancer research that includes the identification of significant differences in the frequency and expression of various genes and biomarkers associated with cancer in men of African descent. This group is often diagnosed with prostate cancer at younger ages than their white or Asian counterparts, and the cancer has been proven to be more aggressive.
- Why are Asian Americans in the nearby neighborhood suffering from liver cancer more than any other one population group? The Center is working with a team of laboratory investigators to enhance screening and to determine more effective treatment options.

### Taking it on the Road

With more than 30 years of global health knowledge and extensive travels in the worlds of medicine and the military, Dr. Mitchell leads the charge even beyond the laboratory, bringing news about the Center's groundbreaking research and new life-saving tests and treatments through presentations nationally and internationally. She also embraces the opportunity to spread the word through her leadership positions with the American Society of Clinical Oncology, the National Medical Association (its 2015 president-elect), the *Journal of the National Medical Association* and others.

And spreading knowledge is the starting point to winning the battle.

"The first step in eliminating cancer disparities is to raise awareness through public and professional education about what resources are available to these groups in their fight against cancer," said Dr. Mitchell. "At Jefferson, we're approaching the battle on two fronts: education and research."

With the support of funding from organizations also dedicated to making a positive difference, the fight continues.





Since 2008, 'Get Your Rear In Gear Philadelphia' (GYRIG) has been supporting the important work of the Sidney Kimmel Cancer Center and the Department of Surgery as they care for patients with colon cancer. Accepting the most recent donation from GYRIG Executive Director Maria Grasso (third from left) and her brother, Mark Hepperlen, (second from right) are Lara Allan Goldstein, AVP, Institutional Advancement; Scott Goldstein, MD, Director, Division of Colorectal Surgery; Edith Mitchell, MD, FACP, Director, Center to Eliminate Cancer Disparities; and Elizabeth A. Dale, EdD, EVP, Institutional Advancement.

## Meet the Army of Supporters

The need for research into the growing incidence of colon cancer in the young has found a champion in Maria Grasso, Executive Director of "Get Your Rear in Gear Philadelphia," supported by the Colon Cancer Coalition. While colon cancer has decreased by 30 percent in older adults (particularly those over 65) due to increased use of colonoscopy over the past 10 years, disturbingly, it is rising by two percent a year in the younger segment of the population. Researchers at the Center to Eliminate Cancer Disparities are using the vital funding from Maria's organization to investigate whether age-related differences could warrant a different treatment that is more effective for this age group.

"My father was diagnosed with Stage IV colon cancer at Jefferson in 2004," said Maria, who founded "Get Your Rear in Gear" (GYRIG), with an annual run/walk to raise awareness and funds to help fight colon cancer.

"While my dad only lived 10 months after diagnosis, the care he received at Jefferson was second to none. The personal attention given to patients and families during these most difficult of times is so important. After starting GYRIG Philadelphia in 2008 we decided to support both the Sidney Kimmel Cancer Center and the Department of Surgery so they can continue to offer their superior services and support to other families with loved ones battling colon cancer."

### 'Boots on Ground'

Other groups supporting Dr. Mitchell and the Center for Cancer Disparities include the Centers for Disease Control and Prevention and the Commonwealth of Pennsylvania's Healthy Women's Project. With support from these organizations, the Center is able help stem the tide of two types of cancer – breast and cervical. Screening for these cancers has been proven to save lives, yet women who are financially challenged and don't have health insurance may skip testing in lieu of other life needs.

Since 2008, the Center has reached out to provide free screenings to this at-risk group. Over six years, the Healthy Women's Project has tested more than 1,400 women, leading to some cancer diagnoses. Data gleaned from these ongoing screenings is supplied to the CDC to help the organization maintain an accurate knowledge base that reflects the screenings' impact on survival.

The Center also works with the National Cancer Institute and the renowned ECOG/ACRIN Cancer Research Group—a multidisciplinary, membership-based scientific organization that designs and conducts biomarker-driven cancer research involving adults who have or are at risk of developing cancer.







Takami Sato, MD, PhD

## In the Blink of an Eye

The word melanoma is unlikely to make most people think of their eyes. Yet, uveal melanoma is one of the most dangerous eye cancers in adults because it doesn't respond to conventional chemotherapy regimens like other cancers. The disease returns and metastasizes in half of all cases in which the primary tumor was successfully treated. On average, a patient whose disease has spread to the liver survives from one and a half to two years after the metastasis is confirmed. This is a significant increase in survivorship from just two years ago when life expectancy was six months. Although the incidence of uveal melanoma is rare – affecting six or seven people in every million – it is the most common primary cancer in the eye. Yet the expertise and therapies available to fight it are limited.

### Seeking Treatment From Afar

Takami Sato, MD, PhD, the first K. Hasumi Professor of Medical Oncology at the Sidney Kimmel Cancer Center at Thomas Jefferson University, has spent his career studying and treating uveal melanoma metastasis. In collaboration with physicians from Wills Eye Hospital and Jefferson's interventional radiologists, David Eschelman, MD, and Carin Gonsalves, MD, Dr. Sato and his team have been able to translate promising research into clinical treatments that suppress the spread of uveal melanoma cancer cells and extend life. Encouraged by Dr. Sato's outcomes, two-thirds of patients travel from outside of the tri-state area to benefit from his wide range of therapies – establishing Jefferson as a national referral center.

Dr. Sato is best known for the development of liver-directed treatments for uveal melanoma, including immunoembolization. Jefferson is the only institution to offer this therapy, which can

increase survival from only a few months to almost two years. Immunoembolization involves injecting drugs called cytokines directly into the arteries supplying the liver to stimulate or modulate immune responses, and is combined with deliberate blocking of the hepatic artery, known as embolization. Approximately 400 liver-directed treatment procedures are performed annually for uveal melanoma patients with hepatic metastasis at Thomas Jefferson University Hospitals.

Dr. Sato has also teamed up with Jefferson's Andrew Aplin, PhD, whose lab has consistently garnered national recognition and scholar awards for its work in the field of melanoma research. Drs. Sato and Aplin's approach employs a search-and-destroy drug therapy that targets and disables cancer cells' primary and secondary signals, inhibiting growth and causing cells to die.

"Our ability to improve the prospects for patients with metastatic uveal melanoma is due in part to our partnerships with fellow research labs that share a common passion for working towards better cancer immunotherapies, both here at Jefferson and as far away as Japan. We are consistently challenging and supporting each other to enhance the lives of our patients by developing innovative treatments," says Dr. Sato.

Each of Dr. Sato's clinical trials builds on the advancements achieved in the previous one, allowing for new treatments to become available and progressively improving the prognosis of each new uveal melanoma case. His research is enriching the lives of patients in a real and very practical way, every day.

Uveal melanoma moves quickly, and so must the work of Jefferson researchers to save lives.





## Changing the Course of Cancer

The great irony of uveal melanoma is that it often goes unseen—until the stakes are highest for patients, who typically have minimal knowledge of the disease with little time to fight for their lives. Ted Popp, Jr., and Terry Willoughby are two patients who faced this same dilemma, traveling from Texas and Kansas to benefit from Dr. Sato's expertise.

Motivated by their own positive experiences with Dr. Sato's life-saving treatments, both Ted and Terry became significant donors to funding the fight against uveal melanoma, even producing an educational video for Jefferson (see [advancement.jefferson.edu/sato](http://advancement.jefferson.edu/sato)) about this devastating cancer with the hope of compelling others to contribute to the advancement of Dr. Sato's research.

"We each have a profound opportunity to change the course of this cancer by writing a check and raising awareness," says Ted Popp. "The donations that we provide are desperately needed and can be put to immediate use by researchers to fund the fundamental research necessary to identify treatments for this disease. We can help position researchers and care teams for success by keeping this cancer in the spotlight, subsequently brightening the outlook for uveal melanoma patients everywhere."

**"We have a profound opportunity to change the course of this cancer."**

For Terry Willoughby, finding out the "why's" behind clinical trial successes is important.

"Dr. Sato is on the verge of something really big," says Terry. "If he has the funds to continue discovering why the clinical trials are working for us, then he can help more people. Research is really the key to curing uveal melanoma."



(Above) Husband Russ Willoughby and uveal melanoma patient Terry Willoughby aren't giving up the fight to find a cure for this rare and dangerous form of eye cancer. The clinical trial Terry is enrolled in is working. For her, the bigger question is, why? The answer may someday lead to a cure.

(Left) Patient Ted Popp, Jr.'s mission is to keep uveal melanoma in the spotlight by raising awareness and important research funds. He and Terry are so committed they created an educational video for Jefferson on this rare cancer to compel others to advance Dr. Sato's research.





Neal Flomenberg, MD

## Match Game

Some people take their birthday off. Some spend it doing something special. On September 20, 1995, medical oncologist Neal Flomenberg, MD, spent his birthday on the job, doing something very special – performing the first-ever bone marrow transplant as part of Jefferson’s Bone and Marrow Transplant (BMT) Program – an initiative he and his colleagues established.

Today, Dr. Flomenberg is Chair and Professor of Jefferson’s Department of Medical Oncology, as well as the Sidney Kimmel Cancer Center’s Clinical Deputy Director. This year, his birthday will mark the 20th anniversary of Jefferson’s BMT Program. To mark the occasion, he’s planning a special celebration.

“We’ll invite all available surviving Jefferson BMT patients and their families,” says Dr. Flomenberg. “We’re going to celebrate and draw strength from each other.”

### The Region’s Highest Survival Rates

Since its inception, Jefferson’s BMT Program has completed more than 1,000 bone marrow transplants, with increasingly impressive outcomes. These include the region’s highest actual one-year patient survival rates, according to National Marrow Donor Program Center Specific analyses for 2013 and 2014.

Especially remarkable are our outcomes for patients with only half-matched (haploidentical) related donors (usually siblings). Since 2006, Dr. Flomenberg and his team have performed more than 200 transplants on these higher-risk patients utilizing a “two-step” approach they developed over the course of several clinical trials at Jefferson. Patients in these trials who were transplanted while their leukemia was in remission have demonstrated a projected overall

survival of 75 percent three years later. In fact, many of them have survived since 2006, when Jefferson first originated two-step transplantation.

“Jefferson is the only institution in the nation that’s using the two-step procedure,” says Dr. Flomenberg. “And our outcomes are as good as or even better than anything that’s been published anywhere in the haploidentical transplant field. In fact,” he emphasizes, “half-matched transplants can now generate outcomes that are every bit as good as fully matched transplants.”

The two-step procedure has also benefitted physically fit senior patients who were without a fully matched related donor. In one of the initial trials at Jefferson, the median age of the patient was 67 years, which is far older than most reports of reduced intensity regimens at other institutions.

### Modern Family

Human leukocyte antigen (HLA), a protein – or marker – found on most cells in bodies, is used to match patients with donors for blood and marrow transplants. Traditionally, the best transplant outcome occurs when a patient’s HLA and the donor’s HLA fully or closely match. Half of everyone’s HLA markers are inherited from their mothers and half from their fathers. Each brother and sister has a 25 percent, or one in four chance of matching a transplant patient if that patient has the same biological mother and father. The more brothers and sisters with the same mother and father that a patient has, the greater that patient’s chances are of having a suitably matched donor.

“The issue of what to do about patients without fully matched donors has increased significantly since the first bone marrow transplantation in

**“Families are becoming more nuclear. The divorce rate is high, the number of single-parent families is growing, and so is the number of patients who have more half-siblings than full siblings. That has driven our development of the two-step approach.”**

— Neal Flomenberg, MD



leukemia patients was reported in 1979,” says Dr. Flomenberg. “Families are becoming more nuclear. The divorce rate is high, the number of single-parent families is growing, and so is the number of patients who have more half-siblings than full siblings. That has driven our development of the two-step approach.”

### Timing Is Everything

In traditional bone marrow transplants, patients receive chemotherapy to treat the underlying malignancy before being infused with donor T-cells and then stem cells. The patients receive immune suppressive drugs to prevent graft-versus-host disease (GVHD), a life-threatening complication after transplant. This can weaken the patient’s immune system, which may cause infections and even secondary cancers.

In the BMT approach developed at Jefferson, however, chemotherapy drugs are administered after the introduction of T-cells but before stem cells. This alteration in timing kills GVHD cells but spares cells that restore normal bone marrow function.

“The beauty of this approach is that it’s within every institution’s grasp, regardless of its access to advanced technologies,” Dr. Flomenberg notes. “All we’ve really altered is the timing of the application of chemotherapy. The other advantage, of course, is that it increases the number of potential candidates for successful transplants.”

### From Vanilla to Chocolate Chip

The two-step procedure for blood and marrow transplants is a quintessential example of a promising new cancer treatment developed by Jefferson physicians and scientists through a series of clinical trials. Dr. Flomenberg and his team are currently performing additional clinical trials to try out variations that may further improve the two-step approach. For example, they’re currently investigating whether waiting a bit longer following chemotherapy before transplanting immune stem cells might be advantageous in terms of killing off more cancer cells and reducing the chances of relapse after transplant. In the future, more effective drugs



for chemotherapy may be introduced. But these are incremental tweaks, he insists – the fundamentals of the procedure are set.

“A good clinical trial to me is like chocolate chip ice cream,” suggests Dr. Flomenberg. “Standard treatment is like vanilla; a trial is mostly vanilla, but as we go along, we tweak the procedure just a little bit, like adding chocolate chips to vanilla ice cream. It’s not a radical change in treatment, like going from vanilla to say, tutti-frutti. It’s a subtle change. So, our patients certainly need not fear clinical trials, which we generally conduct to test thoughtful and incremental changes to a proven therapy.”

Although several months away, Dr. Flomenberg is already eagerly awaiting the 20th anniversary reunion party for Jefferson’s BMT program.

“I anticipate that celebrating with patients and their families that we have been able to help and honoring the memory of those who played such heroic roles in making longer survival rates possible for so many will be the best birthday present I ever receive.”

Neal Flomenberg, MD, receiving a check from donor Jack Biddulph at the foundation's most recent golf tournament.



## The Program's Real Heroes

Andrea Bartolomeo was in her early 20s when she became Dr. Flomenberg's first two-step transplant patient in late 2005. Following transplant, she survived for a year and a half before succumbing to recurrent leukemia. Andrea's participation laid the groundwork for the many subsequent survivors of Jefferson's two-step clinical trials. Her absence will be felt – and her spirit celebrated – especially keenly at this year's 20th anniversary party for the BMT Program.

"Andrea was a sweet young woman," recalls Dr. Flomenberg. "She was very gentle on the outside but had true grit on the inside. I'd like her parents to know what a hero she was, blazing the way for our other patients. I'd like to tell them, in front of a room full of survivors, 'These are all people who Andrea helped and touched. They are your daughter's legacy!'"

**"I was determined to do something so other families did not have to go through what we did."**

Two more heroes in Dr. Flomenberg's estimation are Jack and Roseanne Biddulph, who, for the past 14 years, have organized an annual golf tournament in memory of their son, Patrick Shane Biddulph, to raise money for the BMT Program. Through the Patrick Shane Biddulph Foundation, Jack and Roseanne have raised more than \$187,000 to support BMT research.

"Patrick was not transplanted at Jefferson," Jack Biddulph explains. "After his procedure, he developed graft-versus-host disease, which

led to his passing. Roseanne and I looked around for an institution that was doing research in preventing this disease. Our research kept leading us to Jefferson and to Dr. Flomenberg. We knew we made the right choice. Patrick's passing was devastating for us, and I was determined to do something so other families did not have to go through what we did. We have taken that personal tragedy and turned it into something positive. We're not especially wealthy people, but through hard work, we've raised a substantial amount for Jefferson's BMT Program. We know that it's very much appreciated and that we are making a difference."



## Reasons to Believe

Pancreatic cancer incidence has been slowly rising over the past decade or so while other cancers have been declining. The American Cancer Society estimated about 46,420 new cases in 2014.

"Pancreatic cancer is a major life event and stressor for patients," acknowledges Charles J. Yeo, MD, the Samuel D. Gross Professor and Chair of the Department of Surgery at Thomas Jefferson University and Hospitals and Co-Director of the Sidney Kimmel Cancer Center's multidisciplinary Jefferson Pancreas, Biliary and Related Cancer Center. "Nevertheless, we have guarded enthusiasm in the field – there is much to be excited about."

Dr. Yeo's view is highly credible. His career is filled with major accomplishments in surgical education, clinical care of patients with complex gastrointestinal tract diseases and molecular research. As an author and editor, he has made significant contributions to surgical literature and his design and completion of numerous prospective randomized clinical trials have dramatically impacted the field of pancreatic surgery.

Dr. Yeo's leadership of large teams of physicians and scientists has generated much new

knowledge relevant to the early detection, screening, categorization and therapy of pancreatic and related types of cancer. He was instrumental in organizing the Jefferson Pancreas, Biliary and Related Cancer Center, which offers a comprehensive approach vital to treating cancers of the pancreas, bile ducts and other anatomically related tumors.

Jefferson's multidisciplinary center enables patients to benefit from the collective expertise of specialized surgeons, oncologists, gastroenterologists, endoscopists, radiologists, pathologists, pain specialists, pharmacologists, molecular biologists, molecular geneticists and others who share a commitment to reducing the burden of disease.

### Enhancing Chances for Early Detection

Early detection of pancreatic abnormalities and accurate diagnosis are paramount to treating cancer at a curable stage. But early pancreatic cancer often does not cause any signs or symptoms. By the time it does, it's often already grown locally or spread beyond the pancreas.

Jefferson gastroenterologists are using a new state-of-the-art endoscopy suite that allows for superior visualization of the disease. One area of particular research interest is the use of



A little rain this day couldn't keep some of our docs away. Isidore Rigoutsos, PhD, Jonathan Brody, MD, Charles Yeo, MD, and medical student, Geoffrey Kozak helped raise important research funds during the annual Pancreatic Cancer Action Network's Purple Stride Philadelphia Walk. Dr. Yeo served as the 2014 Honorary Chair for the walk.



endoscopic ultrasound-guided fine needle aspiration to obtain tissue samples from the pancreas and surrounding areas to determine if subtle radiographic abnormalities are benign, precancerous or true cancer. When a patient with a pancreatic abnormality undergoes a needle aspirate that is equivocal, the Jefferson pancreas and biliary team analyzes the fluid for abnormal DNA that can help with the diagnosis and treatment of early pancreatic cancer.

### **Surgical Technique and Experience Improve Outcomes**

Dr. Yeo and fellow surgeons perform more than 200 pancreatic resections annually, which include more than 125 Whipple and mini-Whipple procedures. The Whipple procedure is a major surgical operation involving removal of portions of the pancreas, bile duct and duodenum, and is typically performed to treat malignant tumors involving the pancreas, common bile duct, ampulla or duodenum.

Research is pointing more and more to the importance of surgical volume in developing expertise in complex procedures and reducing perioperative mortality and morbidity. Jefferson's large patient volume for pancreatic resections, more than any other hospital in Pennsylvania, results in better outcomes. Our complication rate for the Whipple operation falls in the lowest 10 percent by the measure of the American College of Surgeons' National Surgical Quality Improvement Program.

"We use the mini-Whipple whenever possible," notes Dr. Yeo, who helped to pioneer its development. "Unlike a 'classic' Whipple procedure, this modified resection preserves the entire stomach and pylorus. Other upsides include shorter hospital stays and fewer complications."

At our National Cancer Institute (NCI)-designated Sidney Kimmel Cancer Center, Jefferson offers a full range of innovative medical therapies and new approaches to combining therapies.

Patients have access to the latest treatments that can help improve surgical success and boost the effectiveness of standard drugs. Two examples of therapies at Jefferson under investigation:

- The APACT trial, which randomizes patients with pancreatic cancer post-resection to the standard drug gemcitabine vs. gemcitabine plus nab-paclitaxel.
- Trial NLG-0505, which is designed for patients with locally advanced or borderline disease, and offers modern chemotherapy with or without a pancreas cancer vaccine.
- In the case of bile duct cancer, Jefferson gastroenterologists have one of the largest experiences in the U.S. in treating tumors with photodynamic therapy and radiofrequency ablation. Using locally ablative treatments, physicians have been able to downstage, or reduce the size of tumors so that patients can undergo surgery, improve bile flow to remove percutaneous drains and extend life.

### **Repository for the Future**

Dr. Yeo also helped to establish the Jefferson Pancreas Tumor Registry, focused on identifying genetic, environmental and occupational risk factors for pancreatic and related cancers. The registry serves as a repository for tumor tissue and DNA samples collected from patients, patient data on occupational and environmental exposures such as tobacco smoke and chemicals, and detailed family histories. These elements drive Jefferson's basic science program to study the biology, causes and treatments for pancreatic and related cancers. Among the research projects underway are studies on the genetics of the disease, the cancer cell cycle and mechanism of cancer resistance to chemotherapy.

"Taking care of patients today is very gratifying," Dr. Yeo concludes. "But the contributions of more than 400 patients and family members who are already part of the Jefferson Pancreas Tumor Registry will inform patient care for decades to come."



Donor Bob Halinski honored his wife, Mary, by setting up a fund to support pancreatic cancer research.

## Raising Awareness, Support and Hope

Jefferson is a leader in rapidly applicable “bench-to-bedside” research resulting in better treatments and new surgical techniques that improve survival rates for patients with pancreatic cancer. But more research and advocacy are needed. Fortunately, generous people like Bob Halinski have stepped up with their support.

As a widower, Bob has experienced that generosity in a very powerful and personal way. He set up a fund to support Jefferson’s research in pancreatic cancer to honor the legacy of his wife, Mary, who had been a patient here.

“Mary believed in Jefferson and was grateful for the compassion that they showed, so I set up the fund to continue her support,” says Bob. “A year after her passing, I had a personal epiphany – I realized I was doing much better than I thought I would ever be able to do. I think in large part that was because of giving to Jefferson and what came of that. There was so much positivity given to me – people wanting to support and honor Mary and giving to the Jefferson fund to aid in their research efforts. There was so much kindness there. I think it was helpful to me in the healing process. I think that’s why, a year later, I’m actually doing pretty well.”

Dr. Yeo himself drew additional support for Jefferson in 2014 when he served as honorary chair of the Pancreatic Cancer Action Network’s Purple Stride Philadelphia annual walk. He and 23 team members from Jefferson’s faculty and the Gibbon Surgical Society were on hand in Fairmount Park to raise money and awareness for pancreatic cancer. Jefferson’s team surpassed its fundraising goal to help the organization advance research, support patients and create hope.

**“Mary believed in Jefferson...  
so I set up the fund to continue  
her support.”**

# Population Matters

Understanding what motivates people to make decisions about taking actions that will affect their health is challenging science. Just ask behavioral epidemiologist Ronald E. Myers, PhD, Professor and Director of the Division of Population Science in the Department of Medical Oncology.

"We've been working out answers to those questions in diverse populations for the 20 years that I've been at Jefferson," says Dr. Myers. "We've encouraged people to take well-informed actions that can alter their health risk. As a result, we can move forward in earnest with a program that has the potential to improve the health and well-being of many more individuals."

Dr. Myers is referring to the formal establishment of a Population Science Program within the NCI-designated SKCC. The Population Science Program seeks to identify factors that affect the risk for cancer and the response to therapy, and to develop interventions that decrease risk, improve the quality of personalized treatment and eliminate disparities in cancer care and patient-centered outcomes.

## Time to Engage

The SKCC is a consortium cancer center that involves researchers at Drexel University and Lankenau Institute for Medical Research. Adding the Population Science Program to existing basic and clinical science programs will enable Dr. Myers and his colleagues to accelerate their efforts in cancer prevention and control.

"The new Population Science Program," says Dr. Myers, "will increase our faculty, broaden our expertise, generate new research and expedite our efforts to bring new discoveries into routine care to engage and benefit populations in Greater Philadelphia and beyond."

Dr. Myers is also Associate Director for Population Science for SKCC and partners with his colleague, Ann C. Klassen, PhD, who is SKCC's Associate Co-Director of Population Science and Professor and Associate Dean for Research at Drexel University's School of Public Health. Together, the two organizations are connecting groups of researchers with a shared purpose and are

also focusing their efforts on education and community engagement in cancer prevention and control. None of this would have been possible if the institutional leaders had not taken the bold step of defining population science as a critical component of Jefferson's vision for achieving quality health care for all.

## A Call to Action

Dr. Myers's areas of expertise in Population Science include patient adherence to cancer screening, physician follow-up of abnormal cancer screening test results, informed decision making in cancer susceptibility testing and cancer clinical trials participation. During his two decades conducting cancer prevention and control research at Jefferson, he has been a principal investigator on numerous peer-reviewed research grants and has produced more than 100 peer-reviewed publications in the field.

One study led by Dr. Myers established that among the general population, receipt of a reminder by phone or mail to get screened for colorectal cancer significantly increases the likelihood that people will do so. Dr. Myers' research team performed a randomized, controlled trial of 945 people aged 50-79, who were patients in primary care practices. Patients who received a mailed screening kit and a follow-up telephone call to navigate, or instruct them, in the usage of the kit, were almost three times as likely to undergo screening six months later compared to those who received usual care. The study results were published in the January 2013 issue of *Cancer Epidemiology, Biomarkers and Prevention*, a journal published by the American Association for Cancer Research.

Subsequently, Dr. Myers led another study regarding colon cancer screenings – this one funded by the American Cancer Society and targeted solely at the African-American population. The study showed that sending a screening kit and making navigational telephone calls were highly effective at increasing screenings among African Americans. This finding is important because colon cancer screening rates are substantially lower among this group as compared to Caucasians – resulting in higher cancer mortality.





Translating this intervention into routine care could have a major impact on reducing these disparities. These study results will be published in an upcoming issue of the *Journal of the National Cancer Institute*.

Now, Dr. Myers and his team are beginning a similar study among Hispanics, another population that has relatively low colon cancer screening rates. This study, funded by a Patient-Centered Outcomes Research Institute (PCORI) grant, will test the impact of adding information to the mailed screening kit and navigation intervention to support recipients' informed decision making in screening participation.

Dr. Myers feels tremendous personal satisfaction in seeing Population Science grow at Jefferson.

"When I left the Peace Corps 40 years ago, I wanted to knit together my interests, knowledge and training in health policy analysis, medical sociology and epidemiology as well as my education and experience in immigrant, race and ethnic relations into a career that had a chance of making a difference. At the time, no such clear career path existed at any academic institution. If you had those interests, you had to fashion your own educational program and take advantage of opportunities as they arose. Now, Jefferson has instituted a strong Population Science Program that can prepare the next generation of policy makers and researchers to make the world a better and healthier place."



Paolo M. Fortina, MD, PhD

# One Size Does Not Fit All

## Jefferson offers genomically informed therapy for individual patients

In Greek mythology, evil Procrustes lured weary travelers with the promise of a perfectly sized bed. Surprisingly, no one was an exact fit, so he made *them* fit the bed instead of vice versa, either by stretching or removing their legs!

Until recently, suggests Stephen Peiper, MD, the Peter A. Herbut Professor and Chair of Jefferson's Department of Pathology, Anatomy and Cell Biology, cancer treatment was a "Procrustean bed," administered arbitrarily. But the past several years have seen the dawn of precision – or genomically informed – medicine which is profoundly changing how we treat cancer.

"By combining genomic data with bioinformatics and clinical knowledge," explains Dr. Peiper, "the Sidney Kimmel Cancer Center at Thomas Jefferson University identifies suitable, effective therapy personalized to the genetic blueprint of an individual patient's tumor. Instead of a cookie-cutter approach to treatment, we apply genomics testing to give patients an accurate assessment of their individual disease risk and biology and then select the best options earlier in their care."

## Reading Genomic Letters

To appreciate the specificity of genomic testing, consider that the entire DNA contained in each organism's cells makes up that individual's genome, composed of billions of DNA letters.

"The letters in our genomes make words to communicate information just as the letters in books do," says Paolo Fortina, MD, PhD, Professor of Cancer Biology and Scientific Leader of the Cancer Genomics Laboratory at Jefferson. "Genomics is the study of the sequence of these letters in your DNA and how each string of letters passes information to help each cell in your body work properly."

"In Jefferson's Cancer Genomics Lab, we are able to read the information within an individual's tumor cells. Now and then, we may find a unique variation in the genomic letters that manifests itself as a form of cancer in that particular individual."

A changed letter in the genetic code can cause the cell to make a protein which prevents that

cell from functioning properly. Such proteins can make cells grow quickly and cause damage to neighboring cells. According to Dr. Fortina, studying the cancer genome may enable physicians to discover which letter changes are causing a cell to become a cancer, and as a result, select a suitable treatment, such as a medication already approved by the U.S. Food & Drug Administration (FDA) or one being tested in a clinical trial at institutions like the SKCC.

In addition, Dr. Fortina, in collaboration with a team led by Massimo Cristofanilli, MD, FACP, Professor of Medical Oncology, Director of the Jefferson Breast Care Center and Deputy Director of Translational Research at SKCC, is involved in isolating circulating tumor cells (CTC) from peripheral blood in patients with breast cancer. Doing so may help to develop a noninvasive approach to identifying molecular markers in CTC that would be predictive of disease progression.

In another study, Dr. Fortina is using genomics approaches to identify genes involved in agranulocytosis, a condition in which white blood cells are depleted. Agranulocytosis can occur in different forms of cancer after chemotherapy.

## Melanoma Activation

"When it comes to providing more precise and personalized therapy," notes Dr. Peiper, "we need modern and advanced tests because every tumor is different."

For example, Jefferson was the first academic medical center in the U.S. to offer the FDA-approved diagnostic assay that tests melanoma patients for the BRAF mutation (which occurs in about half of all cases) and ultimately determines if they'll benefit from taking the oral drug vemurafenib. Both the drug and its companion diagnostic test were developed by Roche Pharmaceuticals and approved in 2011 by the FDA after clinical trials showed that this medication significantly extended survival *only* in metastatic melanoma patients with the BRAF mutation.

"Melanoma is a deadly skin cancer, and the BRAF mutation test plays a pivotal role in our approach to it," says Dr. Peiper. "It allows us to quickly and



**“Instead of a cookie-cutter approach to treatment, we apply genomics testing to give patients an accurate assessment of their individual disease risk and biology and then select the best options earlier in their care.”**

**—Stephen Peiper, MD**



**Stephen Peiper, MD**

accurately identify Jefferson patients who will respond positively to vemurafenib.”

### **Targeting Lung Cancer**

Similarly, testing patients with non-small-cell lung cancer for the presence of certain somatic mutations, or genetic changes in their tumors, can help doctors select the right treatment with the best chance of success. Jefferson offers two such tests. One test identifies patients with mutations in the epidermal growth factor receptor (EGFR) gene who may respond positively to and benefit from the medications erlotinib and gefitinib. The other test reveals anaplastic lymphoma kinase (ALK) mutations, for which the chemotherapy drug crizotinib can be a lifesaver (see next page).

### **Prognosticating Breast Cancer**

In October 2014, Jefferson became the first academic medical center in the region, and one in a small, elite group in the nation, to perform the Prosigna™ Breast Cancer Prognostic Gene Signature Assay.

Prosigna uses a patient’s tumor resection and analyzes its genomic expression signature for 50 genes important to breast cancer growth and spread. It determines how much of each gene is expressed as RNA by the cancer, which helps predict whether the cancer is aggressive or not. The Prosigna software then combines the data from the genomic expression signature with information from a surgical pathologist about the size of the tumor and whether the lymph nodes are involved, in order to determine risk of recurrence.

“Prosigna enables us to grasp quickly how threatening the disease is and how likely it is to recur, so we can prescribe a course of treatment that is most likely to succeed,” says Dr. Peiper. “Being able to perform it here in Jefferson’s

Molecular & Genomic Pathology Laboratory significantly reduces turn-around time for test results, allowing patients to begin effective treatment sooner.”

### **More to Come**

Dr. Peiper adds, “We have put together a great team in clinical genomic oncology that will provide Jefferson oncologists with diagnostic information that offers a new approach to clinical trials. Therapy in these so-called ‘basket trials’ consists of agents targeted to specific genetic mutations that drive tumor behavior instead of the site of origin.”

Meanwhile, in Jefferson’s Cancer Genomics Lab, Dr. Fortina and his team, in collaboration with Isidore Rigoutsos, PhD, Director of the Center for Computational Medicine at SKCC, and his laboratory, are conducting research into RNA molecules that are not involved directly in coding for proteins. These non-coding RNAs are highly abundant, and their precise function is unknown; however, recent studies suggest they may play a critical role in cancer development and progression.

Dr. Fortina is also studying the role of epigenetics in cancer using genomics approaches. Epigenetics involves, for example, how changes in protein modification can influence the reading of the human genome and, additionally, how cancer evolves.

Ideally, the hard work of Dr. Fortina’s group will lead to discoveries that Dr. Peiper’s team will eventually be able to translate into advanced diagnostic tests and genomically informed medicine.



Jefferson X-ray specialist Nick Lamina with his wife, Caroline, and their daughters, Lauren (front) and Cara (back).



## Genomically Informed Care for a Jefferson Caregiver

As an X-ray specialist in endovascular neurosurgery at Jefferson Hospital for Neuroscience, Nicholas Lamina has helped to diagnose and treat patients with neurovascular conditions such as cerebral aneurysms and AVMs for 15 years. But in 2011, Nick himself became a Jefferson patient at the Sidney Kimmel Cancer Center, where a multidisciplinary team diagnosed and began treating him for adenocarcinoma of the lung, a type of non-small-cell lung cancer.

Early in 2012, Nick had a mediastinoscopy, a minimally invasive surgical procedure to extract a small amount of tissue from his lymph node. Leading-edge genomics testing of that tissue showed mutations in the anaplastic lymphoma kinase (ALK) gene. That inspired his Jefferson medical oncologists, Rita

S. Axelrod, MD, and Barbara Campling, MD, to prescribe him a twice-daily regimen of XALKORI (crizotinib). This targeted therapy had only recently been FDA-approved after a clinical trial had demonstrated its effectiveness in suppressing the effects of ALK rearrangements in tumors harboring this mutation.

Three months later, a PET scan revealed that Nick's tumors had shrunk to an infinitesimal size, and his lungs were pronounced "metabolically clear." Since then, he's been back at work and enjoying life with his wife and two young daughters. He commends Dr.

Peiper for making the test for ALK mutations available in his lab, as well as other "companion diagnostic" procedures that can determine patients' suitability for certain new and emerging treatments.

"My illness has given me a greater appreciation for what our patients experience," Nick says. "The support of my multidisciplinary Jefferson treatment team – that also includes neurosurgeons Pascal Jabbour, MD, and James Harrop, MD, radiation oncologist Maria Werner-Wasik, MD, and pulmonologist John R. Cohn, MD – has been wonderful. My family and I cannot find enough words to adequately thank them for all their work and dedication."

**"My family and I cannot find enough words to adequately thank them for all their work and dedication."**

“Yesterday I dared to struggle.  
Today I dare to win.”

— Bernadette Devlin

*Civil rights activist and the youngest woman  
elected to the British Parliament*

**Sidney Kimmel Cancer Network members include:**

---

- Aria Health
- Brandywine Hospital
- Delta Medix
- Einstein Medical Center Philadelphia
- Hematology & Oncology Associates of Northeastern PA PC
- Holy Redeemer Hospital
- Hudson Valley Oncology Associates
- Inspira Medical Center Vineland
- Inspira Medical Center Woodbury
- Jefferson Hospital for Neuroscience
- Jennersville Regional Hospital
- Mercy Fitzgerald Hospital
- Mercy Philadelphia Hospital
- Mercy Suburban Hospital
- Jefferson's Methodist Hospital
- Nazareth Hospital
- Nazha Cancer Center
- Nemours/Alfred I. DuPont Hospital for Children
- Northeast Radiation Oncology Center
- Pocono Medical Center
- Reading Hospital
- Riddle Hospital
- Sacred Heart Hospital
- Sidney Kimmel Cancer Center at Jefferson
- Sparta Cancer Treatment Center
- Saint Francis Hospital (Wilmington)
- St. Francis Medical Center
- Trinitas Regional Medical Center
- Upper Delaware Valley Cancer Center
- Wills Eye



# **Sidney Kimmel Cancer Center™**

at Thomas Jefferson University  
NCI – designated

Bluemle Life Science Building  
233 South 10th Street, Suite 1050  
Philadelphia, PA 19107