

New drug
for advanced
kidney cancer



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Nine-year-old
raises money to
honor her dad



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Novel cause of
ovarian cancer
drug resistance

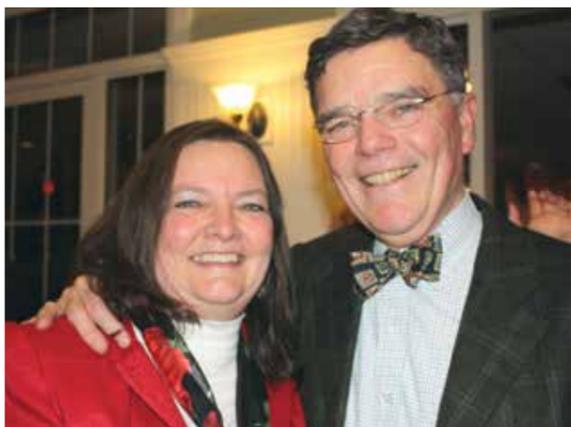


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Nurse leader marks retirement with fund to help patients

Throughout her 35-year oncology nursing career, Shirley Shuster, NP, met patients who were struggling financially. Now, upon her retirement this month as director of clinical operations for Dana-Farber Community Cancer Care (DFCCC), Shuster has taken a step to help these individuals and their families make ends meet while undergoing treatment.

The nursing leader and her husband, John – who retired in December – have named the Shuster Patient Support Fund to assist active patients and families in DFCCC locations with everyday expenses like groceries, utilities, transportation, child care, and short-term lodging. The fund was established with a significant gift by the Shusters.



Shirley Shuster, left, is pictured with James Everett, Senior Network Physician at Dana-Farber Community Cancer Care in Weymouth.

The Division of Development and the Jimmy Fund at Dana-Farber helped create a page on the Jimmy Fund Giving Pages so that the fund can continue to grow from additional gifts made there.

“I have been drawn to the care of cancer patients since I was in nursing school in the early 1970s,” says Shuster. “I have ‘grown up’ with cancer care. Through every patient, I learned lessons that have helped me to be a better person. I have been privileged to be part of their lives at an extraordinarily difficult time.”

Shuster says she has always wanted to help patients with “the relief they need so they can focus on their treatment and care.” She is also serving as a trendsetter of sorts. Many doctors and physician-researchers have established funds when retiring from Dana-Farber, but she may be the first nurse practitioner to do so.

“Shirley and her husband have made an incredibly generous gesture, one that will benefit countless DFCCC patients for years to come,” says DFCCC Chief Medical Officer Andrew Norden, MD, MPH.

Nurse leader, page 3



Icandace Woods, left, is satellite program coordinator for Young and Strong: A Program for Young Women with Breast Cancer at the Susan F. Smith Center for Women’s Cancers. She is pictured with patient Joy Yang.

For Icandace Woods, a career forged by learning

On Dec. 31, more than a dozen young women treated at Dana-Farber for breast cancer received a call from Icandace Woods asking how they were doing and if there was anything she could do to help. “Who wants to spend New Year’s Eve worrying?” she reasoned. “If I can answer a question, it could make a difference.”

The patients responded with appreciation and surprise in equal measure. “So many of them asked

why I was working that day,” Woods says. “Didn’t I know it was New Year’s Eve?”

To those who know Woods, stories of her sensitivity to others come as no surprise. Since arriving at Dana-Farber through a high school Workforce Development Program a decade ago, she has advanced through six positions in six departments, motivated by an ambition kindled on first contact with the Institute, a desire to learn, and a

Icandace Woods, page 4

Research in brief

Study yields three-for-one results

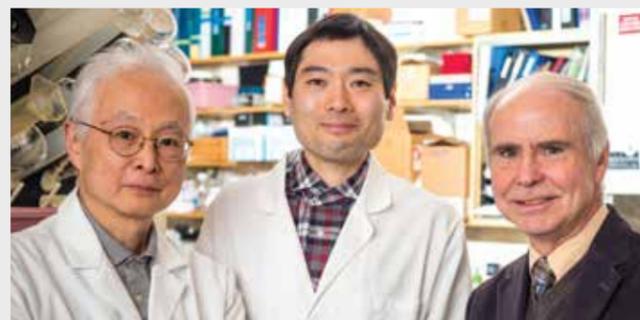
The components of a cell’s genetic machinery are so prodigiously interconnected that an investigation into a single gene can yield a trove of contributors to cancer – each a potential target for new therapies.

That was the case in a recent study by Jerome Lipper Multiple Myeloma Center and LeBow Institute for Myeloma Therapeutics scientists of an errant gene in multiple myeloma. In a study published recently by *Nature Communications*, the researchers discovered

that an interplay between three genes – *KDM3A*, *KLF2*, and *IRF4* – allows myeloma cells to avoid the normal cell-death process and directs them to the bone marrow, where they can thrive.

Focusing first on *KDM3A*, which has been implicated in several types of cancer, the researchers found that shutting down the gene caused myeloma cells to die, both in the laboratory and in animal models. They then found that *KDM3A* spurs *KLF2* and *IRF4* into action, and that stifling *KLF2* causes the cells to die. It also turns out that *KLF2* and *IRF4* form a kind of mutual booster club: *KLF2* activates *IRF4*, and *IRF4* activates *KLF2*. Squelching any of the three genes interferes with myeloma cells’ homing instinct for the bone marrow and decreases their ability to adhere there.

“These findings both elucidate the course of myeloma development and provide the rationale for developing novel therapies directed at these hallmark abnormalities in the disease,” says Teru Hideshima, MD, PhD, who led the study with Hiroto Ohguchi, MD, PhD, and Ken Anderson, MD, director of the Lipper Center. [RL](#)



Teru Hideshima, Hiroto Ohguchi, and Ken Anderson (l to r) discovered that an interplay between genes allows myeloma cells to avoid the cell-death process.



Anna Muriel

New textbook is guide to issues faced by young patients

Anna Muriel, MD, of Pediatric Psychosocial Oncology, is a co-editor of *Pediatric Psychosocial Oncology: A Textbook for Multidisciplinary Care*, published this year to guide clinicians through the challenges faced by children and adolescents with cancer and their families. The book is designed to help clinicians understand the physical and emotional impact of the disease and assist them in working with patients and their families to diagnose and treat a range of behavioral and psychological issues. Topic areas include communication and ethics, psychosocial assessment, and a wide variety of therapeutic interventions. There is also attention to the growing fields of social media, complementary therapies, palliative care, and survivorship, and to the voices of patients and parents who have experienced childhood cancer.

Contributing chapters to the book were Dana-Farber's **Daniel Benedetti, MD; Sarah Brand, PhD; Candice Chow, PhD; Jennifer Kesselheim, MD; Cori Liptak, PhD; Jennifer Mack, MD; Andrea Patenaude, PhD; Christopher Recklitis, PhD; Sarah Tarquini, PhD; Joanne Wolfe, MD; and Eric Zhou, PhD.** [ITI]



Mike Makrigiorgos

DFCI inventor receives tech transfer grant

The National Institutes of Health is funding collaborative research by Dana-Farber and a biotech company to improve the performance of an invention by **Mike Makrigiorgos, PhD**, of Radiation Oncology.

In 2008, Makrigiorgos invented a powerful method for magnifying subtle DNA mutations that could have wide application in cancer precision medicine, infectious disease research, and prenatal testing. It is called ICE COLD-PCR (improved and complete enrichment co-amplification at lower denaturation temperature-PCR).

The invention was licensed to Transgenomic, a biotech firm based in Omaha, Neb. Dana-Farber and Transgenomic will be partners under the two-year, \$1.5 million NIH Small Business Technology Transfer grant.

The expected improvements in the technology will potentially make ICE COLD-PCR useful for identifying drug-resistance mutations, indicating remaining cancer in a patient, and providing physicians with early indications of relapse using sequencing of blood-based liquid biopsies, according to Makrigiorgos. [ITI]



Krietta Bowens Jones

Bowens Jones appointed co-chair of Boston Bar Association section

Krietta Bowens Jones, associate general counsel at Dana-Farber, has been appointed to a two-year term as co-chair of the Delivery of Legal Services (DLS) section of the Boston Bar Association (BBA).

The DLS section's mission is to improve access to Boston area legal services, especially for members of middle- and low-income communities. The DLS section sponsors BBA programs that address access to justice for the city's most vulnerable populations.

Bowens Jones joined Dana-Farber's Office of the General Counsel in 2009. She serves as counsel to the Diversity Subcommittee of the Governance Committee of the Dana-Farber Board of Trustees. She is also lead attorney for DFCI's pro bono legal services program for low-income patients. [ITI]

Four chosen for Clinical Faculty Awards

Four Dana-Farber faculty members have been selected to receive Clinical Faculty Awards for 2016. They are:

Bridging Boundaries Award to a clinician in a subspecialty who is dedicated to oncology and particularly skilled in interacting with other disciplines.

Awardee: **Faina Nakhlis, MD**, of Surgical Oncology

Nominees: **Jennifer Bellon, MD**, Radiation Oncology

Francisco Marty, MD, Medical Oncology

Clinical Mentoring Award to a clinician whose approach and behavior are an outstanding example for trainees.

Awardees: **Jane deLima Thomas, MD**, Psychosocial Oncology and

Palliative Care, and **Daniel Deangelo, MD, PhD**, Medical Oncology

Nominees: **Toni Choueiri, MD**, Medical Oncology; **Ian Krop, MD, PhD**,

Medical Oncology; **Erica Mayer, MD**, Medical Oncology

Innovation Award to a Dana-Farber clinician who provides outstanding patient care combined with a commitment to clinical research and clinical trial recruitment.

Awardee: **Raymond Mak, MD**, Radiation Oncology

Nominees: **Vincent Ho, MD**, Medical Oncology; **Jacob Laubach, MD**,

Medical Oncology; **Sara Tolaney, MD**, Medical Oncology

The awards will be presented Feb. 7 at the clinical faculty brunch at the Boston Museum of Science.

Clinical faculty nominate individuals for the awards, which are decided by a committee of senior clinical faculty. [ITI]

National Wear Red Day: Friday, Feb. 5

Heart disease affects people of all ages and races and is one of the primary killers of women.

This year is the 12th anniversary of **Go Red for Women**, an initiative sponsored by the American Heart Association to raise awareness in the fight against heart disease in women.



This year is for YOU!

By considering your own health well-being and wearing red on Feb. 5, you are prioritizing your own personal heart health and becoming a valuable partner in promoting the need for better research and awareness of heart disease, which claims the lives of one out of every three women each year.

So please wear something red – a tie, dress, suit, scrubs, scarf, pin, or necklace – on Feb. 5, and join staff across DFCI in celebrating National Wear Red Day.

For more information, visit the heart health table outside the Lavine Family Dining Pavilion from 11 a.m. – 1 p.m. on Feb. 5, or visit www.goredforwomen.org.



New drug is superior to standard treatment for advanced kidney cancer



Toni Choueiri

A powerful new drug has improved progression-free survival and increased the response rate in patients with advanced kidney cancer, compared with standard treatment in a clinical trial.

There are also hints that it may help patients live longer.

Dana-Farber oncologist Toni Choueiri, MD, is the senior author on a report of the latest findings from the METEOR phase 3 clinical trial, which is comparing the drugs cabozantinib and everolimus (Afinitor) – currently the standard treatment. The report says cabozantinib shrank tumors in more patients (75 percent) than everolimus (48 percent).

The most recent findings were presented at the 2016 Genitourinary Cancers Symposium in San Francisco held Jan. 7-9.

New drug, continued on page 3

Inside the Institute is published by the Dana-Farber Communications Department for staff members and friends of **Dana-Farber Cancer Institute**. The next issue is scheduled for **Tuesday, Feb. 9**.

Story ideas are welcome. Please contact Naomi Funkhouser at 617-632-5560 or Naomi_Funkhouser@dfci.harvard.edu. Visit the Dana-Farber website at www.dana-farber.org or the intranet at www.dfcionline.org.

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Nine-year-old honors dad's cancer journey by supporting other patients

Peter Silveira took to calling his daughter, Hannah, a good luck charm during his treatment for gray-zone lymphoma in 2014-15. Now, with her dad's cancer in remission, the grade-schooler – who accompanied him to several of his treatments at Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC) – has taken it upon herself to pass some of that luck on to others.

During one of Silveira's recent checkups with oncologist Caron Jacobson, MD, at DF/BWCC, Hannah brought a transparent, hot pink pencil case stuffed with crumpled bills and change. She handed it to the doctor, who read the accompanying note:

"Dr. Caron Jacobson, here is \$25 I saved to help with research for gray-zone lymphoma. From Hannah Silveira, age 9. You helped my dad, so I would like to help someone."

For both caregiver and patient, it was an unforgettable gesture. Silveira had a decades-long aversion to doctors and hospitals dating back to 1984, when he was treated at Dana-Farber for Hodgkin lymphoma – when he was Hannah's age. He and his wife, Jennifer, didn't tell Hannah

or her older brothers, Aiden and Josh, much about dad's childhood cancer experience, and Silveira did everything he could to avoid even routine physicals.

It was only when Jennifer noticed bumps on her husband's neck that he went in for tests that revealed his second cancer diagnosis, after which he shared the whole story with the kids. "They all have big hearts, and have really been there for me," says Silveira. "I knew I couldn't be afraid anymore, because I had to take care of myself for Jennifer and them."

Now, in a place that once terrified him, his little girl had given him one of his proudest moments.

"I still tear up just talking about it," says Peter. "When you are a parent and your kids make a choice like this – well, it really gets to you. I just looked at Jennifer and said, 'We must be doing something right.'"

Although Peter learned about Hannah's idea before the appointment, Jacobson was surprised by the gift. She's been telling colleagues about it ever since.

"I was so impressed and touched by Hannah's gesture, and found the whole experience incredibly



Hannah Silveira brought a pencil case stuffed with crumpled bills to one of her dad's recent checkups with oncologist Caron Jacobson. Peter Silveira is now in remission after being treated for gray-zone lymphoma.

moving," says Jacobson. "For her to have such a generous spirit at a young age, and also to have so much gratitude and relief that her dad is doing well, was fantastic to see."

Jacobson plans to put Hannah's gift toward translational research

underway here on Hodgkin lymphoma and gray-zone lymphoma – both of Silveira's cancers. She also says she has shared the story with her 2- and 5-year-old kids, "so they can see how even someone young can make a big difference." [SW](#)

New drug, continued from page 2

In the first 375 patients treated in METEOR, cabozantinib lengthened the median period of time before the cancer worsened – 7.4 months versus 3.8 months with everolimus. In addition, early analysis has detected a trend toward improved survival in cabozantinib-treated kidney cancer patients. A total of 658 patients with advanced clear cell kidney cancer were enrolled in the trial.

The improvements were seen in previously treated patients, including those who received immunotherapy with checkpoint inhibitor drugs.

Cabozantinib is an oral drug known as a tyrosine kinase inhibitor (TKI). It blocks the growth of tumor blood vessels and the key signaling pathways that drive tumor growth and spread. It has been designated a "breakthrough therapy" by the Food and Drug Administration, which accelerates review of clinical data toward potential marketing approval.

"These are very encouraging results, and for the first time since 2011, we have a new potent TKI that won against the standard of care," says Choueiri. "If the overall survival is improved when further data are updated, this will be the only oral TKI with a survival benefit in advanced kidney cancer."

Choueiri is clinical director of the Lank Center for Genitourinary Oncology and director of the Kidney Cancer Center at Dana-Farber. [RS](#)

Nurse leader, continued from page 1

"What a fitting legacy in light of her lifelong commitment to cancer patients and their families."

There are six DFCCC practices; in addition to Quincy, where Shuster worked as a nurse practitioner as well as overseeing clinical operations for all DFCCC sites, there are locations in Dorchester, Lawrence, Methuen, Milton, and Weymouth. All oncologists, nurse practitioners, and nurses at the practices collaborate closely with colleagues at Dana-Farber in Boston.

Michael Anderson, MD, and DFCCC Patient Advocate Donna Lynch will oversee the Shuster Fund, along with help from Clinical Services Administrator Emily Etienne and Kathy Ryan, office manager at the Weymouth site.

"For me, [the fund] is also a way for me to thank our staff for all that they do for patients," says Shuster. "The beauty of what we have created at Dana-Farber Community Cancer Care is a sense of family taking care of family." [SW](#)

"I have been drawn to the care of cancer patients since I was in nursing school in the early 1970s."

– Shirley Shuster



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DFCI researchers identify novel cause of ovarian cancer drug resistance

Dana-Farber scientists have shed new light on why some ovarian cancers don't respond to, or learn to evade, standard chemotherapy and targeted drugs. They say the discovery could aid in developing strategies to combat ovarian drug resistance.

The investigators' research, posted online by the journal *Cell Reports*, identified a previously unknown resistance culprit – a tiny piece of genetic material called a microRNA, or miRNA – that the cancer cells use to regain their DNA repair powers.

The study focused on the 15 to 20 percent of epithelial ovarian cancers harboring inherited *BRCA1* or *BRCA2* mutations. Because such tumors can't repair damage to their DNA effectively, they are vulnerable to platinum-based chemotherapy agents and newer targeted drugs called PARP inhibitors that shred the tumors' DNA molecules.

However, a substantial number of patients don't respond to or become

resistant to the drugs, reducing their long-term survival. One way that *BRCA1*- and *BRCA2*- mutant ovarian tumors outwit treatment is by gaining additional mutations that restore their molecular DNA-repair pathways.

In the new research, however, senior authors Dipanjan Chowdhury, PhD, of Radiation Oncology, and Panagiotis Konstantinopoulos, MD, PhD, of the Susan F. Smith Center for Women's Cancers, discovered a different resistance mechanism that doesn't involve acquiring new mutations. Instead, the ovarian cancer cells turn off one of two competing DNA repair pathways and turn on the other – known as homologous recombination – that enables the tumor to resist platinum drugs and PARP inhibitors. This repair pathway switch occurs in cancer cells that make increased levels of a specific micro-RNA, miR-622, which turns out to be a regulator of DNA repair.

The scientists found that laboratory-grown cancer cells overproducing



Dipanjan Chowdhury, pictured at left, and Panagiotis Konstantinopoulos identified a new resistance mechanism in which ovarian cancer cells turn off one of two competing DNA repair pathways and turn on the other that enables the tumor to resist platinum drugs and PARP inhibitors.

miR-622 were resistant to the PARP inhibitors olaparib and veliparib and also to the chemotherapy agents carboplatin and cisplatin. Next, they looked for an association between increased levels of miR-622 and treatment results in ovarian cancer patients in a database compiled by The Cancer Genome Atlas project. They examined data from 89 patients with *BRCA1*-mutated ovarian cancer who had undergone surgery followed by treatment with platinum-based chemotherapy.

"In all cases," the researchers note, "we consistently found that tumors with higher miR-622 expression were associated with inferior response to first-

line platinum-based chemotherapy and worse survival." Patients with higher expression of miR-622 survived a median of 39 months compared with 49.3 months for patients with lower levels of miR-622.

As a result of their discovery, levels of miR-622 in *BRCA1*-mutant ovarian cancer could help guide treatment of the tumors in the future. Moreover, "miR-622 may be a promising target for augmenting response to PARP inhibitors and platinum chemotherapy for these tumors," according to the researchers. [RS](#)

Icandace Woods, continued from page 1

ready empathy for people facing difficult times.

Since October, she has been the satellite program coordinator for Young and Strong: A Program for Young Women with Breast Cancer at the Susan F. Smith Center for Women's Cancers. Her role involves contacting patients age 44 and younger at Dana-Farber's satellite centers and affiliates to assess which aspects of supportive care were important to them while undergoing treatment. When the survey is complete, she and the program's director, Ann Partridge, MD, MPH, will meet with leadership at each satellite to discuss the findings and decide how to implement Young and Strong at each site.

The program was founded in 2005 on the Longwood campus and in 2014 began expanding to Dana-Farber satellites and affiliates with a grant from the Centers for Disease Control. Focusing on young patients with breast cancer, the program helps participants deal with issues unique to their time of life – fertility, parenting young children, managing a career, and maintaining relationships.

Because of a recent vacancy, Woods also has been meeting with patients on the Longwood campus to introduce them to the program. "When some patients are first diagnosed with cancer, they feel alone," she comments. "I try to put them at ease and explain we have resources that can help them. Some say they'd heard about the program and came to Dana-Farber specifically because of it."

Woods' own route to Dana-Farber, and her career path since coming here, also owe something to the qualities that make the Institute unique. She first entered the Institute as a high school senior in the Workforce Development Program. "I knew it was for me," she says. "When I saw how passionate my colleagues were and how patients looked up to them, I wanted to be a part of it."

Working as a part-time intern at the Institute through the remainder of high school and four years at Lesley University – first in Friends' Place, then Medical Oncology Administration and Human Resources – she didn't have to look far for inspiration. In Human Resources, for example, her responsibilities included checking job applicants' references. "When I looked at their resumes and saw what they'd accomplished, it gave me ambition to try to do more," she remarks.



Ever Wonder?

Why do stem cells have a strong odor?

The odor, which has been compared to that of creamed corn, comes from the protective solution in which the cells are frozen and stored, rather than from the cells themselves, say Richard Kaufman, MD, medical director of the Adult Transfusion Service at Brigham and Women's Hospital, and William Savage, MD, PhD, medical director of the Kraft Family Blood Donor Center.

When blood-making, or hematopoietic, stem cells are collected from a patient undergoing an autologous transplant – a "self" transplant in which the cells are later returned to the patient – they're processed and stored in Dana-Farber's Connell and O'Reilly Families Cell Manipulation Core Facility. The cells are frozen using a protectant substance called dimethyl sulfoxide (DMSO), which prevents them from getting damaged. When it's time to perform the transplant, the cells are thawed and infused intravenously back into the patient. It is the DMSO that gives stem cell products their characteristic and peculiar odor. [ITI](#)

After college, she worked as a clinical administrative specialist in an Adult Ambulatory Service infusion unit, scheduling patient appointments, then as a team lead in the Jimmy Fund Clinic. Each job provided lessons for the next – and the ones that followed. On the infusion unit, she says, "a light went on. I learned to be super-organized, to have patience. Patients taught me to be thankful for what I have. I learned to be receptive to everything: If there's an opportunity to learn, take it."

It's a message she's taken to heart, enrolling in numerous training classes at Dana-Farber, still incredulous that they're offered for free.

In Woods' view, knowledge gained on the job and in life is only as valuable as its ability to help someone else. "It's important to share what you've learned," she says, "like a torch that you pass to bring success to others."

With that in mind, two years ago she established the Women's Inspirational Group, a monthly support group for women that addresses issues such as domestic violence, financial management, career development, and relationships.

The connection between her work in the Young and Strong Program and the support group she created isn't lost on Woods. "When I've gone through difficulties in my life, I've benefited from others' experiences," she says. "People don't have to struggle alone." [RL](#)