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Administrative fellows develop leadership skills

Before last summer, Marian “Manny” Hill had never visited the Dana-Farber campus. Now, just a year after college, she’s participating in meetings with the Institute’s top leaders and learning skills needed to build a health care management career.

What is the secret of her success? Hill is part of what has become one of Dana-Farber’s most successful avenues for advancement: the Administrative Fellowship Program (AFP). Established in 2007, the one-year program allows individuals to develop their leadership style and analytical skills while gaining expertise in such areas as Finance, Human Resources, Patient Care Services, Research Administration, and Clinical Operations.

Selected from more than 100 candidates with master’s degrees in health care administration, business administration, public health, or related fields, Hill – who has a master’s in biomedical engineering from the University of Michigan – started her fellowship on July 1 and is spending her first two months shadowing executive

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Fellowship gives students inside look at oncology nursing

Kayla Costigan grew up admiring her mother, an oncology nurse for more than 20 years. Lauren Guerra remembers reading to her toddler cousin in the hospital during his cancer treatment.

Rising seniors at Boston College, both Costigan and Guerra have long had a passion for cancer care. Now, thanks to a new program at Dana-Farber, they are getting a glimpse at adult oncology nursing.

Through a fellowship program made possible by

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Lauren Guerra (left) and Kayla Costigan are participating in an oncology nursing fellowship program established by Frederick C. Flynn Jr. (center) in honor of his late wife.



Michaela Reagan (left) and Irene Ghobrial are studying a delivery system using nanoparticles that target bone cancer cells and release a drug to slow the progress of multiple myeloma.

Nanoparticles deliver drugs to fight bone cancer

Scientists have demonstrated in mice a delivery system using drug-filled microscopic nanoparticles that home in on bone cancer cells and release the drug to slow the progress of multiple myeloma. They report that the treatment enhanced the strength and volume of the bone as well.

Such a system could be used to treat patients with multiple myeloma or other cancers that metastasize to the bone, say researchers from Dana-Farber

and Brigham and Women’s Hospital (BWH) who collaborated on the project. A report on the study was published June 30 in *Proceedings of the National Academy of Sciences*.

“There are limited treatment options for bone cancers,” notes Michaela Reagan, PhD, of Dana-Farber’s Center for Hematologic Oncology, co-lead study author. “Our engineered targeted therapies manipulate the tumor cells in the bone and the surrounding microenvironment

Nanoparticles, page 3

Fat cell protein signal found to stimulate insulin production

Researchers have shown in diabetic mice that a protein made by fat cells is critical to the normal production of insulin, the hormone that enables the body to maintain a healthy level of blood sugar.

Dana-Farber’s Bruce Spiegelman, PhD, senior author of the report in *Cell*, says the newly discovered role of the protein, adiponectin, could have implications for treatment of type 2 diabetes, a growing epidemic affecting an estimated 382 million people globally.

In an experiment with obese, diabetic mice that lacked adiponectin, restoring the protein to the animals improved the health of beta cells in the pancreas. Beta cells secrete insulin, which helps muscle cells use sugar (glucose) for fuel. The beta cells malfunction in severe diabetes.

The scientists also discovered that adiponectin is deficient

in human patients with severe type 2 diabetes.

“This suggests a new approach to treating type 2 diabetes in patients whose pancreatic beta cells work poorly, leaving them dependent on injected insulin,” says Spiegelman, of the Department of Cancer Biology.

“If humans respond similarly to the mice in this study,” he continues, “correcting their deficiency of adiponectin would improve beta cell function and perhaps maintain enough natural insulin production to avoid or delay the need for insulin injections.”

Per-Olof Berggren, PhD, of Karolinska Institutet in Stockholm, Sweden, and a co-investigator of the study, adds that adiponectin “might be the long-sought molecule linking fat tissue metabolism to pancreatic beta cell function.” James Lo, MD, PhD, a cardiologist in the Spiegelman lab, is the report’s

Fat cell protein, page 3



David Reardon

Novel immunotherapies to be tested in brain tumor patients

With the support of a three-year grant from the Ben and Catherine Ivy Foundation, Dana-Farber researchers are preparing a multi-pronged attack on glioblastoma brain tumors with a combination of immunotherapy methods.

A small pilot clinical trial of a cutting-edge vaccine could begin enrolling glioblastoma patients later this year, according to **David Reardon, MD**, principal investigator on the \$1.5 million grant from the foundation, which funds research to improve the survival of patients with these aggressive brain tumors. Reardon is the clinical director of Dana-Farber's Center for Neuro-Oncology.

The vaccine, called NeoVax, was developed by a research team at Dana-Farber and the Broad Institute of MIT and Harvard led by Cathy Wu, MD. NeoVax is tailored to each patient's tumor cells that carry on their surface highly specific identifying molecules created by mutations that are unique to each patient's glioblastoma. The vaccine treatment is designed to "teach" the patient's immune system to identify and react against those cancer cells. NeoVax is currently being tested at Dana-Farber in patients with advanced melanoma.

In a second project, carried out in collaboration with David Mooney, PhD, and other colleagues at the Wyss Institute, researchers will test an implantable vaccine delivery device that "reprograms" the immune system to generate an immune attack on glioblastoma cells.

The third part of the research focuses on how glioblastomas, like many other tumors, shield themselves from the body's immune defenses, which otherwise would attack the cancer. Drugs based on discoveries by Gordon Freeman, PhD, of Dana-Farber, have showed great promise in some forms of cancer by blocking the "immune checkpoints" that shield the tumors from attack. With the Ivy grant support, scientists will continue studies in mice in which these drugs achieved long-lasting elimination of glioblastomas.

The ultimate goal is to combine these three approaches into a unified treatment approach that can generate long-term anti-tumor activity and potentially eradicate glioblastomas, says Reardon. RS



Andrew Wagner

Wagner receives grant for liposarcoma research

The Liddy Shriver Sarcoma Initiative has selected **Andrew Wagner, MD, PhD**, for an international team grant aimed at improving the understanding and treatment of liposarcoma, a rare form of sarcoma. The two-year, \$250,000 International Collaborative Grant is funded in partnership with The Wendy Walk.

The Liddy Shriver Sarcoma Initiative supports research on the estimated 50 different types of sarcomas. It is named in honor of Liddy Shriver, daughter of Bruce and Bev Shriver, who passed away at age 37 after battling Ewing sarcoma. The Wendy Walk was formed by the children of sarcoma patient Wendy Landes, who fought liposarcoma and passed away in March 2013.

Wagner will work with three other scientists – two from Norway and one from Australia – to identify genetic factors that distinguish two forms of liposarcoma. One form of the disease grows gradually and is not a danger to spread, while the other form is more aggressive and can quickly become fatal.

"I'm thrilled to be joining this group of outstanding researchers and collaborators in our approaches to improving our understanding and treatment of liposarcoma," says Wagner. If the research pinpoints genes that trigger the change to the more aggressive form, "we will potentially be able to test drugs that specifically target these alterations," Wagner says. MG

Dana-Farber researchers awarded Melanoma Research Alliance grants

Seven Dana-Farber doctors were awarded research grants by the Melanoma Research Alliance (MRA). MRA is the largest private funder of melanoma research and this year awarded a record-breaking \$8 million in new research grants.

MRA awards research grants to "both individual investigator and collaborative team projects focused on translational, innovative research that will impact the prevention, diagnosis, staging, and treatment of melanoma in the near and immediate future," the award statement reads.

Dana-Farber doctors were awarded three Team Science Awards and one Academic Industry Award. **F. Stephen Hodi, MD**, received the Academic Industry Award, one of three awards offered annually. This award is unique because it "represents a novel mechanism for collaboration among academic researchers, industry, and MRA through a corporate match of MRA's funding," according to MRA.

Team Science Award recipients were chosen based upon the goal of the award, "to foster a collaborative research process that promotes transformational melanoma research advances with the potential for rapid clinical translation." They include **Loren Walensky, MD, PhD; Levi Garraway, MD, PhD; James Bradner, MD; Jason Luke, MD; Kai Wucherpennig, PhD; and Michael Goldberg, PhD**.

"These grants are infused with MRA's spirit of collaboration, reflecting geographic diversity and drawing from many scientific disciplines," says MRA co-founder and chair Debra Black. "Together, we are making huge strides against this disease." WE

Jon Lester jersey giveaway

For more than 60 years, the Red Sox have had a special bond with the Jimmy Fund and Dana-Farber Cancer Institute – the longest and most successful partnership between a professional sports team and charity in North America. The Red Sox have helped the Jimmy Fund raise millions of dollars for cancer care and research at Dana-Farber through appearances and appeals, while befriending patients of all ages.

In honor of this partnership, we're giving away a signed Jon Lester jersey to one lucky fan. Encourage your patients and friends to vote for their favorite Red Sox star on the Dana-Farber Facebook page to be entered to win.

Contest ends at 11:59 p.m. on Tuesday, August 12. Dana-Farber employees and their immediate family members are not eligible to win.



New MASCO shuttle buses on the road

If you're a frequent rider of the MASCO shuttles, you may have noticed a recent upgrade to the bus fleet.

On June 30, MASCO rolled out 30 new large shuttle buses. The clean diesel buses run on all MASCO shuttle routes and feature quieter engines, controlled interior temperature, and comfier seats.

In addition to the 30 buses, MASCO has also purchased seven smaller vans for its shuttle routes. The vans will hit the road in fall 2014.

"MASCO is committed to providing safe, comfortable, and timely transportation to our riders," says Marilyn Swartz-Lloyd, president and CEO of MASCO. "They are hard-working, mission-driven employees, so it is extremely important to us that we provide our riders the very best in comfortable, efficient, and safe transportation," she said.

MASCO purchased the new fleet using a \$13.4 million tax-exempt lease through JP Morgan. The lease was made possible through a partnership with MassDevelopment, the state's finance and development agency. MG



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Research takes aim at cancer's genetic 'addictions'

Breaking an addiction to illegal drugs can bring a chance at a new life. Breaking a cancer cell's addiction to certain growth-spurring genes can spell the cell's death.

In some cases, that's a relatively straightforward task: design a drug that can block the abnormal gene from continually issuing growth commands. But what if that gene isn't abnormal – harbors no mutations – but has been whipped into hyperactivity by some other actor within the cell?

If so, proteins called transcription factors may be the culprits. They control how genetic information is converted to a ready-to-use form, and thus serve as on-off switches for genes. Unfortunately, transcription factors are notoriously difficult to target with drug compounds.

It's now known that transcription factors don't work solo; they often rely on "co-factor" enzymes to perform their function. While these co-factors bring an additional level of complexity to the transcription process, they also offer an enticing array of targets for new therapies. Blocking a co-factor with a drug could,

in theory, disable a key transcription factor, thereby shutting down a gene relentlessly sending growth signals to the cell.

In new research published in the journal *Nature*, scientists at Dana-Farber and other institutions succeeded in killing laboratory-grown leukemia cells with this type of molecular sneak attack. They used an agent that, instead of directly targeting a co-factor, targets an exquisitely sensitive part of the genome that has an outsize influence on the co-factor's ability to function. It represents one of the first times an enzymatic co-factor has been stymied with this technique.

"We've known for many years that some cancer cells are dependent on the continual transcription of certain genes. Without the constant growth signals sent by these genes, such cells won't survive," says Dana-Farber's Nathanael Gray, PhD, the study's senior author. "In this study, we've used a novel technique to disrupt such transcription and bring about cancer cell death."

Previous research had shown that T-cell acute lymphocytic leukemia (T-ALL) cells are highly

susceptible to a drug compound called THZ1. In the current study, Gray and his colleagues set out to discover why this is so.

They found that THZ1 latches onto a long DNA segment known as a "super-enhancer" because of its exceptional power over gene activity. About 10 times the size of standard enhancers, and with a jumble of proteins attached, super-enhancers are the giants of the cell's gene-controlling machinery. But like the biblical giant Goliath, super-enhancers are not only massive, they're also highly vulnerable, easily disrupted with a pinpoint strike.

That's what THZ1 accomplishes, Gray and his colleagues discovered: it disables a super-enhancer by blocking an enzymatic co-factor called CDK7. That, in turn, halts transcription of the genes *MYC* and *RUNX1*, which are overactive in the T-ALL cells. The result is death of the leukemia cells.

Gray notes that while the technique has worked admirably in laboratory cell cultures, more work is needed to determine if it can succeed in patients without producing severe side effects. [RL](#)

Fat cell protein, continued from page 1 *Nanoparticles, continued from page 1*

first author.

Checking for adipin levels in diabetic patients might help doctors predict which individuals are at highest risk of impending beta cell failure so they can begin treatment earlier, the authors note.

Adipin was the first of a class of proteins called adipokines to be discovered. These proteins, which are secreted into the bloodstream by adipocytes, or fat cells, continuously circulate to influence a variety of metabolic and immune functions. Spiegelman's research group discovered the protein and its connection to the immune system in 1987, but its newly identified role in controlling insulin production by the pancreas was entirely unsuspected.

The Spiegelman lab and other researchers have recently found some immune system components are present in fat cells, where they help maintain the body's energy balance. This growing area of investigation prompted Lo and Spiegelman to revisit the function of adipin. Lower levels of adipin had been reported in obese and diabetic animals, but overweight and diabetic humans experienced unchanged or elevated levels, leaving it unclear how the protein functions in those conditions.

In this study, the Dana-Farber investigators used "knockout" mice lacking the adipin gene and "wild type" mice with normal adipin levels. Both sets of animals became obese on a high-fat diet and developed excess blood sugar – a pre-diabetic state. The symptoms were worse in the adipin knockout mice.

In the report, the scientists say the difference in symptoms is explained by "an unexpected and striking requirement of adipin for proper insulin secretion by the pancreatic beta cells." [RS](#)

to effectively prevent cancer from spreading in bone with minimal unwanted effects."

Reagan is a postdoctoral fellow in the laboratory of Irene Ghobrial, MD, a medical oncologist in the Jerome Lipper Multiple Myeloma Center at Dana-Farber/Brigham and Women's Cancer Center and co-senior author of the study with Omid Farokhzad, MD, director of the BWH Laboratory of Nanomedicine and Biomaterials.

"Bone is a favorable microenvironment for the growth of cancer cells that migrate from tumors in distant organs of the body, such as breast, prostate, and blood, during disease progression," explains Archana Swami, PhD, of the Laboratory of Nanomedicine and Biomaterials. She is a co-lead author of the study.

"We engineered and tested a nanoparticle system to selectively target the bone microenvironment and release a therapeutic drug in a controlled manner, leading to prevention of disease progression," says Swami.

The scientists developed nanoparticles made up of biodegradable materials, coated with alendronate, a type of drug that binds to calcium. The mice were pre-treated with nanoparticles loaded with the anti-cancer drug bortezomib before being injected with myeloma cells. The treatment resulted in slower myeloma growth and prolonged survival of the mice. Moreover, the researchers also observed that bortezomib, as a pre-treatment agent, changed the makeup of bone, enhancing its strength and volume.

"This study provides the proof-of-concept that targeting the bone marrow niche can prevent or delay bone metastasis," says Ghobrial. "This work will pave the way for the development of innovative clinical trials in patients with myeloma to prevent progression from early precursor stages, or in patients with breast, prostate, or lung cancer who are at high risk of developing bone metastasis." [RS](#)



An Epic Journey

A conversation with Michael Hassett

Michael Hassett, MD, MPH, assistant professor of medicine and medical oncologist in the Breast Oncology Program at the Susan F. Smith Center for Women's Cancers at Dana-Farber, sat down with the Epic group to discuss the Epic implementation and how it will positively affect Dana-Farber and the entire Partners community.

How are you involved with the Epic project?

I am assisting with the DFCI Epic implementation and serve as the clinical lead for oncology for the Partners Clinical Content Team. I work with the Epic Systems Corporation and the Partners organization to collaborate on new developments for the Epic system. I also oversee Epic's oncology module, Beacon [used for cancer staging and chemotherapy treatment plans].

How do you envision the Epic implementation impacting the fight against cancer?

Although DFCI operates on a variety of IT systems that do their job very well, the specialization of each has led to an overall weaker system. With the Epic implementation, we are transitioning to a strong, system-wide infrastructure that will help with care coordination across providers and sites. For instance, providers will be able to see test results and notes from all clinicians regardless of the setting's inpatient or outpatient status.

A core value of DFCI is "Discovery." How will this project help further research efforts?

Because Epic will provide more coordination of care, there is hope that we will be able to better identify patients eligible for clinical trials. Epic also contains a large number of structured data fields, thereby giving DFCI the ability to further discovery by using patient data for approved clinical research.

Do you have any advice for your colleagues for how to thrive in this time of change?

This is going to be a challenging transition, and we all must be prepared, open, and patient. Preparation depends on completion of all necessary training and pre-conversion prep work. We should be open to doing things differently, as our current applications will differ from those we are adopting. Lastly, patience will be key during implementation; this will be a change for the better. [MB](#)

To read a transcript of the full interview, visit <http://dfcionline.org/partnersecare> and click on "Resources."

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DFCI nurse supports research, raises awareness in memory of her sister

By 2003, Eileen Lind, RN, MSN, CPNP, had several years of experience handling treatment protocols and diagnoses, and delivering difficult information to patients and families as a pediatric nurse practitioner at Dana-Farber/Boston Children's Cancer and Blood Disorders Center.

But those experiences would hardly prepare her for the news that her older sister, Maureen Russo, had cervical cancer.

"I thought because I deal with cancer on a regular basis that I could handle her diagnosis, but the dual role of caretaker and oncology nurse was one of the most difficult challenges I've ever faced," Lind says.

Her sister, with her infectious laugh and warm personality, was just 34 years old when she was diagnosed. She sought treatment with Ursula Matulonis, MD, medical director of the Gynecologic Oncology Program at the Susan F. Smith Center for Women's Cancers at Dana-Farber, who worked with Russo through every step of treatment.

"Dr. Matulonis made Maureen feel like she was her only patient; she never made her feel rushed and she was always available to listen to her concerns," Lind says.

After chemotherapy and radiation, Russo eventually



Eileen Lind holds a photograph of her sister, Maureen Russo, who died in 2006 after a three-year battle with cervical cancer.

went into remission, but three years later the disease came back. In December 2006, just six months after her cancer returned, Russo passed away.

In the years since her death, Lind has maintained her relationship with Matulonis, teaming up to raise awareness for cervical cancer prevention and research. Last fall, Lind and Matulonis organized the first annual HPV/Cervical Cancer Summit, held in November 2013. Hosted by the Susan F. Smith Center in collaboration with the American Cancer Society, the event brought together more than

100 public health officials to discuss the expansion of community cervical cancer prevention programs. This year's summit will be held on November 7.

Lind and her family have also worked to keep Russo's spirit alive through Team Maureen, a nonprofit organization that began as a Pan-Mass Challenge (PMC) team. The organization aims to improve the lives of women affected by gynecological cancers by raising money for cancer research and community outreach.

This year, 13 cyclists will join Team Maureen for the PMC, including Russo's husband, Mike.

"It's exciting to see the money we raise support Dana-Farber researchers," Lind says. "The research makes a real difference and helps develop treatments that give patients more time than my sister had."

Lind and Team Maureen also work with Dana-Farber's Community Benefits Program and the Department of Public Health to spread awareness about cancer prevention. Joined by Russo's daughter, Gabrielle, Lind and other health professionals travel throughout the state to educate people, particularly teens, about HPV vaccines, early detection, and screening opportunities.

The goal of these programs, Lind says, is to keep her sister's spirit alive, while reducing the stigma around cervical cancer and educating as many people as possible about how to prevent the disease.

"If we can get away from the stigma and focus on prevention, we can really make a difference," Lind says. [MG](#)

Oncology nursing, continued from page 1

the Susan D. Flynn Oncology Nurse Training and Development Fund, Costigan and Guerra spent June and July training alongside veteran nurse preceptors Maura Dacey, RN; Erin Drury, RN; Suzanne Oliver, RN; and Michaëlle Renard, MS, RN, at Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC). Frederick C. Flynn Jr., a retired business executive, established the fund in honor of the nursing care his late wife, Susan Flynn, experienced before dying of ovarian cancer in May 2013.

Although both students have completed clinical rotations with other students and one nursing faculty member, Costigan and Guerra say the opportunity to work one-on-one with oncology mentors and develop relationships with patients has confirmed their career aspirations.

"We're not exposed to oncology much in our school training," says Costigan. "Being able to watch what veteran nurses do, you learn so much about connecting with families. My mom is quizzing me to see what I've learned."

Like Costigan, Guerra has learned about many specialized areas of oncology nursing, including social work, spiritual care, radiation oncology, integrative therapies, and palliative care, and even observed an operation. With input from their preceptors, they also created presentations – Costigan

on the prevention and treatment of chemotherapy-induced nausea, and Guerra on the role of palliative care in pain management and quality of life.

"Everybody on the staff has been willing to teach us, and the patients have been wonderful," says Guerra. "What surprised me the most was how the positives about the cancer care experience far outweigh the negatives. The patients feel it's their job to get better, and as a nurse you focus on helping them get there."

This is the message Clinical Nurse Specialists Anne Elperin, MSN, ANP-BC, AOCNP, and Mary Lou Siefert, DNSc, AOCN, envisioned when coordinating the program. "We're socializing them to the role of an oncology nurse at a comprehensive cancer center, and preparing them for the situations they will encounter in that role," says Elperin. Siefert, noting DF/BWCC has never offered such a program before, adds, "What makes it such a rich experience is that they are able to observe patients along the entire continuum of care."

For Flynn, it's also a lasting legacy to his wife: "I hope the fellowship can better equip and inspire participants to pursue a career in this critical field and give DF/BWCC's next generation of oncology nurses valuable exposure to the mission." [SW](#)

Fellows, continued from page 1

leadership across the Institute. This inside access to decision-making at a major cancer center is invigorating for Hill, who still remembers her mother's battle with breast cancer during Hill's high school and undergraduate years.

"That experience drew me to the field of biomedical engineering, so I could improve the lives of those with cancer," explains Hill. "When I heard about the mission and culture of Dana-Farber, and then the AFP, it really resonated. I felt driven to apply."

In doing so, Hill joins a list of past fellows that includes many who have gone on to full-time positions at the Institute. Julie Bryar Porter spent her AFP year of 2010-2011 helping transition patient clinics from the Dana building to the Yawkey Center, overseeing documentation for a Department of Public Health survey, and organizing daily huddles for leadership after the move. Now she is manager of Quality and Patient Safety.

"The AFP confirmed to me that health care management is almost always about the people, especially making sure you have the right staff involved in a decision or a job," says Porter.

Remembering how generous senior leaders were to her as a fellow, Porter enjoys helping others in the role. This feeling of "paying it forward" is shared by Hill's immediate AFP predecessor, Mary Tyson, who has transitioned into a full-time role as manager of clinical strategy in Clinical Planning and Network Operations.

"As a fellow, I had exposure to the highest level of executive decision-making, and was also given the flexibility to gain hands-on analytic and project management experience as a contributing member of project teams," says Tyson. "This balance of observation and active contribution was an incredible learning opportunity."

And a great indicator of future success.

"From the Institute's perspective, we get to see young talent in action," says David Read, vice president of Ambulatory Practice Management and chief administrator for Medical Oncology, who supervises the AFP recipients. "Our administrative fellows are then ready for more senior level leadership positions sooner. Hopefully, if we can convince them to stay at Dana-Farber, their ramp-up time is much shorter." [SW](#)



Pictured left to right are Julie Bryar Porter and Mary Tyson, both former administrative fellows, with current fellow Marian Hill.



Dana-Farber designated as Magnet® organization for third time

Dana-Farber was recently reaccredited with Magnet® status from the American Nurses Credentialing Center (ANCC). This prestigious designation recognizes excellence in nursing and health care delivery and has been given to only 7 percent of hospitals nationwide. In 2005, Dana-Farber became the first cancer center in New England to receive Magnet status. We were redesignated in 2009.

"The ANCC Magnet credential recognizes excellence in nursing care delivery, innovation, and evidenced-based practice," says Patricia Reid Ponte, RN, DNSc, FAAN, NEA-BC, Dana-Farber's senior vice president for patient care services and chief nursing officer. "It highlights the exquisite nature of our interdisciplinary practice model and demonstrates, through quality, workforce, and organizational outcomes, that our practice is outstanding, while constantly striving for improvement. It is an honor for me to be working alongside such extraordinary nurses."