Dana-Farber Cancer Institute

INSIDE THE INSTITUTE

March 3, 2020 Volume 25, Issue 5

Hilary Libka helps protect the discoveries, inventions, and original works of authorship developed at Dana-Farber.

Hilary Libka Promoted to Chief Intellectual Property Counsel

True to the mission of Dana-Farber's founder, Sidney Farber, MD, the Institute remains dedicated to not only delivering compassionate, patient-centered care, but also to advancing cancer research. To remain a leader in this field, it is crucial to protect the groundbreaking discoveries that happen here. For that, Dana-Farber turns to Hilary Libka.

In December, Libka was promoted to Chief Intellectual Property Counsel. She is now developing a team within the Office of General Counsel (OGC) that manages matters related to intellectual property – including inventions, discoveries, and original works of authorship.

"My goal is to devise unique, creative solutions to get our work out there so it can be developed, while also safeguarding it," explains Libka.

Dana-Farber owns thousands of intellectual property (IP) rights in the form of patents, trademarks, and copyrights. Securing a patent is a multi-year process, and the Institute currently has more than 2,000 pending applications. Because of this, two major responsibilities of Libka's include learning about advancements in technology and deciding how they can be protected.

Libka meets with Institute researchers to understand the work they're doing, and then advises the Innovation Office as to which discoveries or inventions can be patented and which aren't yet ready. This can require a touch of clairvoyance. Many times, current industry research or technology isn't capable of utilizing the advancement until many years after the patent application is filed.

Libka, page 3

Researchers Resolve How the Intestine Heals Itself

Deep within the lining of the human intestine lies the source of the organ's ability to renew itself and recover from damage: Intestinal stem cells (ISCs), lodged in pockets of tissue called crypts, generate the cells that continuously repopulate the intestinal lining. Even the stem cells themselves have a safety net: When they're damaged, healthy replacements appear in less than a week.

For years, scientists have debated how the ISCs' re-emergence occurs. Some have held that the intestine keeps a pool of ISCs on reserve – a kind of backup-backup supply – to replenish the cache of front-line ISCs that have been lost. Others have maintained that something more cyclical is at work: The ISCs, like queen bees, give rise to more specialized, or "differentiated," progeny – in this case, daughter cells that form the inner lining of the intestine. When the ISCs are damaged, this school of thought held, the daughter cells reverse course and "de-differentiate" – reverting into the ISCs from which they arose.

A new study by Dana-Farber scientists comes down solidly on the latter. As reported in the journal *Cell Stem Cell*, the researchers found that ISCs and their daughter cells have a strikingly reciprocal relationship: Under normal conditions, ISCs differentiate into daughter cells, and, if the ISCs are lost, the daughter cells simply reverse course and become ISCs.

"Our findings suggest that the restoration of intestinal stem cells occurs entirely by the process of de-differentiation," says the study's senior author, Ramesh Shivdasani, MD, PhD, of Dana-Farber, Brigham and Women's Hospital (BWH), and the Harvard Stem Cell Institute. "We showed there's no need for a reserve set of ISCs."

Bolstering their findings, the researchers tracked the de-differentiation process in real time. When cells begin to de-differentiate, they switch on a gene that allows them to be isolated and collected with laboratory

Resolve, page 4

Painting with Purpose

The first time Becky O'Toole picked up a paintbrush, she never imagined anyone would want the finished canvas. Having recently completed radiation treatment for breast cancer, the mother of two was looking for a way to process her diagnosis. From this humble beginning, a passion morphed into a growing business.

O'Toole's original breast cancer diagnosis came in 2014, when a biopsy revealed she had early stage, ER-positive (ER+) breast cancer. The discovery was made after a mammogram she felt compelled to do following her mother's stage II breast cancer diagnosis only two weeks prior.

A resident of Scituate, Massachusetts, O'Toole was able to receive care close to home at Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC) in clinical affiliation with South Shore Hospital. Under the guidance of Meredith Faggen, MD, medical director, Medical Oncology at the South Shore location, O'Toole underwent a lumpectomy, radiation, and maintenance hormone therapy.

Shocking News

As O'Toole began to feel better, her painting took a backseat to raising her two young daughters. Slowly, she returned to the life she had built before her diagnosis – and for almost three years she remained cancer-free. But in the summer of 2017, she sensed something wasn't right.

A dedicated runner, O'Toole began feeling perpetually tired during her time hitting the pavement. When she developed what looked like mosquito bites on her legs and swollen masses behind her ears, she went to

Purpose, page 4

Becky O'Toole used painting as a way to manage the stress a cancer diagnosis can bring.

News of Note

Stuart H. Orkin

Orkin named 2020 King Faisal Prize Laureate in Medicine

Stuart H. Orkin, MD, of Dana-Farber/Boston Children's Cancer and Blood Disorders Center, a David G. Nathan Professor of Pediatrics at Harvard Medical School, and an investigator at the Howard Hughes Medical Institute, has been named a 2020 King Faisal Prize Laureate in Medicine for his research contributions in hemoglobin disorders.

"I am honored to receive this award, which recognizes many exceptionally talented trainees in my laboratory over more than three decades," says Orkin.

Launched by the King Faisal Foundation (KFF) and granted for the first time in 1979, the prize honors the outstanding works of individuals and institutions in five major categories.

Prizes for Medicine were first awarded in 1982. Individuals are considered qualified to win the King Faisal International Prize for Medicine if they have carried out and published an original scientific research on the prize's topic, with major benefits to humanity, and meeting one or more of the prize's objectives as determined by a Selection Committee.

"Stu is incredibly deserving of this recognition as a true pioneer in this field, and especially all he has done to advance the understanding of sickle cell disease and other hemoglobinopathies over more than 30 years," says Scott Armstrong, MD, PhD, president of Dana-Farber/Boston Children's Cancer and Blood Disorders Center. "On behalf of all the faculty at Dana-Farber/Boston Children's, congratulations to Stu and gratitude for all that he has contributed to our program."

The King Faisal Prize (KFP) was initiated by the King Faisal Foundation inspired by its humanitarian objectives and its commitment to preserve the Islamic values for which King Faisal stood.

This year is the 40th anniversary of KFP and previous KFP winners have gone on to win 21 Nobel Prizes, 13 Gairdner Foundation International Awards, 11 American National Medals of Science, 10 Laster Awards, and many other honors. ITI

Harvey Cantor

AAI Recognizes Cantor with High Honor

Harvey Cantor, MD, the Baruj Benacerraf Professor of Immunology at Harvard Medical School, has recently been named a 2020 Distinguished Fellow of the American Association of Immunologists (AAI).

Established in 2019, the program annually recognizes long-term members (25 or more years) that have demonstrated one or more of the following: excellence in research accomplishment in the field of immunology; exceptional leadership to the immunology community in academia, foundations, nonprofits, industry, or government at a national or international level; notable distinction as an educator. It is among the highest honors presented by AAI.

Cantor's work has greatly advanced the understanding of different immune cells by developing an approach that uses antibodies to identify different subsets and determine their functions. For his accomplishments, he has been elected to the National Academy of Sciences and the American Association for the Advancement of Science. His current work continues to characterize how T cells and natural killer cells develop and the mechanisms that they use to defend us against pathogens as well as protect us from potential autoimmune damage. ITI

Toys Help Pediatric Patients in Major Life Transitions

To many children, the specially crafted dolls, stuffed animals, and action figures may look unusual. To orthopedic oncology nurse Sara Swaim, BSN, RN, and her young patients, they are just right.

A Spiderman has a prosthesis that can be removed and reattached, just like the young boy for whom it was made. Then, there is a fluffy pink pig, with one shortened leg capped by a backwards ankle and foot. When fit into a tiny prosthesis, the reversed lower leg functions like a knee joint, allowing for full flexibility. This makes the pig an ideal companion for a young girl about to undergo surgery known as rotationplasty, after which she hopes to run and jump with the help of her own reversed ankle and foot.

Swaim has toys like these customized for her preteen patients, most of whom have malignant bone tumors that require one of three orthopedic surgeries performed at Dana-Farber/Boston Children's Cancer and Blood Disorders Center: amputation, rotationplasty, or limb-salvage surgery. In the latter procedure, an internal extendable metal prosthesis is placed in a growing child's tumor-shortened leg and extended intermittently to keep pace with his or her healthy limb.

The idea of starting a program to help young children and their families better understand their surgical options, and then grow comfortable with them, came to Swaim six years ago. Two patients – a 2-year-old and a 3-year-old – were scheduled for amputations. Another child, 23 months of age, was readying for rotationplasty.

"These were young children who were full weight-bearing with normal-appearing limbs right up until surgery, and they were going to wake up to a different situation," says Swaim. "We wanted a way to show them the vastly different appearance and mobility restrictions each would face, and to help them and their parents be as ready as possible for those changes."

Now the orthopedics team can do just that. During initial sessions in which Swaim, surgeons, and other on the team meet with patient families, she brings along her two teaching dolls – an Elmo that has undergone an amputation, and a post-rotationplasty doll. Later, away from

A New Visual Identity

For more than 70 years, Dana-Farber has viewed cancer research through a special lens – one that blends innovative science and exceptional patient care into transformative medicine. This unique approach has brought hope to cancer patients worldwide.

The Institute's new logo – the Dana-Farber Lens – was recently installed outside of the Yawkey Center and visually represents the interplay of science and care as an integrated and unified approach. The colors represent synergy and optimism while the intertwined "D" for "Dana" and "F" for "Farber" connects patients, physicians, researchers, and loved ones to each other and to the Institute's rich history. ITI

Learn more about the new logo on the Brand Resource Center on *DFCI Online*.

Register to Volunteer on Marathon Weekend

Be a part of the Boston Marathon® by volunteering with the Dana-Farber Marathon Challenge (DFMC) team. Shifts are available Friday, April 17 – Monday, April 20. Opportunities that are still available include:

- **Pasta Party Guest Check-In:** Check in runners and their guests to DFMC's pre-race celebration dinner.
- **Hopkinton Pre-Race Runner Refuge:** Welcome runners on the morning of the marathon as they prepare for the starting line.
- **Massage Therapy Staff:** Provide post-race massages to DFMC runners after the race. (Licensed professionals and massage students only.)
- **Runner and Fan Zone Crew:** Greet and direct runners and families to the appropriate locations. Help check in runners after the race and coordinate communication between the runner and family areas.

Inside the Institute is produced by Communications.
The next issue will publish on **Tuesday, March 17, 2020**.

Story ideas are welcome. Email Jessica Cassidy.

Dana-Farber shares patient stories that may include descriptions of actual medical results but are not intended to represent typical results. Dana-Farber provides personalized care for each patient based on their unique needs, and their experiences will vary.

Steven R. Singer
senior vice president for Communications

Michael Buller
senior director, Content and Creative Services

Gillian Buckley
associate director, Content and Creative Services

Naomi Funkhouser
manager, Content and Creative Services

Jessica L. Cassidy
managing editor

Deanna L. Finlayson
designer

Sam Ogden
senior photographer

contributors
John Digianni, Austin Fontanella, Robert Levy, Richard Saltus, Lee Whale, Saul Wisnia, Christina Runnals Photography

Inside the Institute is printed on 30% recycled post-industrial fiber.

Sara Swaim has toys specially made to help young patients better understand their surgical options.

the hospital, preop patients have the option to meet with children who have had different surgeries to further help in decision-making.

Once a family has made its choice, Swaim will ask if the patient wants a favorite toy that has already "had" the procedure. She works with Boston Orthotics and Prosthetics – located on the Boston Children's Hospital campus – to make toys with shortened limbs, and then add the prosthetics. Swaim has been known to do some final limb-sewing herself.

"The goal is to give the child their toy before surgery," says Swaim. "That allows them time to play with it and really visualize limb loss and the prosthesis, as well as to learn how the fitting will work."

Surgeons and patient families praise Swaim's efforts for helping make the pre- and post-surgery periods easier.

"Abby was ecstatic to have her favorite animal now be just like her," says Janell Leavitt, whose daughter, Abby, prepared for her rotationplasty with her beloved retrofitted pig. "It helped tremendously when she went back to school too. Using her pig, she was able to explain to classmates what had happened to her, without taking off her prosthetic.

"For an eight-year-old girl, it made all the difference in the world." SW

Libka, continued from page 1

"My role involves unpacking where the investment opportunities are, and how to get the technology to the clinic quickly," says Libka. "My office works as a conduit to give researchers the best chance to make that happen."

From Researcher to Guardian

Libka's current role is far-removed from what she thought her career path would be as a college student. Her original plan was to treat patients and produce the kind of intellectual property she now protects. Libka is a graduate of Columbia University, where she earned her bachelor's degree in biomedical engineering. While she loved lab research, Libka admits that she was more intrigued by opportunities to describe and promote new technologies and their applications.

Still looking for a way to intersect health care and technology, Libka attended the University of Michigan Law School, where she studied to become an intellectual property attorney – a goal that formed when she interned for former United States President Bill Clinton, and worked with intellectual property attorneys negotiating drug prices on behalf of the Clinton Health Access Initiative.

Libka later became a consultant at the World Intellectual Property Organization in Switzerland and then a senior associate at two major Boston law firms until an opportunity arose to serve on a temporary basis as Dana-Farber's IP counsel.

"I fell in love with the people and technology," she says. "I saw what this position could be, and I kept thinking 'I wish I had more time.'" Fortunately, Dana-Farber's General Counsel Richard Boskey felt the same way. "I knew almost from the first day that we needed to be sure she stayed," he says. "Her intellect, curiosity, and energy were obvious. She was a fantastic complement to the other attorneys in the OGC."

Since coming to Dana-Farber, Libka has expanded her two-person team into a flourishing eight-person – and counting – Intellectual Property Program. Libka designed the program under the Project Thrive Initiative to expand the scope of the OGC's in-house IP services with better quality and at far lower rates than those charged by outside counsel. The IP Program has already assumed coordination of patent application and patent maintenance payments, as well as great savings to the Institute.

"There is no end to what we can get done. We're excited for the future," says Libka. "The investigators here are incredibly smart and prolific. I have so much respect for what they do."

Outside the office, Libka is working on perfecting a piece of her own intellectual property. A graduate of Pennsylvania State's week-long ice cream course, she enjoys experimenting and creating her own flavors of ice cream: her specialty being a maple walnut custard. AF

Nutrition Tips for Younger Patients

- Give your child 5-6 small meals or snacks throughout the day.
- Keep healthy, high-calorie, high-protein snacks on hand, like nuts, cheese, and eggs.
- Give your child a snack before bedtime.
- Give your child high-calorie drinks, such as chocolate milk, whole milk, smoothies, shakes/frappes, or full-fat soy milk.
- Notice the time of day when your child's appetite is at its best, and have them eat then.

High Calorie Recipes

Vanilla Milkshake

- 3-4 scoops ice cream
- 1/2 cup whole-milk
- 3 tablespoons nonfat milk powder or instant breakfast powder
- Blend ingredients

Strawberry Banana Smoothie

- 1 cup whole-milk
- 1/2 cup full-fat yogurt
- 1 banana
- 1/2 cup strawberries
- Blend ingredients

Lactose Intolerance and Colorectal Cancer

A number of research studies suggest that people who consume a lot of milk and other dairy products have a somewhat lower risk of developing colon cancer than those who don't. However, many people avoid or minimize dairy consumption because they are lactose intolerant, meaning they have difficulty digesting lactose – a sugar found in dairy products – due to a deficiency of the enzyme lactase.

Often, this intolerance develops with increasing age, and the proportion of people with the condition varies across ethnic groups, amounting to millions of affected individuals worldwide. So, where does this leave those who are lactose-intolerant and concerned that their diet may impact their risk for colon cancer?

"It's a complicated answer," says Jeffrey Meyerhardt, MD, MPH, clinical director of Gastrointestinal Oncology at Dana-Farber. "Yes, there are multiple epidemiological studies showing a lower risk of colorectal cancer with diets high in dairy and milk, but we really don't know the mechanisms responsible," he says. "It might involve calcium, vitamin D, components of the microbiome, and others."

Most of the research that's looked at the subject is observational, meaning it's difficult to prove cause and effect and identify the specific factors in dairy products that might reduce colon cancer risk.

One review from 2019 looked at 29 studies involving 22,000 case reports and found a consistent and significant decrease in colorectal cancer risk associated with a higher consumption of total dairy products, compared with lower consumption. A 2018 report from the World Cancer Research Fund and the American Institute for Cancer Research concluded, "In general, the more dairy products people consume, the lower the risk of colorectal cancer."

Another review notes that studies conducted in Hungarian and Finnish populations have shown an increased risk of colorectal cancer in individuals who have a genetic variant causing lactose intolerance. According to the review's authors, the enzyme lactase inhibits the development of colon cancer because it produces intestinal galactose, a sugar which binds lectins and helps prevent excessive growth in the intestinal mucosa. While this would suggest deficiency in lactase may contribute to a higher risk of colorectal cancer, the authors said further studies are needed, and similar studies in Italian, British, and Spanish populations failed to find this link.

It's possible that vitamin D and calcium, nutrients found in a dairy-rich diet, may play a role in preventing cancer or helping people live longer with metastatic disease, but the overall picture is complicated, and more studies are needed to understand more about the link between lactose intolerance and colorectal cancer. RS

Purpose, continued from page 1

the emergency room. A blood test revealed O'Toole had acute myeloid leukemia (AML).

"I was in complete shock," recalls O'Toole. "The experience was traumatic. I remember being incredibly scared when they told me I needed to begin treatment right away."

This time, O'Toole was placed under the care of Marlise Luskin, MD, MSCE, an oncologist at Dana-Farber's Adult Leukemia Program. O'Toole's type of AML is characterized by "inversion 16," a chromosome abnormality considered to be more favorable, as the mutation increases the leukemia's sensitivity to chemotherapy. She underwent six months of intense chemotherapy and has been in remission since January 2018.

Becky O'Toole's paintings often incorporate ocean imagery because it has always been a place that brings her a sense of peace and hopefulness.

O'Toole says it was during these treatment sessions when her passion for painting really took off.

"Painting helped me to have some control in my life. It allowed me to work through my stress and do something good with it," O'Toole explains. "I'd bring 40 canvases into my hospital room, and that would become my studio."

The Pink Frame

Encouraged by her husband, Gavin, O'Toole started what is now a flourishing business: The Pink Frame. She began to successfully sell her work and donated a portion from each painting to Dana-Farber. She also gifted her paintings to her care team, and even donated some to the Institute to be offered to patients who might benefit from them.

Most of her work incorporates images of the ocean, a setting O'Toole says has always given her a sense of calmness and hope.

"During her treatment, we'd take turns to come in to admire her work," explains Luskin, who has a pair of O'Toole's paintings displayed in her office directly above her computer. "I love looking at them because it is a wonderful reminder of what my patients can accomplish despite the challenges put in front of them."

"Becky struck me as a strong and resilient person," adds Faggen. "When she was diagnosed with leukemia, I knew that she would get through it with her toughness and strong spirit. I had no idea until recently that she was such an amazing artist, though I am not surprised at all."

Community Driven

O'Toole also uses her work to raise money and awareness for other causes. Last year, she partnered with Scituate-based Untold Brewing and designed four different labels for their products, with proceeds going to four different nonprofits in Scituate.

Moving forward, O'Toole doesn't intend to stop painting. She says she will continue to use her passion as a way to bring positive change in her community and beyond.

"I feel like painting helped save me," adds O'Toole. "A lot of people have empowered me along the way, and I hope my art can help someone in a similar fashion." AF

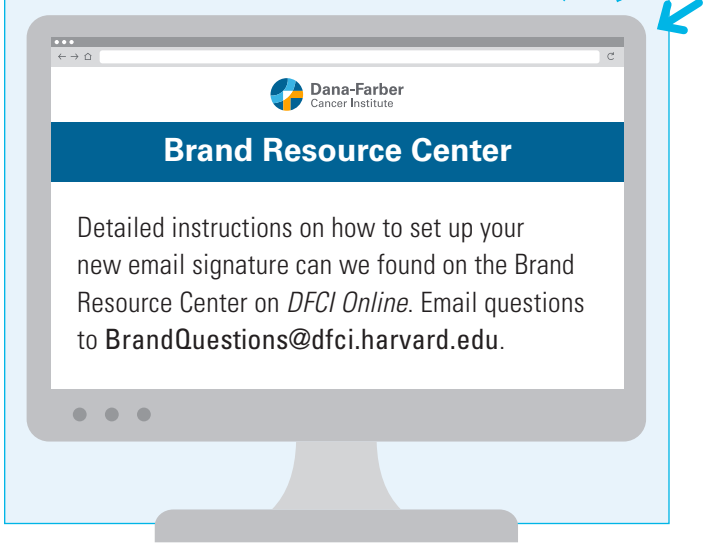
Update Your Email Signature

As we continue to roll out Dana-Faber's new brand architecture, we are pleased to offer two email signature options for all e-communications:

- **Extended Version**
  - Provides the option to incorporate an approved DFCI-affiliated program logo, and includes social media icons for quick access to more information.
- **Condensed version**
  - No social media icons or partner or program logos for a streamlined look.

Note: Personal pronoun use is optional on either version. If included, it should appear below the phone and fax numbers.

Do not make any other modifications to these email signatures. It is important to conform to one of these templates for a clean, clear, and consistent presence of our new brand. Incorporating additional logos, imagery and/or text is not allowed, please reserve that for your personal email signatures.



Resolve, continued from page 1

techniques, Shivdasani explains. Through this process, researchers were able to capture the cells along a continuum of de-differentiation. Shivdasani likens it to a baseball play in which a runner is tagged out between first and second base.

Heavy Turnover

The intestine is one of just three tissues in the body, along with the skin and blood, in which cells are constantly turning over – dying and being replaced by fresh cells. They share this quality because they are the tissues most intimately in contact with material from the environment, and therefore with potentially harmful substances. The constant turnover, it's thought, is a way to prevent toxic substances from having lasting effects on cells and their offspring.

The crypts that hold ISCs are, in a sense, misnamed. Far from being enclosures where dead cells are entombed, they are the sites where ISCs daily generate the billions of daughter cells that take the place of defunct intestinal cells.

One of the chief characteristics of ISCs is that they are extremely radiosensitive, or vulnerable to radiation. People exposed to high levels of radioactivity, in the form of nuclear fallout, for example, can suffer severe intestinal damage because the loss of ISCs halts production of cells to regenerate the damaged tissue. But if ISCs succumb easily to radiation, they also make a rapid return. Patients with radiation-induced intestinal damage who can be kept alive for a week often recover as their ISC levels bounce back.

To determine whether this rebound is due to a reserve stockpile of ISCs or to de-differentiation of daughter cells, Shivdasani and his collaborators performed a kind of time-lapse experiment. They treated a collection of ISCs with the drug tamoxifen, which caused the cells and their offspring to become fluorescent. They waited 48 hours for the label to take hold, then killed the ISCs. If the daughter cells were indeed de-differentiating, any ISCs produced after that point would be fluorescent. That's exactly what researchers found.

While scientists have been able to convert many kinds of differentiated cells into stem cells using laboratory techniques, Shivdasani and his colleagues' discovery demonstrates that de-differentiation is more than a curious act of nature; it is the principal means to restore damaged stem cell in the intestine. It's not known whether cells in other organs and tissues have this capability, but it remains an open avenue of investigation.

"It also isn't clear how the crypt knows that stem cells have died and need to be replaced, or how the daughter cells receive the signal to de-differentiate," Shivdasani remarks. "This is a subject we're currently exploring."

The lead author of the paper is Kazutaka Murata, PhD, of Dana-Farber and BWH. Co-authors include Unmesh Jadhav, PhD, and Alessia Cavazza, PhD, of Dana-Farber and BWH; Shariq Madha; Justin Dean; Kai Wucherpfennig, MD, PhD; and Franziska Michor, PhD, of Dana-Farber; and Johan van Es, PhD, and Hans Clevers, MD, PhD, of the Royal Netherlands Academy of Arts and Sciences and University Medical Centre. RL

Nominate a Nurse

Do you know a special nurse who has had an impact on you or your family? Honor this individual by nominating him or her for the *Boston Globe's* annual Salute to Nurses, appearing May 10 in the *Boston Sunday Globe*, in conjunction with National Nurses Week.

The *Boston Globe* will publish selected stories in the Salute to Nurses section. Submissions are due March 22.
nurses.bostonglobe.com

The Boston Globe Salute to Nurses

Dana-Farber Cancer Institute