Ovarian tumors might begin in fallopian tubes

Research by Dana-Farber investigators is helping expose a malevolent biological impostor.

High-grade serous ovarian cancer (HGSOC), the fifth-deadliest cancer among American women, is thought by many scientists to be a fallopian tube malignancy masquerading as an ovarian one. Pinning down its actual tissue of origin is critical to devising better treatments, but most of the evidence linking HGSOC to the fallopian tubes has so far been circumstantial.

In a new study appearing in Proceedings of the National Academy of Sciences, Dana-Farber scientists report that they’ve developed a laboratory model that mimics the process by which fallopian tube cells may morph into cancer cells that appear to have come from the ovaries. Their demonstration that this process can happen in the lab is powerful evidence that it does happen in patients. “The hypothesis of fallopian tube origin of HGSOC is based primarily on examinations of fallopian tubes surgically removed from women with a genetic predisposition to ovarian cancer,” says senior author Ronny Drapkin, MD, PhD. “Areas of the tubes adjacent to the ovary often had patches of cells that were predecessors of serous cancers. But to convincingly show that these cells are the source of HGSOC, we needed to trace each step of the disease’s development. Our model provides that kind of demonstration.”

The origins of fallopian tube origin of HGSOC have been so difficult to track down because of the insidious nature of the disease. Ovarian tumors often establish themselves without producing warning symptoms. By the time the disease is discovered, the ovaries can be so over-run with cancer that adjacent sections of the fallopian tube are obscured, making them difficult to examine. Late detection is one reason why ovarian cancer is notoriously difficult to treat. Approximately 22,900 women in the United States are diagnosed with HGSOC each year, and 14,000 die of it.

In work published last year, Dana-Farber researchers created a labora-

Cord blood transplants shown safe

An innovative treatment for boosting the effectiveness of stem-cell transplants with umbilical cord blood has a favorable safety profile in long-term animal studies, report scientists from Dana-Farber, Children’s Hospital Boston (CHB), and Beth Israel Deaconess Medical Center (BIDMC).

Analysis of long-term safety testing in nonhuman primates, published online by the journal Cell Stem Cell, revealed that one year after transplant, umbilical cord blood units treated with a signaling molecule called 16,16-dimethyl PGE2 had reconstituted all the normal types of blood cells – and none of the animals receiving treated cord blood units developed cancer.

Wolfram Goessling, MD, PhD, of Dana-Farber/Brigham and Women’s Cancer Center is the first author of the paper.

Mukherjee speaks at capital campaign celebration

In a strange serendipity, Dana-Farber’s seven-year capital campaign parallels the period of time Siddhartha Mukherjee, MD, PhD, was writing The Emperor of All Maladies: A Biography of Cancer.


The Emperor of All Maladies was included among the “10 best books of 2010” by The New York Times and won the 2011 Pulitzer Prize for general nonfiction in April. “Every life will be touched by the family of diseases we call cancer,” said Mukherjee, who gave a brief summary of cancer’s “biography,” beginning with Egyptian hieroglyphs that reference a woman with a disease we now know to be breast cancer.

The book features several Dana-Farber staff physicians,

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Interpreter Services at the push of a button

It’s hard enough to arrive at a cancer center for the first time as a patient. Now imagine the experience if you didn’t speak English.

If such a patient arrives in Central Registration on the second floor of theYawkey Center for Cancer Care, the first stop for all new adult patients, staff can now communicate – even with those who speak the rarest of languages – with the push of a button.

This new pilot program, spearheaded by Interpreter Services, involves a set of cordless phones that simultaneously connect the registrar and the patient to an Interpreter Services, page 4

Dedicated to Discovery...Committed to Care
Animal facility earns high marks

Manning, director of the facility, and exceptional standard operating procedures, says Heather among ARF staff, a prominent animal enrichment program, which recommended full certification for another three years. According to Manning, the AAALAC reviewers commented that these systems contributed to the unparalleled veterinary care seen throughout the site visit. ARF is responsible for the health and care of about 60,000 animals used in research – nearly all of them mice – at Dana-Farber. Barbara Smith, DVM, PhD, senior director and attending veterinarian, is the operational supervisor.

What does your job involve?

DF/HCC combines the cancer research efforts of seven Harvard-affiliated institutions, with the common goal of finding innovative ways to combat cancer. As the DF/HCC business analyst, I have two primary responsibilities. First, I am responsible for collecting, reporting, and analyzing data on grants that fund cancer research across the seven member institutions, as well as cancer-related clinical trials and DF/HCC membership.

Secondly, I am part of an administrative team that is responsible for the renewal of the Cancer Center Support Grant. This grant is for more than $10 million (in direct costs) per year, and supports much of the infrastructure that cancer researchers use to conduct clinical, basic, and population science research. We submitted the grant in January and are awaiting the results of the review.

Outside of my DF/HCC role, I serve as the co-chair of the Dana-Farber Cultural Observances Committee. The committee highlights and recognizes the cultural observances of the Dana-Farber patient and employee community, such as the annual Martin Luther King Jr., Celebration, National Women’s History Month, Asian Pacific American Heritage Month, Latino-Hispanic Heritage Month, and International Day.

What attracted you to the Cultural Observances Committee?

About five years ago, I was new to Dana-Farber and wanted to establish connections here, so I signed up as a participant in the Martin Luther King Jr., and the Asian Pacific American Heritage Month celebrations. Inspired by the events and the committee, I became increasingly involved each year and went from participant to event organizer. The results of my participation are long-lasting friendships and enhanced organization, planning, management, and leadership skills. Furthermore, I learned to appreciate, enjoy, and respect cultures from other countries and regions, and now I have a more intimate connection to the world and a bigger heart to care for people from other cultures.

What brought you to Dana-Farber?

I was a management information system manager back in Taiwan, and my family moved to the U.S. in 1993. My husband passed away in 1997 from pancreatic cancer. At that time, I had limited work experience in the U.S. I started with a part-time job and studied at Harvard Extension School to prepare myself for professional work. Soon I was fortunate to work fulltime as a computer programmer and database administrator. During those rough years of working, going to school, and raising my daughter, I made a wish that one day I could help those in need. I consider it a blessing that I can work at Dana-Farber in my current role.

With support and encouragement from DFCl executive leadership, my supervisor, colleagues, and family, I recently earned my MBA from Northeastern University. It would have been impossible to achieve my dreams and this goal without my DFCl community, which is like a home to me.

What is your proudest work achievement?

A recent challenge was to prepare the competing renewal grant application for submission to the National Cancer Institute. We learned to work and function as a productive, effective, and efficient team to accomplish many complicated and highly detailed projects involved in preparing the grant. In addition, we developed a new database that integrates data from many areas. The database has improved the quality of our work and decreased the amount of labor necessary to produce the grant.
No one is an island

By Larry Kwong, PhD, a postdoctoral fellow in Medical Oncology

The lone geniuses are out there; they do exist. These scientists, hunkered over books and labware, decipher riddles of nature over long and laborious tenures. Some of them even get Nobel Prizes. But today’s scientist is increasingly a plural, as teams—not individuals—have become the drivers of today’s most astute discoveries. This happens at a few different levels: institutions, head investigators, and then us postdocs and students.

At the higher levels, it’s been a slowly turning tide through the decades towards collaboration over competition. An optimist like me might suggest that a balance is being refined here: that we can get more done by working together, yet still have a healthy spur of competition. Another major part of it has been an increasing demand from technology and statistics. A lot of studies now require a large network of institutions, doctors, and researchers to recruit thousands of patients and healthy individuals from whom to collect and analyze biological samples.

A postdoc’s set of projects is often a microcosm of this broad arrangement: we must seek out collaborators and learn the ropes of networking and politics (in a good way). Early on, a good mentor will help a postdoc by introducing him or her to potential collaborators, if not setting the partnerships up directly. In general, however, initiative is the key word. Even when collaborations are already set up, we have to begin marshalling our own resources.

On one level, such collaborations help my projects. A few weeks ago, I was trying to cut extremely thin slices of a frozen tumor, but found the slices always curled up or broke apart. I was too proud (and embarrassed) to ask for help right away. As with all such things, I found pride isn’t worth much: as soon as I asked, I found out that I was holding the handle on the machine wrong.

On another level, science just works better when it’s attacked at several different angles. Not only with ideas, but with different types of assays looking at the same thing, providing a multi-dimensional (not to mention time-saving) way of understanding complicated biological processes. If I were stubborn last year, I could have spent several days painstakingly isolating DNA from a hundred tumors. Instead, I asked if my collaborators would do it, and their expert DNA sequencing data will greatly complement my RNA data.

Overall, it’s tough to be an island these days. It can and is being done, but even grants tend to be geared towards collections of labs. Everyone is recognizing that as the depth and complexity of our knowledge about cancer grows, so too must the research infrastructure that continues to prove it. A successful postdoc learns how to incorporate this vital aspect of the emerging research world. Lone genius is a great thing—but working toward a common goal can provide moments of group genius.

Cover your cough—no matter the season

Springtime’s arrival means rising temperatures and blooming flowers, but for many people it also means allergy season—when pollen can cause runny noses, itchy, watery eyes, sneezing, and coughing. And even though spring signals the end of cold and flu season, good respiratory etiquette is still important.

For staff and patients alike, taking steps to prevent cold and flu throughout the year can make all the difference in staying healthy and keeping patient safety at the top of our priorities. Here are some tips to remember:

• Cover your cough or sneeze with a tissue and then throw the tissue away. If you don’t have a tissue handy, use your elbow or upper arm to cover your cough.
• Clean your hands with an alcohol-based hand sanitizer or wash them with soap and water. You should do either regularly, but especially after coughing, blowing your nose, or touching items that others have touched. Throughout the Institute, you’ll find hand-hygiene stations with Purell dispensers, tissues, and surgical masks.
• Stay home if you are ill and avoid contact with people who are sick. Do not visit patients or come to work if you have a fever. Patients coming to the Institute with a cough or a fever accompanied by either a runny nose or a sore throat should be given a mask to wear. Staff members who are ill and have a fever need to check with Occupational Health before returning to work.
• Prevent the spread of germs. Follow the tips listed above and try not to touch your eyes, nose, or mouth.

You can also help prevent the spread of illness by keeping your immune system strong. This means getting enough sleep every night, exercising regularly, and eating a nutritious, balanced diet.

Cord blood—continued from page 1

and Trista North, PhD, of BIDMC, is the senior author.

One of the limitations of cord blood as a transplant source is that the cells engraft in a recipient’s bone marrow more slowly than do matched donor cells from bone marrow. In addition, there is a higher failure rate for cord blood transplants. Thus there is a need for ways to improve the speed and quality of cord blood transplantation.

Goessling and North were postdoctoral fellows in the laboratory of coauthor Leonard Zon, MD, a stem cell researcher at CHB, when they hit upon 16,16-dimethyl PGE2 while looking for compounds that could regulate the production of blood-forming stem cells. The initial testing used zebrafish models, and, according to Goessling, “this is the first time a compound discovered in zebrafish has received a nod from the Food and Drug Administration for a clinical trial.” A phase I clinical trial under way at DFCI and Massachusetts General Hospital, led by Corey Cutler, MD, has enrolled more than a dozen patients who underwent stem cell transplants using frozen blood units harvested from umbilical cords. Each patient receives one untreated cord blood unit and one treated with 16,16-dimethyl PGE2. Full results have not yet been reported.

Research by Wolfram Goessling has lead to enhanced cord blood transplants getting safety approval from the Food and Drug Administration.

Visit DFCI Online and search “Patient Safety” or “Infection Control” to learn more.

FastFact

7,278 — Number of units donated by platelet donors in 2010.
Ovarian cancer continued from page 1

Rony Drapkin and Alison Karst created a new model that allows scientists to genetically alter fallopian tube cells to gain insights into the development of high-grade serious ovarian cancers. For the new study, researchers removed secretory cells from the fallopian tube tissue model and “immortalized” them—altered the cells’ genetic programming so they could divide indefinitely, as cancer cells do. As the Cancer Genome Atlas Project has shown, ovarian cancer cells don’t have a consistent pattern of gene mutations (other than in the p53 tumor suppressor gene). Instead, they show broad irregularities in the number of copies of key genes—too many, too few, or none at all. The gene most commonly missing from ovarian cancer cells is hRb, the one most often overduplicated is c-Myc. The Dana-Farber researchers, including lead author Alison Karst, PhD, and Keren Levanon, MD, PhD, made the immortalized cells mimic those abnormalities by shutting down hRb and sending c-Myc into overdrive. Like true tumor cells, these “artificial” cancer cells proliferated rapidly and had a 35 percent reduced risk for breast cancer recurrence. This is the largest study that examines soy consumption in breast cancer patients, and is based on tracking the diets of 9,515 American and Chinese women (average follow-up was seven years). Previous study results, which led to soy’s bad reputation for breast cancer patients, focused on the effects of isoflavones in laboratory animals.

Myth 1: Breast cancer recurrence risk can be reduced by adding soy into my diet.

Reality: Maybe. The women who exhibited the greatest benefits from soy were born and raised in China and had been consuming large amounts of soy from birth. In the U.S., soy consumption was much lower overall and started later in life. Therefore, it is unknown if starting soy consumption after turning 30 would be as helpful.

Does soy do a body good?

In 1947, a few months after establishing the Children’s Cancer Research Foundation (now Dana-Farber), its founder, Sidney Farber, MD, (above) formed a team to help him in his studies of children with acute lymphoblastic leukemia (ALL) — then a universally fatal disease. Although many in the medical community scorned such efforts as futile, pediatric hematologist Louis Diamond, MD, and fellows Robert Mercer, MD, Robert Sylvester, MD, and James Wolff, MD, joined Farber in his work. Testing the impact of folic acid antagonists on 16 children with ALL, the most common childhood cancer, they achieved temporary remissions in five patients and published their results in the June 3, 1948 issue of the New England Journal of Medicine. Soon physician-scientists worldwide were sending patients to Boston for Farber’s team to treat, and their work became the springboard for decades of advances leading to today’s pediatric ALL five-year survival rate of about 85 percent.

Myth 2:

Breast cancer survivors should avoid soy.

Reality: Not true. Soy foods are a beneficial part of a healthy diet, and may actually improve your health. For example, says Chen, researchers found that women who ate the greatest amount of isoflavones — nearly 12 milligrams per day — actually decreased estrogen-like properties in laboratory studies, increasing fears about their impact on breast cancer recurrence and tamoxifen treatment. However, a new study presented at the American Association for Cancer Research annual meeting in April found that soy products are, in fact, safe. We checked in with one of the study’s investigators, Wendy Chen, MD, MPH, of Medical Oncology, to get the skinny on soy.

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Interpreter Services continued from page 1

available-on-demand interpreter. Rather than passing a phone back and forth, or using a speakerphone, the system provides a more seamless—and private—way to communicate.

“The goal is always to provide an in-person interpreter. But when we cannot assign an interpreter immediately, or in cases where we have requests for a rare language, this technology provides one more option to ensure that all of our patients can be understood,” says Laura Nakazawa, manager of Interpreter Services.

Last year alone, Interpreter Services assisted 15,800 patients in person and 2,400 by phone, with tasks that varied from scheduling appointments to interpreting doctor’s visits. Requests have been growing steadily during the past few years, at about 10 to 12 percent per year. As demand has increased, so too has the number of interpreters. The department now has 52 linguists available, between full-time and per diems, including those who can speak Indone-

sian, Twi, Somali, and Urdu.

Next May, with the support of Telecommunications, Nakazawa hopes to expand the phone service to the Yawkey Center’s clinical floors, as well as the Jimmy Fund Clinic and Imaging.

Ovarian cancer continued from page 1

Q: Who were the first doctors to work at Dana-Farber?

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