UC Leads Study on Male Breast Cancer Drug Combination

By Amanda Harper
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Medical oncologist Zeina Nahleh, MD, wants to know whether a certain drug combination can slow the progression of male breast cancer, a rare disease that often goes undiagnosed until it’s at an advanced stage.

Nahleh is leading a national phase-2 clinical trial to test a combination of the drug anastrozole (Arimidex), currently approved by the Food and Drug Administration (FDA), for treating breast cancer in postmenopausal women, can effectively fight the same disease in men.

“IF we’re going to make significant advances against the disease, we need better male-specific treatment strategies,” says Nahleh, director of breast oncology in UC’s division of hematology and oncology.

Previous research has shown that the female hormone estrogen promotes the growth of certain types of breast cancer. Anastrozole is one of a class of drugs, known as non-steroidal aromatase inhibitors, that block the tumor’s use of estrogen and slow its development.

By treating male breast cancer with a combination of anastrozole and a synthetic hormone called aromatase, Nahleh said that results could be promising.

See CANCER page 5

Hoxworth Sees Influx of Minority Donors

Targeted Recruitment Campaign Helps Center Increase Minority Blood Supplies By 14 Percent

By Michael Anderson
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More minorities are rolling up their sleeves to donate blood in Cincinnati and give the “gift of life.”

Hoxworth Blood Center recently reported that more than 4,000 minority donors came to the center or a community blood drive between April 2005 and March 2006, a 14 percent increase over the same time period a year ago.

This increase was reported as the result of a Minority Donor Recruitment Campaign that Hoxworth launched in April 2005.

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Hoxworth saw the biggest jump in minority donors from high school students. There were 1,086 minority donors at high school blood drives between April 2005 and March 2006, a 35 percent increase over the same time period in 2004-05. Annually, over 190 high schools in 17 area counties host blood drives at their schools, combining for more than 10,000 individual donations.

See HOXWORTH page 3

Medical Students’ Diagnostic Skills Improved Through Art

New Course Redefines Connection Between Art and Medicine

By Sheryl Hilton
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UC medical students are studying works of art in order to appreciate that medicine is often more of an art than a science.

Based on the premise that art is the way we make observations, and that medicine is often more of an art than a science, UC medical students are studying works of art from ancient to modern times. The course is run by Barbara Tobias, MD, and Nancy Elder, MD, both associate professors of family medicine, with the help of Amber Lucero-Criswell of the Cincinnati Art Museum.

Using paintings and sculptures at the art museum, says Tobias, “We’re attempting to teach students to think about conclusions made on the basis of their observations. For example, what is it about this person that makes us think they are sad, and what are the observer’s personal frames of references and biases?”

“A greater awareness of the differences between our objective and subjective views allows us to be more careful about the judgments we make about patients, and people in general,” Tobias says. “It’s very easy for a doctor to seize upon an obvious diagnosis, and overlook other complicating conditions.”

The field trips to the art museum are not just a reprieve from the welter of medical facts that students are expected to absorb.

“Taking this class has been one of the highlights in my medical

Physicians who provide care to Hamilton County children with chronic neurological conditions and other disabilities can take advantage of a new UC program that offers no-cost magnetic resonance imaging (MRI) exams.

Kenneth Weiss, MD, associate professor of radiology and psychiatry at UC, has developed a noninvasive, computer-automated MRI technique—known as the automated scan survey iterative scan technique (ASSIST)—that allows physicians to obtain rapid, high-quality MRI scans without exposing the patient to radiation or sedation.

MRI is an imaging procedure that uses a magnetic field and radio-wave energy pulses to create pictures of organs and body structures. The test is used to detect, diagnose and plan treatment for a variety of disorders.

The new ASSIST procedure is used to screen, assess and monitor medical conditions related to the neuroaxis (brain and spine).

“Spine and brain imaging in kids is challenging because the patient usually can’t hold still for the duration of the scan,” Weiss says. “This is especially true in children with neurologic disabilities. So unfortunately, the procedure usually requires sedation or external radiation to get useful results.”

Scientists say radiation exposure and sedating medications may have immediate and long-term cumulative effects in children, he says, so they often seek alternatives to minimize or avoid these risks.

Weiss believes the ASSIST technique, which is currently being refined in adults, could also improve the detection and diagnosis of child brain and spine conditions and injuries—ultimately leading to better care.

“Brain and spine abnormalities are a leading cause of death, disability and reduced quality of life in children,” he says. “We hope that by providing physicians with a technique that is scientifically valid but lower in cost, MRI can become a more feasible neurological screening and diagnostic tool in day-to-day patient care.”

See MRI page 2

Golfing for Cancer Research

The first UC Cancer Center/Barnett Center Golf Classic raised $7,500 to support cancer research programs at UC. Seventy-five people came out to swing for a good cause at the 18-hole golf scramble held June 19 at the Snow Hill Country Club in New Vienna. Volunteers (from left to right) Lori McDonald, Barb Shapiro and Sandra Terry served as event chairs.

See ART page 4
High Blood Sugar Puts Intensive Care Patients at Risk

By Jamie Davis
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If you or a loved one has high blood sugar and are treated for a heart attack or stroke in an intensive care (ICU), you are more likely to die.

Researchers at the Veterans Affairs (VA) Impaired Evaluation Center located at the Cincinnati VA and UC examined the records of 216,000 critically ill patients, 97 percent of whom were male, admitted at 177 VA intensive care units throughout the country. They found patients with certain diseases and conditions, especially cardiovascular problems such as heart attack and stroke, faced a significantly higher risk of dying.

“Our finding that mortality risk varied depending on the disease that led to a patient’s hospitalization was consistent with our expectations,” says Mercedes Falciglia, MD, assistant professor of medicine at the Cincinnati VA.

“But what did surprise us is that intensive-care patients with high blood sugar who had no diagnosis of diabetes were more likely to die than patients with diagnosed diabetes and the same degree of elevated blood sugar.”

High blood sugar, referred to as hyperglycemia, increased heart attack patients’ risk of death from up to five times that expected among non-hyperglycemic patients of similar age and with similar associated illnesses. Hyperglycemia raised the death risk of stroke patients anywhere from 5.4 to 15.1 times, and that of unstable angina patients from 1.7 to 6.2 times. Early, small trials have already associated hyperglycemia with increased mortality in hospitalized patients. However, the potential benefits of reducing high blood sugar levels have been questioned, because results from intervention trials with intensive insulin therapy have varied—some trials showing improved outcomes with treatment and others having no effect.

“It’s not clear why hyperglycemia occurs in hospitalized patients who don’t have diagnosed diabetes, nor why they may have worse outcomes in some cases than people with diagnosed diabetes,” says Falciglia. “That’s why further studies are necessary.”

According to Falciglia, intensive-care personnel routinely obtain blood for various tests, including blood sugar levels.

“For many of the conditions typically found in the ICU setting it’s important that someone look at the patient’s blood sugar level information and act on it,” says Falciglia. “Physicians are increasing their awareness of the potential harm from hyperglycemia and a systematic approach for lowering blood sugar levels in hospitalized patients is important in order to do so effectively and safely. The good news is that such initiatives are becoming a priority throughout the country.”

Locally, Falciglia is leading a team of physicians, nurses and pharmacists from UC and University Hospital who have established DiabetesNOW!, a new program providing cutting-edge resources and education for practitioners caring for diabetes and hyperglycemia inpatients. The program offers intensive practitioner education and a protocol on insulin use, and establishes diabetes resource specialists for every unit in the hospital.

Falciglia presented their findings at the American Diabetes Association’s (ADA) 66th annual scientific sessions last month.

The ADA estimates that 6.2 million Americans have undiagnosed diabetes. Caused by high blood sugar levels resulting from the body’s inability to produce or use insulin, diabetes affects 20.8 million children and adults in the United States.

Collaborators in the study were Marta Renda, MD, professor of medicine in the pulmonary and critical care division and director of the VA’s Impairment Evaluation Center, and David D’Alessio, MD, professor of medicine and division director of endocrinology. The research was funded by the VA.

UC Research Awards Interdisciplinary Grants

Six faculty members from the College of Medicine have received $25,000 University Research Council grants under the new Interdisciplinary Grant Program, sponsored by UC’s research office.

The program’s goal is to encourage campuswide, interdisciplinary research projects that will result in applications to federal granting agencies.

Thirty-eight grant applications were received from 129 faculty members representing nearly every UC college, the Institute for the Study of Health and Cincinnati Children’s Hospital Research Foundation. Faculty will work with other UC researchers in the following projects:

• Electrode for Deep Brain Stimulation: Michael Bethelhan, PhD, and Raymond Pun, PhD, both of molecular and cellular physiology, with Raymond Li, ScD, of the College of Engineering.
• Mapping of Transduction in Olivary Cilia: Steven Kleene, PhD, of cell biology, neurobiology and anatomy, with Donald French, PhD, of the McMicken College of Arts and Sciences.
• Development of Diagnostics and Therapeutics for Shiga Toxin: Alison Weiss, PhD, of molecular genetics, with Suri Iyer, PhD, of the McMicken College of Arts and Sciences.
• Managing Cognitive Workload and Stresses in Minimally Invasive and Robotic Surgery Interfaces: James Donovan, MD, and Krishnanath Gaitonde, MD, both of surgery, with William Ball, PhD, College of Engineering, and Gerald Matthews, PhD, Michael Rokok, PhD, and Joel Warm, PhD, all of the McMicken College of Arts and Sciences.

This allows physicians to get numerous high-quality images in a very short timeframe—without exposing a vulnerable population to potentially harmful ionizing radiation.”

Kenneth Weiss, MD
Initiative, Weiss is currently working with that country’s leading researchers to refine his MRI technology. The international team hopes to increase MRI scanner productivity so that more patients in highly populated countries have access to diagnostic imaging services.

This UC MRI program is funded by a $100,000 State of Ohio grant. Weiss and his advanced neuroradiography team will begin seeing patients at UC’s Varsity Village Imaging Center and other facilities this fall.

The project is being conducted in collaboration with Cincinnati Children’s Hospital Medical Center physicians and UC faculty Tom DeGrauw, MD, and Kerry Cron, MD.

For more information, physicians should call (513) 584-1384.

Space is limited and children must be referred into the program by a qualified physician.

MRI: Noninvasive Technique Offers Better Brain and Spine Scanning Capabilities from page 1

The UC-developed technique uses computer-automated software to obtain and analyze brain and spine MRI studies. With Weiss’ technique, a total neutron scan takes as little as five minutes. Traditional total brain and spine MRI exams can take more than 1.5 hours to complete.

Weiss stresses that the neutron scanning exam is not as comprehensive as a standard MRI, but it may be sufficient to answer pressing clinical questions.

“For cases that involve fidgeting or claustrophobic children, the rapid image sequencing may actually yield more information than a longer—but motion-degraded—exam,” he says.

“This allows physicians to get numerous high-quality images in a very short timeframe—without exposing a vulnerable population to potentially harmful ionizing radiation.”

Kenneth Weiss, MD

Academic Health Center

Launch Center

Brain and Spine Scanning Capabilities

Dr. Kenneth Weiss, COO of the University of Cincinnati Academic Health Center, presented on Thursday at the McMicken College of Arts and Sciences.

The center is the largest academic health center in the state, with more than 17,000 employees and a medical school.
One Marathon Down, Olympics Yet to Go

Focus and Some Luck Fuel Researcher’s Multi-Career as Student, Epidemiologist and Semi-Professional Runner

By Jill Hafner
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It was just two months ago that UC research associate and PhD candidate Norah Shire captured Cincinnati’s crown jewel, the 2006 Flying Pig Marathon. And already she has her eyes set on something bigger—qualifying for the Olympic Marathon.

Shire plans to shave nine minutes off of her Flying Pig time when she competes in the Columbus Marathon this fall. That time of 2:47:00 would place her in the company of other athletes—professional runners who spend countless hours training solely for the ultimate Olympic race. But Shire is different.

Besides running nine miles to jump-start her day and logging another three miles or so in the evening, Shire spends 40-plus hours at her day job in UC’s digestive diseases division. On top of that, she is wrapping up her dissertation in epidemiology and biostatics. But this “jack of all trades” thinks nothing of her workload. “It’s all about mental focus and persistence for me,” says Shire. “I think running almost parallels my research or dissertation and completely on that, and I can work on that while I’m running,” she says.

Sometimes I find myself running faster, and sometimes I get really excited if I get a ‘eureka!’ kind of moment—thinking ‘that’s it, that’s the model I need to use!’ Admittedly, Shire says she fell into running just as she did studying epidemiology and landing a job at UC with Ken Sherman, MD, PhD.

The 36-year-old Washington, D.C., native, who graduated from Williams College with double degrees in English literature and pre-medicine, walked onto her college cross country and track teams.

“In college, I tried to keep my options open,” she says. “I liked science and writing, but wasn’t sure what I wanted to do.”

“I also wasn’t a very good runner,” she adds. “The college coaches noticed that I had good form and asked if I wanted to walk on the team. I didn’t do well.”

Shire says she was a much better cyclist than she was a runner. So much so that after graduation she pursued professional cycling—a passion she developed while studying in Scotland during her junior year.

Shire says she competed against the best, including many former and aspiring Olympians. However, after suffering a hard crash in 1999, she decided to call it quits and focus on her other passion—science.

“After I looked down and saw how much skin I actually lost, I knew that it was time to retire,” she says. “I also knew that I wanted to become an epidemiologist.”

Shire enrolled at Johns Hopkins University to earn a master’s degree in public health with a focus in biostatics and viral epidemiology. To help make ends meet, she worked as a pharmaceutical representative for Procter & Gamble. Although Shire says sales was not her cup of tea, it did put her one step closer to where she is today.

“P&G transferred me to Cincinnati. While I was working, I called on Ken Sherman, and ended up doing my master’s thesis with him,” she says. “ Afterwards, he recruited me to work full time for him while I started my doctorate.”

Moving to Cincinnati also inspired Shire to begin running again. What began as “something to do” has escalated into something much more serious.

“I didn’t start running seriously until last October,” says Shire. “I now have a coach who sets a schedule for me. I run about 70 miles a week.”

The Flying Pig was Shire’s third marathon. And although the Olympics might be yet another thing she “falls into,” it certainly won’t be anything she passes up.

“I never considered running in the Olympics until I finished the Flying Pig, and I felt so comfortable,” she says. “Sometimes it takes a really big win to give you the confidence to reach higher. It’s like getting your first grant. Your first grant will always lead to others.”

“My goal is to become a research assistant professor at UC and continue to compete as a regional runner.”

“However,” she adds, “if I do make the Olympics, a sabbatical may be in order!”

Norah Shire, digestive diseases research associate and PhD candidate.
Omega-3s Are Important for More Than Just Heart Health

By Dama Kimmon
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If recent news about mercury levels in fish and recommendations about adding this “heart-healthy” staple to our diet is confusing enough, here’s some food for thought.

The same fish we’re warned against—and those still considered safe to eat in larger portions—actually provide our brains with essential omega-3 fatty acids. The omega-3 fatty acid in our brain—called docosahexaenoic acid (DHA)—plays an important role in brain development and function, and can only be obtained through our diet. And compared to people in other countries, says UC psychiatry researcher Robert McNamara, PhD, American diets are suffering from a “DHA deficit.”

“Fear of mercury and dietary trends in the United States has really impacted the amount of omega-3 fatty acid-rich foods that we consume on a daily basis,” says McNamara.

Omega-3 fatty acids, particularly DHA, can be found in high levels in fatty fish, including salmon, trout and tuna.

A recent committee assembled by the American Psychiatric Association evaluated published data on the link between omega-3 fatty acid consumption and major mental disorders, and concluded that omega-3 fatty acids could potentially be a safe and effective treatment for depression and bipolar disorder, and they say further studies are warranted.

But it’s the DHA we stock up on during critical periods of brain development that McNamara is so intrigued by. Lack of this fatty acid during associated with deficits in brain dopamine and serotonin levels which may contribute to attention problems and depression in young children, he says.

McNamara is now conducting a study to find out if “adding back” DHA in the form of a fish-free supplement to the diets of young children can reverse DHA shortfalls and associated activity in brain regions involved in attention.

“For babies in utero, their only source of DHA is their mother,” he says. “After birth, an infant’s DHA comes from breast milk or fortified formula. If moms aren’t getting enough DHA, then the child’s developing brain will be deficient.”

And, he says, DHA fortified formula did not become commercially available in the U.S. until 2002.

Brain gray matter expansion continues until about the age of 12, says McNamara. Knowing that, he hypothesizes that adding DHA to diets of children under 12 may be a way to “restock” this fatty acid in their brains, impacting cognitive function.

McNamara is currently studying 8- to 10-year-old right-handed boys over the course of two months. Some will receive fish-free DHA supplements and others will receive a placebo.

A functional MRI (fMRI) test will be given at the beginning and end of the study to gather information about brain activity and metabolism during the testing.

The study is specific to right-handed boys, McNamara says, because handedness makes a difference in which brain hemispheres researchers monitor.

“We hope to determine whether dietary DHA intake can improve brain activity and function,” says McNamara.

To find out more about McNamara’s research, or to participate in the study, call (513) 558-5601.

“Fear of mercury and dietary trends in the United States has really impacted the amount of omega-3 fatty acid-rich foods that we consume on a daily basis.”

Robert McNamara, PhD

In short, Greater Cincinnati has played a major and important role in this disastrous disorder. Needless to say, on behalf of all the patients and families, we hope it will be possible in the future to prevent HIV/AIDS and to have much more effective treatments.

We at the UC Academic Health Center are committed to that.
CANCER: Investigating Drug Combo on Male Breast Cancer

from page 1

goserelin, Nahleh believes she may be able to stop the transition of the male hormone testosterone to the estrogen estradiol, significantly lowering the man’s overall estrogen levels and limiting breast tumor growth.

Approval for the treatment of prostate cancer, endometriosis and advanced premenopausal and perimenopausal breast cancer.

“Combination therapy of breast cancer is different in men and women, so identical treatment methods are not the best solution,” explains Nahleh.

“We believe that anastrozole—when used in conjunction with a gonadotropin-releasing hormone injection—will lower the amount of male estrogen in the body, resulting in better control of the breast tumor.”

The trial, sponsored by the National Cancer Institute’s Southwest Oncology Group, is the first to test this specific drug combination in men with advanced breast cancer.

“We’ve seen a 26 percent increase in the number of male breast cancer cases since 1973, but the disease is so rare that there’s been little research to determine the best ways to detect and treat the disease specifically in men,” explains Nahleh.

Current male breast cancer treatment methods are based on accepted approaches to the disease in women. Unlike female breast cancer, however, says Nahleh, the relationship between the estrogen receptor and overall survival is unclear.

Under Nahleh’s direction, researchers from medical centers nationwide will test the drug combination on about 68 male patients—age 18 or older—who have recurrent or advanced breast cancer.

Patients will receive an anastrozole pill every day and a goserelin injection on the first day of 12-month-long cycles. Every two months researchers will collect serum samples to evaluate blood estrogen levels. They will also obtain CAT scan and X-ray images of the tumor to determine how the patient is responding.

After the treatment, Nahleh and her team will follow patients for three years to determine whether the approach is a sustainable option for managing male breast cancer.

The American Cancer Society estimates that nearly 1,700 men were diagnosed with breast cancer in 2005 and about 27 percent will die from the disease.
### Teaching Excellence Awards
The College of Medicine recently announced winners of its Gold and Silver Apple Awards, which honor excellence in teaching, and the Arnold P. Gold Foundation Humanism and Excellence in Teaching awards.

### Low Endowment Created
The anesthesiology department recently established an endowed lectureship in honor of Edward Lowe, MD, a professor emeritus.

### Recognizing Humanism
Bruce Gebhardt, MD, of family medicine, and Matthew Meier, a fourth-year medical student, are the recipients of the 2006 Leonard Tow Humanism in Medicine Awards, presented by the Arnold P. Gold Foundation.

### First Rectal Microsurgery
UC has become the first in the Tristate to use this new approach for removing rectal cancers without creating external incisions.

### Bone Drug Prevents Cancer
Comparing the osteoporosis drug raloxifene (Evista) with the widely used breast cancer medication tamoxifen (Nolvadex), researchers noticed that women taking raloxifene were less likely to develop breast cancer, but that raloxifene had fewer side effects. 

### Chemical Found in Plastics Linked to Prostate Cancer
By Amanda Harper

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These everyday product producers all have one thing in common: bisphenol A (BPA), a potentially dangerous chemical used in the manufacturing of plastics that currently UC research suggests provides an important clue as to why some males are more likely to develop prostate cancer.

Shuk-Mei Ho, PhD, chair of UC’s environmental health department, recently identified the first evidence of a direct link between BPA exposure while in the womb and prostate cancer development later in life.

In a laboratory study, Ho found that animal subjects exposed to BPA developed prostate cancer (prostatic intraepithelial neoplasia) than those that were not.

These findings imply that exposure to environmental and natural estrogens during fetal development could affect the way prostate genes behave, leading to higher rates of prostate disease during aging.

BPA, which can leach out of plastics when heated, is one of many man-made chemicals known as “endocrine disruptors,” which permanently alter the function of the endocrine system by mimicking the role of the body’s natural hormones.

In this study, early BPA exposure made the prostate more susceptible to precancerous lesions, which are brought on by the adult animal’s exposure to estradiol, says Ho.

“This is an important discovery, because BPA has been found in human maternal and fetal circulation. If it has such a long-lasting effect, we need to know how adult tissues respond many years later—then potential exposure sources during pregnancy need to be scrutinized and minimized.”

Ho’s research team showed that early BPA exposure permanently changed methylation or “tagging” of specific stretches of DNA and the chromatin structure within the nuclei of prostate cells. The gene expression changes, but the DNA sequences and content do not, says Ho.

They found that a specific altered gene—known as phosphodiesterase 4 (PDE4D)—did not shut down through the natural aging process. Although the gene should normally phase out in adult life, when exposed to estradiol or BPA early in life the animals continued to produce it at high levels.

“We know now that PDE4D plays an important role in regulating cellular function, so when it doesn’t shut down as it should, it begins to promote prostate disease instead,” says Ho.

Any application of these findings, she says, to human prostate disease require further study.

“We need to understand the mechanism behind disease to inspire better lifestyle changes and smart manufacturing changes that will make a broader impact on human health,” says Ho. “If we can develop strong biomarkers, we can manage and prevent diseases much earlier.”

More than 1.6 million pounds of BPA, the molecular building block of polycarbonate plastics, are produced in the United States annually. This research was done in conjunction with Gad Priss, PhD, of the University of Illinois and funded by National Institutes of Health and U.S. Department of Defense grants.

### UC’s Waddell Center Affiliates with National MS Society
By Sheryl Hilton

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Multiple Sclerosis patients, physicians, researchers and supporters gathered at the Vonte Center for Molecular Studies on June 6 to celebrate the affiliation of the Academic Health Center’s Waddell Center for Multiple Sclerosis (MS) with the Ohio Valley Chapter of the National MS Society (NMSS).

“The partnership between the Waddell Center and the NMSS provides collaborations that will help disseminate educational information to our patients,” said Bibiana Bielekova, MD, director of the Waddell Center. “Through our link to the NMSS, patients can find answers to a variety of frequently asked questions, such as how to get a wheelchair, legal support or specialty physical therapy.”

Linda Stetson, president of the Ohio Valley Chapter, noted that the chapter will assist in funding research at UC to find ways to overcome this devastating disease.

The Waddell Center is named for Oliver and Virgilee Waddell, who initiated a $5 million gift to bring world-class MS neurologists and laboratory scientists to the region. Oliver Waddell served as president of the First National Bank of Cincinnati and his wife, Virgilee, suffers from multiple sclerosis and is a 1956 UC alumna.

The Waddell Center is a comprehensive center with doctors and nurses who understand how MS can affect many parts of the body, including the eyes and bladder. It is part of The Neuroscience Institute, a collaborative effort of nine academic departments at the UC College of Medicine, University Hospital and independent physician practice groups.

### Bone Drug Prevents Cancer

Comparing the osteoporosis drug raloxifene (Evista) with the widely used breast cancer medication tamoxifen (Nolvadex), researchers noticed that women taking raloxifene were less likely to develop breast cancer, but that raloxifene had fewer side effects.

Led locally by UC surgeon Elizabeth Shagawaty, MD, PhD, the STAR study (the Study of Tamoxifen and Raloxifene) was part of the National Surgical Adjuvant Breast and Bowel Project. It was funded by the National Cancer Institute.

Shuk-Mei Ho, PhD, chair of UC’s environmental health department.