A PUBLICATION OF UC DAVIS CANCER CENTER VOL 10 · NO 1 · SPRING 2007

Broiling issue: Does overcooked meat cause prostate cancer?

Better brain surgery

Breaking the silence about ovarian cancer

Dear Reader:

Our cancer research program is made up of 286 individuals whose charge is to increase the pace at which cancer patients' lives are made better. This edition of *Synthesis* highlights only a few of the diverse ways in which we are reaching this goal.

While understanding the molecular mechanisms that cause cancer is highly complex, some of the insights are very simple. Dr. Jim Felton, co-leader of our Cancer Etiology, Prevention and Control Program, has found that how you cook your meat may make all the difference in your prostate cancer risk.

Through interactions with Lawrence Livermore National Laboratory and in our own Department of Biomedical Engineering, we are pursuing a number of approaches by which light can be used to fight cancer. Dr. Laura Marcu, an associate professor of biomedical engineering who recently joined our team from Cedars-Sinai Medical Center in Los Angeles, is taking a particularly promising approach. She will tell you how she is harnessing light to help neurosurgeons in the operating room more accurately distinguish malignant from healthy brain tissue, a key to preventing cancer recurrence and limiting side effects.

One of the unique strengths of the Cancer Center is the diverse expertise it can draw upon. Dr. Mary Delany, professor and chair of the renowned UC Davis Department of Animal Sciences, will tell you how she is employing her knowledge of avian genetics to turn chicken eggs into inexpensive, efficient laboratories for the manufacture of antibodies that can be used to treat or image tumors.

As a National Cancer Institute center, we have an obligation, in addition to caring for patients and conducting medical research, to work to improve

the health of everyone in our region, particularly those from medically underserved communities. Toward this end, we recently partnered with Sacramento State to eliminate regional disparities in cancer prevention and control. You will learn about one of the partnership's first major activities, the West Coast debut of a traveling art exhibit designed to spark a dialogue about ovarian cancer.

You will also meet Dina Howard, one of the 9,000 patients we cared for last year. During her treatment for and recovery from breast cancer, Howard recorded an audio journal that became a one-hour radio documentary that aired on Capital Public Radio in December. Her inspirational account reminds all of us there is life after cancer.

Our work cannot be accomplished on grants alone. We must have the help of concerned, philanthropic-minded individuals. Ken and Judy Farrar are such people. You will read about what this Vacaville couple has done to help ensure researchers have the support they need to carry out their studies, whether in the laboratory or the clinic.

I thank you again for your interest in UC Davis Cancer Center, and hope that this edition of *Synthesis* will show you we are using your trust and support to the very best of our abilities.

Sincerely,

d.l.d.l.

Ralph deVere White, M.D. Director, UC Davis Cancer Center Associate Dean for Cancer Programs Professor, Department of Urology



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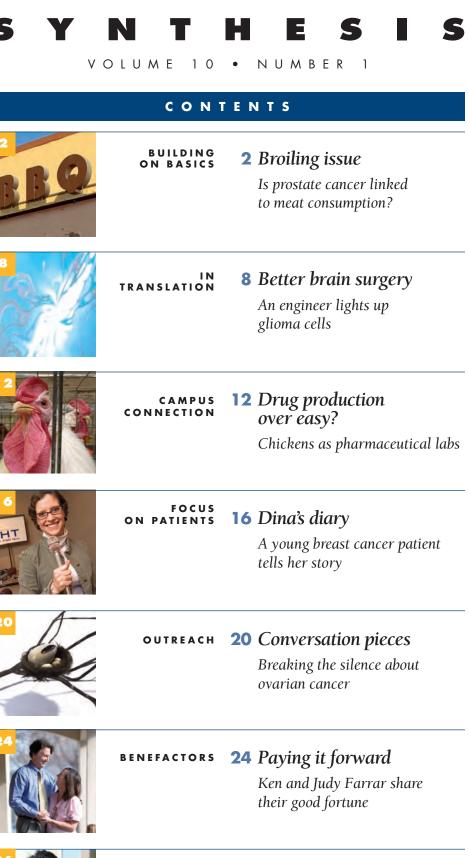
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About the cover:

Carcinogens that form in meat cooked at high temperatures are emerging as a potential culprit in prostate cancer, especially for African-American men.

UCDAVIS CANCER CENTER

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NEWS 26 In brief

Potential blood test for breast cancer, HPV awareness and more



Broiling issue

Well-done meat may be a culprit in prostate cancer, especially for African-American men

Since 2001, hundreds of African-American men have come to the Markstein Cancer Education and Prevention Center at Alta Bates Summit Medical Center in Oakland, Calif., for a blood draw and physical exam to test for prostate cancer. While there, they've answered detailed questions about how frequently they eat chicken, beef, pork and fish, in what quantities, using which cooking methods, and to what degree of doneness.

The 600 men, ages 50 to 70, are part of an ongoing study that may provide answers to a grim mystery: Why do African-American men have the highest prostate cancer rate of any group of men in the world?

"We're increasingly confident that we're onto something," said Kenneth Bogen, an environmental scientist at Lawrence Livermore National Laboratory and head of the Oakland research project. "The hope is that we will really be able to tell people how to lower their risk."

The HCA connection

Bogen launched the study to test an intriguing hypothesis: African-American men are at high risk of prostate cancer because they consume very high quantities of carcinogens formed in cooked meats.

The hypothesis stemmed from decades of research conducted by James Felton, co-leader of UC Davis Cancer Center's Cancer Etiology, Prevention and Control Program and division leader of the Biosciences Directorate at Lawrence Livermore National Laboratory. Felton and Bogen are among the 40 Lawrence Livermore scientists who work as members of UC Davis Cancer Center's Integrated Cancer Research Program, the first formal research partnership uniting a major cancer center and a national laboratory.

Back in the late 1970s, Felton, as well as researchers in Japan, began discovering a range of carcinogens in cooked meats. Eventually, they identified 20 such compounds – known as heterocyclic amines or HCAs – and learned how the compounds form during cooking. In 2002, Felton received a five-year, \$1.5 million P01 grant from the National Cancer Institute to explore the human cancer risk posed by Marion Christian, a research associate involved in the Oakland study, visits barbershops, churches, senior centers and health clinics to recruit study participants. Christian lost his father to prostate cancer.

"As soon as you get over 350 degrees Fahrenheit – in the frying pan, the broiler or on the barbecue – these compounds show up." these mutagens, employing science and technology originally developed for national security uses.

"As soon as you get over 350 degrees Fahrenheit – in the frying pan, the broiler or on the barbecue – these compounds show up," Felton said.

Making the case

Animal studies, meanwhile, were showing that HCAs consumed in food could cause tumors in mice and rats. An HCA called PhIP turned out to be one of the most potent carcinogens ever tested, and it specifically caused prostate cancer in rats. Parallel evidence – nearly 30 epidemiological studies in all – was implicating HCAs in cooked meats as a cause of human cancer.

But to make the case against HCAs, Felton's research team needed more precise estimates of people's typical dietary exposures, particularly to PhIP. So the scientists cooked meats in the lab, made fine-scale measurements of HCAs, and created charts of the kinds and amounts generated.

"At the same temperature, steak has more than hamburger, and chicken has more than either," according to Garrett Keating, a Lawrence Livermore toxicologist who works on the project.

In general, HCAs form more readily when meats are cooked for long periods of time and dry out, Keating said. Fast-food burgers have low amounts, probably because fast-food operations, for the sake of speed and efficiency, try to cook meat as long as necessary to kill E. coli and appeal to customers, but no longer than necessary.

Implicating PhIP

With their HCA data in hand, Bogen and Keating next turned to a U.S. Department of Agriculture diet survey of 25,000 Americans that contained detailed data on meat consumption and doneness preferences. The combined

PHIP-FIGHTING TIPS

Meat cooked at home is the source of most PhIP and other heterocyclic amines in the American diet. These carcinogenic compounds develop when heat acts on amino acids and creatinine in animal muscle.

In general, the longer the cooking time and higher the heat, the more HCAs. Grilling causes the most, followed by pan-frying and broiling. Baking, poaching, stir-frying and stewing produce the least.

Other tips based on work by UC Davis Cancer Center research program members Jim Felton, Garrett Keating and Mark Knize:

- Before grilling, partially cook meat in the microwave, then discard the juices that collect in the cooking dish. Finish on the grill to preferred doneness. Pre-cooking a hamburger for a few minutes in the microwave removes up to 95 percent of HCAs.
- Flip burgers often. Turning patties once a minute reduces HCA formation by up to 100 percent, probably by keeping internal meat temperatures lower.
- Marinate before grilling. A Livermore study showed that marinating chicken for 40 minutes with a mixture of brown sugar, olive oil, cider vinegar, garlic, mustard, lemon juice and salt cut HCAs by 92 to 99 percent.
- Use a meat thermometer. Cook poultry to an internal temperature of 165° to 180° F., ground beef, pork and lamb to between 160° and 170°, and beef steaks and roasts to 145° to 160°. Don't cook meat to "well done."
- Eat cruciferous vegetables, such as broccoli, cabbage, cauliflower, kale and brussel sprouts, one or two days before you barbecue. All contain compounds that activate enzymes in our bodies that detoxify PhIP.



Jim Felton was among the first scientists to discover carcinogens in cooked meats. Now his research team is showing that African-American men consume high quantities of these substances – a potential explanation for their high prostate cancer rates.



information allowed them to determine that the predominant HCA compound Americans consume is PhIP, primarily from pan-fried meats, such as chicken.

But the big surprise was their finding that African-American males were typically consuming two to three times more PhIP than white males.

"A light went on," Keating said. "We thought maybe this would explain their high rates of prostate cancer."

That finding, published in the *Journal of Exposure Analysis and Environmental Epidemiology* in 2001, fit with other dietary surveys suggesting African Americans eat more meat in general, particularly chicken, and prefer it well done.

Cause and effect

To demonstrate that a diet heavy in well-done meats can cause prostate cancer, the researchers next needed to show a dose-response effect: that men who eat more PhIP have more prostate damage.

Preliminary results from the Oakland study suggest there is indeed a significant dose-response: Not only did the study participants have high PhIP intakes, but the higher their intakes, the higher their PSA levels. PSA, for prostate-specific antigen, is a bloodstream marker for prostate damage and early prostate cancer. The findings were published online in the Jan. 16 issue of *Prostate Cancer and Prostatic Diseases.*

PhIP in grilled meats

CONCENTRATIONS OF PHIP* INCREASE WITH COOKING TIME



* in nanograms per gram

Source: Keating, GA, and Bogen, KT. 2004. Estimates of heterocyclic amine intake in the U.S. population. Journal of Chromatography B 802, 127-133.

Specifically, the researchers found that men in the study consumed an average of 17 nanograms of PhIP per kilogram of body weight per day – about double the consumption estimates reported for age-matched white men in the United States. Moreover, the Oakland men who consumed 30 ng/kg per day or more were 30 times more likely to have a highly elevated PSA, defined as 20 nanograms per milliliter of blood or more, when compared to those in the study who consumed less than 10 ng/kg per day. A PSA of less than four is generally considered normal. The association remained significant even after adjusting for family history, saturated fat intake and total calories consumed, and it

was strongest for men over age 50.

Type of meat and cooking method explained about 89 percent of the differences in PhIP intake among study participants. Doneness preference explained the remaining 11 percent.

Study volunteers with high PSA levels, suspicious physical exams, or both were referred for appropriate follow-up care.

Other suspects

But while PhIP is emerging as an important prostate cancer risk factor, it isn't the only one.

Genes are another. Michael Malfatti, another Lawrence Livermore researcher, found that PhIP is detoxified in the body primarily by an enzyme known as UGT1A. As a group, African

ANCESTRY and prostate cancer

A new study under way at UC Davis Cancer Center may give doctors a valuable new tool for making decisions about prostate-cancer screening and treatment for African-American men.

The "Diet and Ancestry Study of Prostate Cancer among African Americans" will analyze blood samples from African-American volunteers living in the Sacramento area for genetic markers of European and African ancestry. The study is seeking 50 men with prostate cancer and 50 who do not have the disease.

As a group, African-American men are twice as likely as white men to develop prostate cancer, and twice as likely to die of the disease. But UC Davis Cancer Center researchers expect to find that not all black men have the same prostate cancer risk. The researchers hypothesize that African Americans of predominantly European ancestry will have a lower prostate-cancer risk than those of predominantly African ancestry.

"It's been assumed that all men who self-identify as African American are at equal risk of developing prostate cancer. Now we can look at this in more detail," said Lesley Butler, an assistant professor of public health sciences and the study's principal investigator.

The researchers will look for genetic markers called Ancestry Informative Markers, which can be used to estimate the African and European contributions to the genetic makeup of an individual. The genetic analysis will be overseen by Michael Seldin, professor and chair of the Rowe Program in Genetics.

The National Cancer Institute, in its recent report, "Accelerating Successes Against Cancer," emphasizes the importance of research to more precisely identify populations with genetic predispositions to particular malignancies, as a first step toward designing screening, chemopreventive and other strategies to reduce these risks and save lives.

Americans tend to have low amounts of this enzyme.

"So not only are African-American men eating more HCAs, they may also have a genetic makeup that means they can't get rid of it – it might be a double whammy," Felton said.

To date, Bogen's Oakland work has been funded by the NCI PO1 and a three-year, \$600,000 grant from the U.S. Department of Defense Cancer Research Program. Now he is seeking funding for a second phase of the study. In it, he hopes to expand the number of volunteers, extend his investigation to include geneenvironment interactions, and find a way to eliminate the excess prostate cancer burden borne by African-American men.

Laura Marcu

Better brain surgery

An engineer sheds new light on brain cancer treatment

For neurosurgeons, the ability to distinguish between healthy and malignant brain tissue with pinpoint accuracy – while the patient is still on the operating table – would be a major advance. For brain cancer patients, it would mean better odds for survival.

A new device under development by Laura Marcu, associate professor of biomedical engineering at UC Davis, promises to make this feat possible.

"Our method allows neurosurgeons to just shine a light on the tissue to determine whether or not it's cancer," said Marcu, who received her undergraduate degree in mechanical engineering at the Polytechnic Institute of Bucharest in Romania, her postgraduate training in spectroscopy, lasers and plasma physics at the University of Bucharest and her Ph.D. in biomedical engineering at the University of Southern California. She joined UC Davis



"The technology may improve the resection of brain tumors – and help save lives." last year from Cedars-Sinai Medical Center in Los Angeles.

Marcu's novel technology uses laser light to excite molecules within tissues or cells. The molecules respond by fluorescing. Different molecules, depending on their chemical properties, emit light of different colors. Using sensitive optoelectronic equipment, Marcu then detects and analyzes this emitted light, gleaning important information about the biochemical status of the tissue. She also employs a process known as "lifetime" or "time-resolved" measurement to determine the wavelength of the emitted light and analyze how long it takes for the fluorescing molecules to revert to their preexcited state.

The portable set-up Marcu has created in her laboratory at the Center for Biophotonics Science and Technology at UC Davis includes a two-way fiberoptic probe that delivers an impulse of laser light and collects



A fiberoptic probe induces fluorescence in a dish of collagen, and instantaneously collects the emitted light. Analysis of the re-emitted light provides important information about the biotechnical status of the tissue – including whether it is malignant. Collagen is the most ubiquitous fluorescent protein in tissues. Such probes can be integrated into biopsy probes, endoscopes and intravascular catheters. the re-emitted light and its decay in nanoseconds.

Precision surgery

"It is very important not to remove normal brain tissue, as this could have devastating effects on the patient. But, if tumor cells are not completely removed, the tumor will recur in a short time," Marcu said. "The techniques we have developed allow us to better identify the infiltrating tumor and the resection margin."

According to Dennis Matthews, director of the biophotonics center, Marcu's cell-screening approach promises to dramatically improve the precision of existing surgical techniques.

"Today a surgeon can take out a tumor, but can't be certain every cell of diseased tissue has been removed, hence the need for additional radiation and chemotherapy," Matthews explained. "This new technology will give surgeons the ability to survey the margins of tumors and determine with great certainty if there is any cancer left."

James Boggan, professor and vice chair of neurological surgery and co-director of the biophotonics center, said Marcu's approach has the potential to improve survival for brain cancer patients.

"Her approach is innovative and seeks to disclose heretofore hidden molecular differences between tumor cells and normal tissue," he said. "As a neurosurgeon, I am especially excited, because this work has the promise of helping me identify sub-microscopic residual brain tumor we cannot detect by our current methods. Doing so would allow us to improve the resection of brain tumors, which may help save lives."



New technology could allow brain surgeons like James Boggan, professor and vice chair of neurological surgery, to identify sub-microscopic residual cancer cells.

Optical biopsy

Marcu's approach, known as timeresolved fluorescence spectroscopy and imaging, is one of several techniques under investigation at UC Davis Cancer Center for near-instantaneous optical "biopsy." A similar technology, under development by researchers at Lawrence Livermore National Laboratory in collaboration with UC Davis surgeons, is expected to enter clinical testing soon; this method relies on measurements of light scattering to distinguish normal from diseased cells.

According to Stavros Demos, a Lawrence Livermore physicist and member of the UC Davis cancer research program, optical devices for real-time tissue screening are the future of oncology.

"The current state of cancer diagnosis involves pathology, and that is a time-consuming process. It takes at least 24 hours to get the result," Demos said. "Optical biopsy technology promises to bring at least a preliminary assessment in real-time, when it would be most beneficial for both the patient and the physician."

Promising early results

Preliminary data suggest Marcu's technology will represent a significant advance in brain cancer surgery. Using her first prototype device, neurosurgeons at Cedars-Sinai Medical Center, where Marcu began her research, were able to correctly identify tumor cells left behind after the removal of glioblastomas from 17 patients. Glioblastomas are irregularly shaped brain tumors with poorly defined borders that invade neighboring tissue.

With her Cedars-Sinai collaborators, Marcu is now recruiting glioblastoma patients for a research clinical trial. The 100-patient study will also include patients being treated at UC Davis Cancer Center.

Applications in heart disease?

Marcu is also working to miniaturize her cell-screening prototype for intravascular applications, and to assess its use in cardiovascular disease. The engineer, who holds several patents, believes the approach could serve as an early warning system to detect potentially problematic atherosclerotic plaques before they can cause a heart attack or stroke.

The opportunity to take new discoveries directly to the bedside where they can benefit patients is what drew Marcu to UC Davis.

"This is a wonderful environment for bringing new technology into practice," she said. "UC Davis has the people and the resources to make new advances happen."

Mary Delany

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Drug production over easy?

Making sophisticated anti-cancer drugs could become as simple as cracking an egg

Chicken soup may be good for the soul and the sniffles. Now scientists are enlisting chickens to help make much stronger medicine – including potential treatments for cancer.

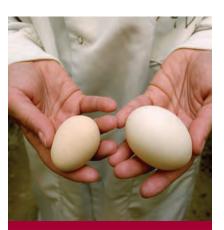
"In the chicken world, we're all very excited. It won't happen this year, but it will happen," said Mary Delany, professor and chair of the UC Davis Department of Animal Science.

One of the world's foremost avian geneticists, Delany is forecasting the day when producing sophisticated anticancer drugs will be a matter of cracking eggs, each egg holding milligram-quantities of a desired agent. The technology would enable pharmaceutical companies to farm human proteins of therapeutic value on an industrial scale, more cheaply and efficiently than currently possible.

"A typical commercial hen house might have 40,000 hens that each lay six eggs a week," Delany noted. "That's 240,000 eggs a week."

Germ of an idea

In the prestigious British journal *Nature* last summer, scientists at a small Bay-Area biotech



"In the chicken world, we're all very excited. It won't happen this year. But it will happen." company, Origen Therapeutics, Inc., reported a major advance in avian transgenics – one that, in principle, should enable scientists to make any genetic modification desired to the chicken genome. Delany collaborated on the project and is an author of the *Nature* paper.

Adding a jellyfish gene

The team's advance involved several feats: isolating and successfully culturing primordial germ cells from the blood of chicken embryos, modifying the cells by adding a jellyfish gene for fluorescence, and then introducing these transgenic cells into the bloodstream of new chicken embryos at precisely the right stage of embryonic development.

The transgenic germ cells migrated to the gonads of the embryos, where they matured, as germ cells are intended, into sperm or egg cells as the embryos grew into chicks. After hatching, males were reared to maturity and crossed with nontransgenic females.

Some of the resulting offspring carried the jellyfish gene. The experiment was



the first demonstration in any species that primordial germ cells can be immortalized, or grown indefinitely, in culture, and the first demonstration that the cells can be genetically manipulated while retaining their ability to mature into viable sperm and eggs that can pass transgenic material to a new generation.

For the birds

The achievement opens the possibility that instead of altering chickens to express a jellyfish protein, scientists will be able to engineer the birds to produce a human monoclonal antibody or other therapeutic protein. Indeed, Origen scientists have already shown in separate experiments that a transgenic protein can be expressed in the whites of chicken eggs.

"They have made an incredible contribution," Delany said of her Origen collaborators.

Delany's own role was pivotal. Her group at UC Davis screened the cultured germ cells for genome organization and stability, making certain that only chromosomally stable cells were used in the project.

"Dr. Delany brought her internationally recognized expertise in avian cytogenetics to the analysis of primordial germ cells that had been in culture for extended periods," said Robert Etches, former vice president of research at Origen Therapeutics. "The combination of in-house expertise and world-class support from the Delany laboratory allowed Origen to complete the technology quickly and efficiently."

The new approach has particular potential for production of monoclonal antibodies used in cancer treatment, including Herceptin for breast cancer and rituximab for lymphoma. Such drugs are now grown in Chinese hamster ovary cells and then turned into drugs at bioreactor plants, a costly and timeconsuming process.

Crucial support

Delany has been studying chickens and their genes since first joining UC Davis in 1995. But it was a modest Institutional Research Grant from the American Cancer Society, matched by funds from the UC Davis School of Medicine, that fixed her focus on cancer.

For research scientists, he early years in academia are demanding. To launch a successful research career, junior faculty must compete for research grants. But to win the grants, they need a track record of research accomplishments. While confronting this catch-22, they also must juggle heavy teaching loads.

Delany's award – intended specifically to support promising young investigators – meant a short respite from grant-writing and the time to, among other things, read the scientific literature on yeast telomeres.

Yeasty question

A telomere is a specialized DNA sequence, found at the end of chromosomes, that plays a critical role in cell replication, normal aging and diseases like cancer.

"I read the body of literature on yeast and wondered, 'What's going on with chickens and telomeres?' There was nothing," she said. "It was one of those 'aha' moments. I knew I'd hit it. I'd found a new area (of scientific inquiry) to move into."

In the decade since, Delany has come to dominate this area. She was the first to characterize the stability of telomeres and regulation by telomerase, the enzyme responsible for keeping telomeres healthy, through the life cycle of the chicken – or indeed of any avian species.

Stopping the clock

In an article in the December 2000 issue of *Development, Growth & Differentiation,* she reported this work and her conclusion that the so-called telomere "clock" – which ensures cells don't live forever – functions in birds as well as mammals, and is disabled by cancer cells in both species as a way to evade mortality.

In 2003, her laboratory and one in Europe reported the characterization of two telomerase RNA genes found in the chicken herpesvirus, which is responsible for an avian cancer known as Marek's disease. And she was part of the international consortium of researchers that analyzed the draft sequence of the chicken genome, a landmark achievement published in the Dec. 9, 2004, issue of *Nature*. With her latest grant, Delany is investigating the role of telomeres in the pathology of Marek's disease in infected chickens.

The avian geneticist is confident the steadily accruing knowledge about the chicken genome will point the way to further advances that will benefit human health.

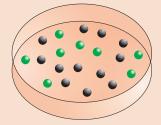
"We can't see now what those will be," she said. "But that's the nature of basic science."

The next leap forward may be an anti-telomerase vaccine to thwart cancer cells' efforts to sabotage telomere clocks. Or something no one has yet imagined – perhaps a development even more fantastic than using hens to fight cancer.

GLOWING CHICKENS

Here's how Mary Delany and the scientists at Origen Therapeutics gave chickens a jellyfish gene for flourescence. The achievement could lead to engineered birds that produce a human monoclonal antibody or other therapeutic protein in their eggs.





 Primordial germ cells are removed from the blood of chick embryos and cultured. An alien gene, in this case a jellyfish gene for fluorescence, is added.



2. The transgenic cells are then injected into the circulatory system of new embryos, where they migrate to the developing gonads. The embryos are incubated until they hatch.



 Hatched males are reared to sexual maturity and mated with ordinary hens. Some of the resulting chicks carry the jellyfish gene.

Dina's story

Radio journal chronicles a year in the life of a young breast cancer patient

By her own admission, Dina Howard is a planner, almost obsessively so. But nothing prepared the 39-year-old Sacramento mother of two for the turn her life took in the fall of 2005 when she was diagnosed with breast cancer.

Over the ensuing year, under the care of UC Davis physicians James Goodnight, Helen Chew and Janice Ryu, Howard made difficult decisions about surgery, chemotherapy and radiation.

"One week ago today, I was diagnosed with breast cancer ... I got a real interesting e-mail from a friend: 'Welcome to the club that nobody wants to be a part of."

Along the way, she recorded her feelings and taped her experiences for a first-person documentary that aired in late December on Capital Public Radio, Sacramento's National Public Radio affiliate. The onehour audio journal remains



Dina's Diary was inspired by a desire to create meaning from illness. available online at www. capradio.org, along with photos and recordings from Howard's husband, her sister and her infusion nurse. In addition, Howard has recorded an update that can be heard on the UC Davis Cancer Center site at www. ucdmc.ucdavis.edu/cancer.

"... I feel very, very lucky, at the same time that I feel totally terrified. The lucky part is that I keep thinking about how much support, love, I have. The other side of the coin is, sometimes I just feel so scared, I can barely see."

Desire for meaning

A desire to create meaning from her illness inspired Howard, shortly after her diagnosis, to approach Capital Public Radio producer Paul Conley with a proposal to record a radio diary of her breast cancer treatment and recovery.

"One of the most valuable



Dina Howard, surrounded by seven members of her treatment team. Clockwise, from first-row left: Radiation oncologist Janice Ryu, social worker Carolyn Guadagnolo, oncology nurses Mia Wilson and Teri Lown, radiation therapist Marianne Kern, oncology pharmacist Amy Tam, and surgical oncologist James Goodnight.

things during the days after my diagnosis was when friends or friends of friends who had already had breast cancer shared their experiences with me," she explained.

Conley provided her with a digital tape recorder and offered to help her edit her audio journal entries into a documentary whenever she was ready.

"... Today I finally got an appointment with a highly recommended surgeon, and I think that's a really big deal ..."

The surgeon was Goodnight, professor and chair of the Department of Surgery at UC Davis and a specialist in breast cancer surgery.

Cancer more extensive

In an initial operation, Goodnight discovered Howard's cancer was more extensive than mammography had been able to detect. She would need a mastectomy of her right breast. Ultimately, to reduce her risk of subsequent cancer, Howard elected to have a bilateral mastectomy.

Howard had her tape recorder with her from the very beginning. It was on in her hospital room following the double mastectomy. She carried it with her to an appointment with Chew, the director of the Clinical Breast Cancer Program at UC Davis, and into the radiation oncology clinic, where Ryu, an associate professor of radiation oncology, oversaw her care. Listen to Dina's hourlong radio documentary at www.capradio. org/news/specials/ dinasdiary/

Hear an update at www. ucdmc.ucdavis.edu/ cancer/survivors/dina



Howard's care team also included oncology pharmacists, radiation therapists, physicists, dosimetrists, a genetic counselor and patient education specialists.

Listeners meet pharmacist Amy Tam, infusion nurse Mia Wilson and a radiation therapist who, in a warm voice, assures Howard, "You're almost done."

"As much as I'm feeling scared and apprehensive ... I know that the people around me are going to help me get through this."

The audio diary ends following Howard's final radiation treatment. The young cancer survivor records her last entry on the beach in Santa Barbara, where she, her husband and children are spending Thanksgiving with her parents.

"... I feel like I taste my life – every moment has a flavor. And I'm so grateful for every single taste."

Bright prognosis

For women like Howard, the prognosis has never been brighter. She benefited from good clinical trial data supporting aggressive adjuvant chemotherapy, genetic testing advances that reassured her she does not carry the breast cancer genes BRCA1 or BRCA2 – good news for her sisters and daughter – and solid research establishing the effectiveness of sentinel node biopsy, a minimally invasive option that spared her the need to have more lymph nodes removed. Over the next five years, she will reduce her risk of a breast cancer recurrence by up to 50 percent by taking tamoxifen, a drug that targets estrogen-positive breast cancers.

But more research is needed. "Breast cancer is common. It is not respecting of age, social status or anything else. It is terribly frightening and mercilessly unjust," Goodnight said. "We must continue to make progress."

Waves crash on the Santa Barbara shore as Howard continues her closing diary entry: "... It's so beautiful here. My beautiful children are on the other side of the beach, digging in the sand, wearing shorts, squishing toes in the sand. I look at them, and my heart just melts. This year has made me incredibly grateful to be alive ... I want to keep that."

CLINICAL breast cancer program

The Clinical Breast Cancer Program at UC Davis Cancer Center provides comprehensive, multidisciplinary care for patients with all types and stages of breast cancer. Patients receive all of their care on one campus, from a team of top academic physicians who specialize in breast cancer. Last year, more than 1,300 breast cancer patients from more than 35 counties came to UC Davis Cancer Center for their treatment.

Specialists

Specialists in different aspects of breast cancer treatment - medical oncology, radiology, surgical oncology, pathology, radiation oncology and plastic and reconstructive surgery – collaborate to design the best treatment plan for each patient. Our multidisciplinary team also includes genetic counselors, dietitians, pain medicine specialists, oncology nurses, oncology pharmacists, clinical trial associates, social workers, patient educators and art therapists.

Services

- New patient orientations specifically for breast cancer patients, funded by the Susan G. Komen Breast Cancer Foundation
- Breast cancer support groups
- "Learn at Lunch" workshops for patients, their families and caregivers

- Cancer Resource Center
- Psychosocial counseling
- Writing as Healing workshops
- Triumph fitness classes
- "Look Good ... Feel Better," an American Cancer Society program held at UC Davis Cancer Center

Clinical trials

UC Davis Cancer Center has one of the largest clinical trials programs in the country, offering breast cancer patients access to the newest drugs and pioneering therapies, often long before they become widely available.

Research

Close collaboration between our physicians and our research scientists means that new drugs and treatments developed in the laboratory can move quickly to the clinic, offering our patients



Dina Howard and Helen Chew

immediate access to the latest breakthroughs.

For example, our surgeons were among the first in the country to pioneer a treatment known as non-surgical lumpectomy, or radiofrequency ablation. This investigational treatment employs heat to destroy small, early stage breast cancers. Our scientists are also developing a new CT breastimaging machine that may detect tumors earlier than standard mammography.

Our physicians conduct research that advances clinical care. For example, a team of UC Davis surgical oncologists, including James Goodnight, professor and chair of the Department of Surgery, recently published a study in the *Annals of Surgical Oncology*, reporting that sentinel node biopsy is more sensitive than axillary lymph node dissection at identifying cancer that has spread to the lymphatic system.



SURVIVOR | by John Magnan. One of the 16 works of art in the body image | body essence exhibit, "Survivor" is dedicated to all women dealing with chemotherapy and hair loss. All but two of the photos of the artist's late wife, Mary Magnan, were taken during her treatment for ovarian cancer.

Conversation pieces

Art exhibit, educational events spark dialogue on ovarian cancer

When his wife, Mary, was diagnosed with ovarian cancer, Massachusetts artist John Magnan responded by channeling his feelings of fear and helplessness into the creation of art that celebrates the resilience of the human spirit. Using a wide variety of materials, Magnan produced 16 works of art that explore hair loss, IV poles, "chemo brain," infertility, exhaustion and triumph in a visual story of hope, courage and love.

The artwork, collected in a traveling exhibit titled "body image | body essence," has its West Coast debut this month at the Library Gallery at California State University, Sacramento, as part of an ovarian cancer awareness project co-sponsored by the Sacramento division of the National Ovarian Cancer Coalition and the Sacramento State/UC Davis Cancer Center Partnership to Reduce Cancer Disparities.

Breaking the silence

The collection, intended to spark conversation about a cancer whose early symptoms are often silent, has made 12 "This disease damages many eggs, defiling many nests." – John Magnan stops, including the Boston Museum of Science, the National Museum of Health and Medicine in Washington, D.C., and the M.D. Anderson Cancer Center in Houston. The Sacramento exhibit will be on display from 10 a.m. to 5 p.m., Tuesdays through Saturdays from March 24 through April 27. The exhibit is free and open to the public.

Related ovarian cancer awareness activities will include an Evening with Experts community forum co-sponsored by the American Cancer Society at UC Davis Cancer Center on April 26, a series of presentations for students at Sacramento State, and a two-day conference for healthcare providers sponsored by the UC Davis Office of Continuing Medical Education.

"Ovarian cancer is sometimes called a silent disease," said Marlene von Friederichs-Fitzwater, director of the Outreach Research and Education Program at UC Davis Cancer Center. "This art exhibit provides powerful visual symbols that will help us break the silence, and, with the other educational activities we have developed,

OPEN TO THE PUBLIC

March 24 – April 27 body image I body essence

10 a.m. to 5 p.m. Tuesday through Saturday

Library Gallery Sacramento State 6000 J St., Sacramento

April 26

Advances in ovarian cancer research and treatment "Evening with experts"

5:30 to 7:30 p.m.

UC Davis Cancer Center 4501 X St., Sacramento

Information: (916) 734-5786 or www.sacstate-ucdcc.com

OVARIAN CANCER: EARLY WARNING SIGNS

According to Lloyd Smith, professor and chair of obstetrics and gynecology at UC Davis, a woman should see a gynecologist if any of the following symptoms persist for over two weeks or recur:

- unexplained pelvic or abdominal pain or discomfort
- unexplained pelvic or abdominal bloating or swelling
- a constant feeling of fullness
- difficulty eating

For more information, visit the National Ovarian Cancer Coalition Web site at www. ovarian.org



WARRIOR 1 A lifecast of Mary Magnan's skull, taken at the height of her chemotherapy treatment, was the inspiration for this bronze helmet. The artist also made a shield, symbolizing the battle waged by his late wife and by all women with ovarian cancer.

spark a public dialogue that will, ultimately, save lives."

No definitive test

Even though ovarian cancer is the leading killer among gynecologic cancers, only 15 percent of women are familiar with its warning signs, and 82 percent have never talked with their doctors about its symptoms or risk factors, according to a recent national survey sponsored by the National Ovarian Cancer Coalition.

Starting the conversation is critical, said Gina Dayton, president of the coalition's Sacramento division and an ovarian cancer survivor.

"If caught in the early stages, the five-year survival rate for ovarian cancer is 90 percent, yet 75 percent of women are still unnecessarily diagnosed in the advanced stages, when prognosis is poor," Dayton said. "Unfortunately, unlike breast or prostate cancer, there is no definitive screening test for ovarian cancer. The Pap smear, which can detect cervical cancer, does not detect ovarian cancer. A woman's best first-line defense is therefore her own awareness of the symptoms. We have to spread that message."

UC Davis Cancer Center and Sacramento State last year formed the Partnership to Reduce Cancer Health Disparities through Education, Research and Training, with a goal of combining the resources of both institutions to promote cancer awareness, prevention and early detection throughout the region, especially in medically underserved communities.

"Faculty and students are excited about opportunities to collaborate with experts at the UC Davis Cancer Center," said



BEYOND EXHAUSTION

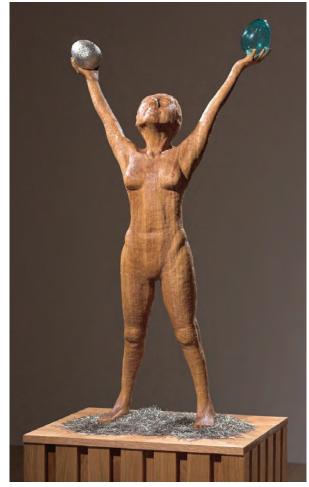
Artist John Magnan created this work of clay and steel to reveal the toll that cancer treatment can take on patients. "The long ordeal is reflected around the eyes," Magnan writes in his description of the piece. "It's a look that's more than tired; it's a look that's beyond exhaustion."

Marilyn Hopkins, dean of the College of Health and Human Services at Sacramento State. " Joint sponsorship of the art exhibit is one of many anticipated ventures that will unite our campuses in efforts to address health disparities in cancer care."

Universal and personal

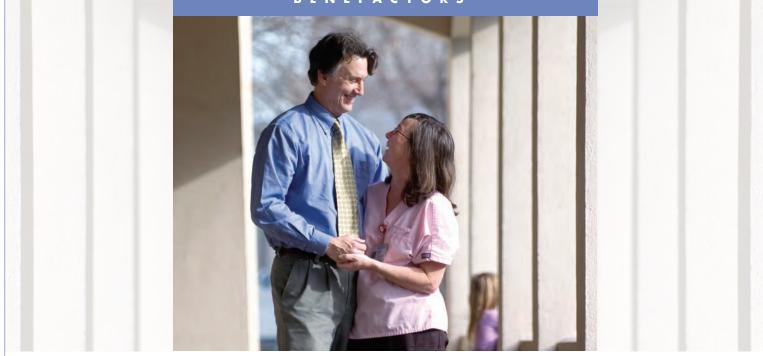
Writing about the initial exhibit of Magnan's collection, *Boston Globe* art reviewer Cate McQuaid characterized the work as "at once universal and personal ... a meditation not only on the struggle, but on the beauty and depth of what he saw ... (the exhibit) attests to his empathy, and to his artistry."

More than 22,000 women will be diagnosed with ovarian cancer this year and more than 16,000 will die of it. Mary Magnan died of ovarian cancer in February, 2006, six years and 10 months after she was diagnosed. She was 59.



ECHO I Made of white oak, pins and glass, this 3¹/2-foot-tall sculpture is intended to reflect the strength and spirit of all women living with and fighting ovarian cancer.

BENEFACTORS



Paying it forward Vacaville couple turns a windfall into a legacy

When Ken Farrar received several hundred thousand shares of stock in a buyout from his partners in an e-commerce Web site not long ago, he and his wife, Judy, a longtime nurse at UC Davis Medical Center, wanted to share their good fortune.

"We were sitting around the dinner table when Judy suggested the idea that we could make a donation to support cancer research at UC Davis," Ken recalled.

That casual conversation led to a \$75,000 gift to the South Placer UC Davis Breast Cancer Endowment, a grassroots group that has pledged to establish the university's first endowment in breast cancer research. With the Farrars' donation, the South Placer Breast Cancer Endowment has raised nearly \$300,000 toward its goal of \$1.5 million.

Ralph deVere White, director of UC Davis Cancer Center, called the gift from the Farrars "a tremendously generous contribution."

"They asked me what they could do to make the very most of their donation, and I suggested the South Placer effort," he said. "I knew Ken and Judy's donation would make a huge impact, that many other people would recognize their generosity and be inspired by it."

Carol Garcia, a breast cancer

survivor who established the South Placer Endowment with eight other area residents whose lives have been touched by cancer, said members of the organization were "blown away" by the Farrars' generosity.

The Farrars' check came as a complete surprise to Garcia, a senior vice president at Granite Community Bank in Roseville. The check was presented to her Oct. 12 at a fundraiser at Austin's Steakhouse at Thunder Valley Casino in Lincoln.

"They kept everything a secret from me," Garcia said. "You should have seen my face – I was in shock when Judy handed me the check. I was just so surprised and grateful that there are people like this who are willing to assist in fundraising for breast cancer research."

Crossing paths

As high school classmates in Fontana, Calif., in the 1970s, Judy and Ken socialized with the same group of friends, but after graduation went their separate ways.

Judy became a nurse in 1981, working at various hospitals before accepting a position as nurse at UC Davis Medical Center. She put down roots in Sacramento, where she bought a house and lived with her two dogs for 13 years as a self-described "confirmed bachelorette."

Ken was living in the Bay Area during those same years, working long hours managing his Internet ventures.

When a mutual friend from high school suggested the two start dating in 1997, it wasn't long before an old friendship was rekindled.

Today the couple have a fiveyear-old daughter, Helen, and a comfortable home in Vacaville.

"We really didn't seriously consider donating the money to any other organization," Judy said. "We wanted our money to stay in the local area, and I knew we would see the results of our donation, because every day I see the tremendous strides being made at the Cancer Center. I was just happy we were in a position to donate, and that it's going to something important."

"I hope more people donate," Ken said. "And with some luck, we hope to make another donation in the future."

thecelebration reaching for a cure for cancer

presented by Comcast

The annual Celebration Gala, a black-tie dinner, dance and silent auction, will be held on Saturday, Aug. 25, beginning at 6 p.m. at the Hyatt Regency Sacramento.

Proceeds support the UC Davis Cancer Center's Outreach Research and Education Program, which develops and tests strategies to reduce cancer disparities affecting medically underserved communities and offers the following services for patients, survivors and the community:

- new patient orientations
- writing, art and fitness classes
- Cancer Resource Center
- Childhood Cancer Resource Center
- "Learn at Lunch" workshops
- "Evening with Experts" series
- National Cancer Survivors Week activities

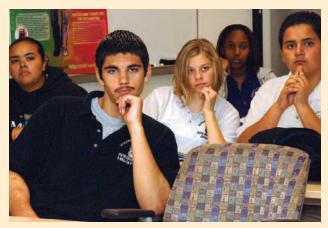
The gala is presented by Comcast with support from the Regent Foundation.

For information about sponsorship opportunities or reserving a table, please call Chantel Hoad at (916) 515-2822.



"CURE" for minority underrepresentation in cancer sciences

Nationally, fewer than 5 percent of all doctorates awarded in the biological sciences go to African Americans. Hispanics, American Indians and some Asian and Pacific Islander groups are similarly under-represented in the ranks of Ph.D. medical researchers.



Sacramento High School students get the preparation they will need to pursue careers in cancer sciences.

With a four-year, \$300,000 "CURE" grant from the National Cancer Institute, UC Davis Cancer Center leaders hope to address this disparity by giving students from under-represented groups the preparation they need to study cancer-related sciences at four-year universities.

The CURE grant, for Continuing Umbrella of Research Experiences, funds an intensive program in basic, clinical and population sciences for promising students at Sacramento High School, a charter school founded by former NBA All Star Kevin Johnson. UC Davis Health System contributed an additional \$40,000 in support. Only National Cancer Institute centers are eligible to apply for CURE grants.

Already, the first class of 20 students – the majority of them from under-represented groups – has embarked on a two-year program of coursework, field study and research experiences centered at the National Science Foundation-funded Center for Biophotonics Science and Technology at UC Davis. Pam Castori, a veteran science teacher, coordinates the program. An all-star cast of Cancer Center and Center for Biophotonics faculty acts as mentors.

Blood test for breast cancer?

In a recent article in *Molecular and Cellular Proteomics,* UC Davis researchers report a promising strategy for discovering biomarkers that could be used to detect breast cancer.

Carlito Lebrilla, professor of chemistry, Suzanne Miyamoto, assistant research biochemist, and a team of collaborators used sophisticated technology to profile and compare the total glycans, or sugars, released from glycoproteins in various breast cancer cell lines, in blood samples of healthy women and women with breast cancer, and in blood samples from a mouse model of breast cancer.

The scientists found that similar breast cancer cell lines had similar glycan profiles, and that these profiles were distinct from the glycan profiles of a healthy cell line and a precancerous, ductal carcinoma cell line. Moreover, the researchers were able to distinguish patients with breast cancer from those without based on their glycan profiles.

Many more patient samples will need to be analyzed, but Lebrilla and Miyamoto hope their approach will enable them to identify glycan "signatures" of breast cancer that will lead to better diagnostic tests for the disease.

Fred Meyers named master of American College of Physicians

In recognition of his pioneering role in the hospice movement in the United States and his research to improve end-of-life care for cancer patients, Frederick Meyers, professor of medicine and pathology and chair of the Department of Internal Medicine, has

been elected a Master of the American College of Physicians, the nation's largest medicalspecialty organization. Only 584 individuals hold the distinction worldwide.

In its citation in support of his mastership, the college describes Meyers as "an internationally known



Frederick Meyers

News in Brief News in Brief News in Brief

researcher in hematology and oncology, credited with pioneering the hospice movement within the academic setting."

Meyers is perhaps best known for his work in "simultaneous care," a model of care for cancer patients undergoing investigational therapy. Meyers has shown that the model improves both patient quality of life and clinical trial participation. He has also been a pioneer in bringing hospice care to dying inmates in prisons and to patients in remote rural communities via telemedicine.



Anne Rodriguez emphasized the need to spread the word about HPV vaccination.

Screen yourself, vaccinate your daughter

A statewide campaign to increase awareness and prevention of cervical cancer and its primary cause, the human papillomavirus, had its kickoff at a January press conference at UC Davis Cancer Center.

about TPV vaccination. Anne Rodriguez, assistant professor of gynecologic oncology, and

Marlene von Friederichs-Fitzwater, assistant professor of internal medicine and director of the Outreach Research and Education Program, underscored the need to spread the word, especially to minority communities.

"Although cervical cancer is an important concern for all California women, ethnic minorities, such as Hispanic and Asian women, are at especially high risk," Rodriguez said. "The lifetime risk of developing cervical cancer for Hispanic and Asian women is more than double the lifetime risk in non-Hispanic white women."

Emphasized von Friederichs-Fitzwater: "We need to get the message of 'screen yourself and vaccinate your daughter' out to every woman, and particularly women who may not see a health-care provider on a regular basis."

The "Screen Yourself, Vaccinate Your Daughter" campaign is a project of the California Medical Association Foundation and endorsed by a long list of health organizations, including the American Cancer Society. It is supported by a grant from Merck & Co.

The U.S. Preventive Health Services Task Force recommends women start having regular Pap tests and pelvic exams at age 21, or within three years of the first time they have sexual intercourse, whichever occurs first. The federal Advisory Committee on Immunization Practices recommends routine HPV vaccination for 11- to 12-year-old girls. The vaccine is approved for females ages 9 through 26.

Triumph in 2007

UC Davis Cancer Center will offer a 10-week Triumph strength-andfitness program for cancer survivors July 9 through Sept. 14. Classes are held twice a week during the day at 650 FIT Fitness Center, 985 Enterprise Drive, Sacramento. There is no cost to participants. Triumph was

established in 2005

by Pam Whitehead, a



Strength-training program can enhance endurance, quality of life.

Sacramento architect and uterine cancer survivor, with an award from the Lance Armstrong Foundation. The program continues to operate free of charge to participants through Whitehead's fundraising and support from UC Davis Cancer Center and 650 FIT.

Through Triumph, participants build muscle mass and strength, increase flexibility and endurance and improve their capacity to perform activities of daily living, from work to play. The program may help to reduce the severity of cancer side effects, prevent unwanted weight changes and improve energy levels and self-esteem. A final goal is to help participants develop their own physical fitness regimens so that they can continue to triumph after completing the program.

For more information, please contact Toni Poppe at UC Davis Cancer Center at (916) 734-5786 or tjpoppe@ucdavis.edu.

News in Brief News in Brief News in Brief

Adolescent and Young Adult Cancer Advisory Board formed

To better meet the special needs of young cancer patients and survivors, UC Davis Cancer Center has established its first Adolescent and Young Adult Cancer Advisory Board. The board's mission is to:

- develop and implement innovative informational, educational and support programs for adolescents and young adults with cancer
- help medical students, physicians, nurses and other health-care professionals learn about the special needs of adolescent and young adult cancer patients and survivors
- raise awareness among secondary and college students of cancer risks, prevention strategies, treatment and survivorship issues

For more information about the board, please contact Toni Poppe at (916) 734-5786 or tjponne@ucdavis.edu.

Colleges to tackle rural tobacco use, colorectal and cervical cancer

The UC Davis Cancer Center/Sacramento State Partnership to Reduce Cancer Health Disparities through Education, Research and Training hosted its first Community-Campus Collaborative Conference in October. The conference featured national speakers on community-based, participatory research as well as presentations on successful local communitycampus projects and activities.

One outcome: three research teams, made



Adele James, program officer for The California Endowment, highlighted the importance of academic-community collaborations.

up of faculty from Sacramento State and UC Davis Cancer Center, together with minority community leaders, formed to explore targeting tobacco and smoking in rural communities, colorectal cancer in American Indians and cervical cancer and HPV vaccination among Hispanics. UC Davis Cancer Center and Sacramento State formed the partnership in 2005 with a goal of reducing cancer disparities throughout the region.

Bright and luminescent



Alexandra Courtis with postdoctoral researcher Andrea Goforth in Susan Kauzlarich's lab

Alexandra Courtis, a senior at Davis Senior High School, won \$5,000, a laptop computer and an allexpenses-paid trip to Washington, D.C., as a finalist in the Intel Science Talent Search. Courtis completed her project during afternoons as a volunteer in the lab of chemistry professor Susan Kauzlarich.

Courtis' project, "Bright Luminescent Silicon Nanoparticles for Biological Applications," involved creating nanoparticles or "quantum dots" of metals such as silicon, germanium and gold that could be used to identify tumors.

As one of 40 Intel finalists, Courtis will have the opportunity to display her research at the National Academy of Sciences.

Kauzlarich, one of the more than 200 UC Davis scientists at work on cancer, focuses on exploring new materials with novel chemical structures and properties.

Land gift will expand cancer services in Placer County

A real estate development firm whose major partners include five prominent local families donated 15 acres of undeveloped land valued at \$8.17 million to UC Davis Health System, the single largest private donation in the health system's history.

News in Brief

The gift is from River South Holdings, LLC, whose partners include five local landowners: Mark Friedman of Fulcrum Properties; Martin Harmon of Western Care Construction; the Tsakopoulos family, represented by Kyriakos Tsakopoulos of AKT Development; Brian Vail of River West Investments; and John Sinadinos, an attorney and developer.

Health system officials plan to use the property, at the northeast corner of Whitney Boulevard and Highway 65 in Rocklin, to develop a health campus offering a range of outpatient services, including cancer care. The health system has submitted plans to the City of Rocklin for a new outpatient facility on a site adjacent to the gift parcel. That facility, to be completed by the end of next year, will include comprehensive imaging services and an infusion center for cancer patients.

Best wishes

A delegation of second- through eighth-grade students visited UC Davis Children's Hospital as part of a school project on cancer, bringing with them more than 100 handmade cards and posters to distribute to pediatric cancer patients.

The students, from Capitol Heights Academy, a charter school located in Sacramento's Oak Park neighborhood, presented the cards to child life specialist Cindy Jones, who talked with the group about childhood cancer and its treatment. Melissa Pelochino, a reading specialist at the school, organized the project.



Khaylani Dove-Austin and Sydnie Mitchell, both 10, with cards they made for cancer patients at UC Davis Children's Hospital.

CALENDAR OF EVENTS

March 24 - April 27

Body Image I Body Essence: Viewing ovarian cancer through the art of sculpture Library Annex Gallery, Sacramento State (916) 734-5786 or tjpoppe@ucdavis.edu for further information

April 26

"Discoveries and Advances in the Detection and Treatment of Ovarian Cancer" An Evening with Experts sponsored by UC Davis Cancer Center and the American Cancer Society UC Davis Cancer Center auditorium, 5:30 to 7:30 p.m. For more information, call (916) 446-7933, option 3, ext. 335

May 5 and 6

Coolest 24-Hour Mountain Bike Race Against Cancer Sponsored by the Auburn Community Cancer Endowment Fund Proceeds benefit UC Davis Cancer Center For more information, call (530) 889-9412 or visit www.thecoolestmtb.com

May 19 - June 2

National Cancer Survivors Week Events to be held at UC Davis Cancer Center For more information, call (916) 734-5786 or e-mail tjpoppe@ucdavis.edu

June 8

Magnussen's Auburn Toyota Charity Golf Tournament Sponsored by the Auburn Community Cancer Endowment Fund Proceeds benefit UC Davis Cancer Center For more information, call (530) 885-8484 or visit www.accef.org

August 25

Celebration Gala Proceeds benefit UC Davis Cancer Center Hyatt Regency, Sacramento, 6 p.m. For more information, call (916) 515-2822

August 25

Sierra Blues Benefest & Crafts Fair Sponsored by the Auburn Community Cancer Endowment Fund Proceeds benefit UC Davis Cancer Center Auburn State Recreational Area, Auburn, 1 to 10 p.m. For more information, visit www.accef.org



S Y N T H E S I S

syn•the•sis (sin' thə sis) n., *pl.* - **ses** (-sez')[[Gr. < *syn*-, together + *tithenai*, to place, DO¹]] **1** the putting together of parts or elements so as to form a whole **2** a whole made up of parts or elements put together **3** Chem. the formation of a complex compound by the combining of two or more simple compounds, elements, or radicals **4** *Philos*. in Hegelian philosophy, the unified whole in which opposites (thesis and antithesis) are reconciled.



UC DAVIS CANCER CENTER

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