

SYNTHESIS

THE MAGAZINE OF UC DAVIS CANCER CENTER

VOL 13 • NO 2 • FALL/WINTER 2010

An expansion for the future

PAGE 2

Researchers explore new cellular avenues to improve survival

PAGE 8

Writing group inspires patients, loved ones affected by cancer

PAGE 12

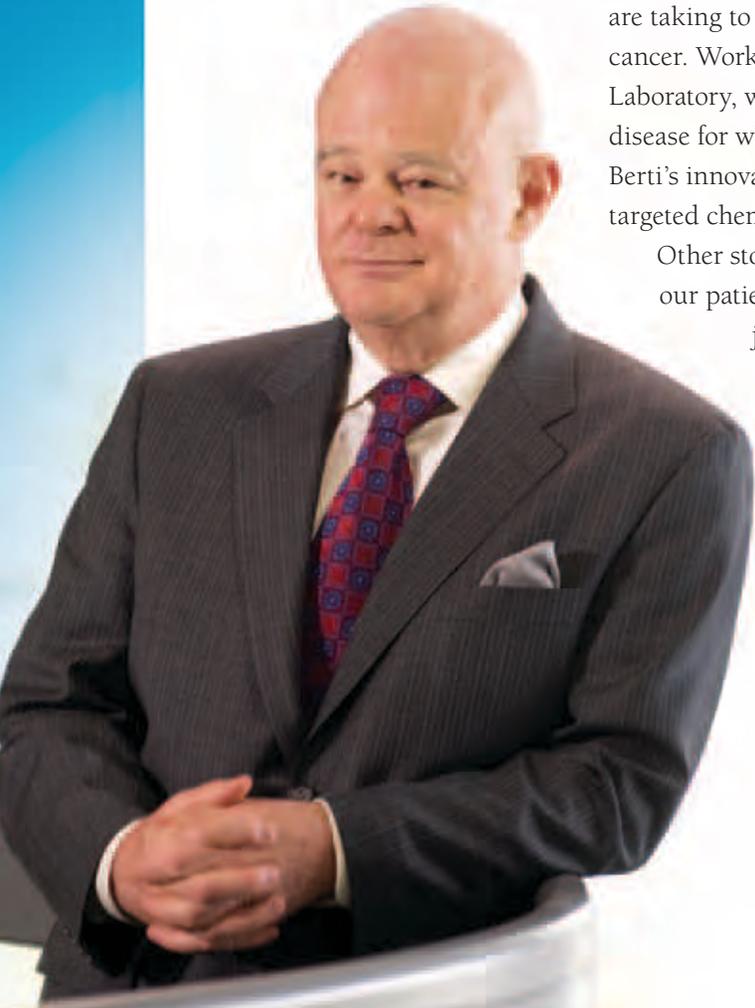
Radiation oncology department assembles world-class team

PAGE 16

Researcher seeks refined approach to drug delivery

PAGE 24





Dear Reader,

In this fall/winter 2010 issue of *Synthesis* I invite our readers to help us celebrate new beginnings as we share our stories of renewal.

After five years of planning, we are so pleased to have broken ground on a major – and much-needed – expansion of the UC Davis Cancer Center, appropriately marked on National Cancer Survivors Day. In this issue you will read about plans to add 46,000 square feet of clinical space to our existing center so that we can treat both our pediatric and adult patients under the same roof. Our hope is that the expanded cancer center will allow us to help even more people become cancer survivors.

We also will introduce you to a cadre of physician-scientists who add breathtaking expertise to our top-notch radiation oncology department. Department chief Richard Valicenti has assembled a powerful team of subspecialists who administer the most advanced and individualized radiation treatment to our patients.

This issue of *Synthesis* also explores the fresh approaches our researchers are taking to improve outcomes for patients with muscle-invasive bladder cancer. Working with our colleagues at Lawrence Livermore National Laboratory, we hope to pave the way toward more effective treatment of a disease for which advances have been too slow in years past. And Lorenzo Berti's innovative research on the use of nanoparticles to deliver more targeted chemotherapy is highlighted in our pages devoted to basic science.

Other stories inside this issue explore the kinds of emotional renewal our patients and their loved ones experience during their cancer journeys. Our "Outreach" feature, for example, describes how those affected by cancer heal as they write when they participate in a popular program coordinated by volunteers. And our "Benefactors" contribution tells the story of one woman whose survival after ovarian cancer sparked a dedication to giving back to bolster UC Davis Cancer Center research.

We hope you enjoy these and other stories in this issue of *Synthesis*.

RALPH DEVERE WHITE

*Director, UC Davis Cancer Center
Associate Dean for Cancer Programs
Professor, Department of Urology*

SYNTHESIS

THE MAGAZINE OF UC DAVIS CANCER CENTER

VOL 13 • NO 2 • FALL/WINTER 2010



INSIDE THIS ISSUE

First steps

- 2 Cancer center marks Cancer Survivors Day with groundbreaking ceremony

In translation

- 8 Researchers explore new cellular avenues to improve bladder cancer survival

Outreach

- 12 Writing group inspires patients, loved ones affected by cancer

Connections

- 16 Radiation oncology department assembles world-class team

Benefactors

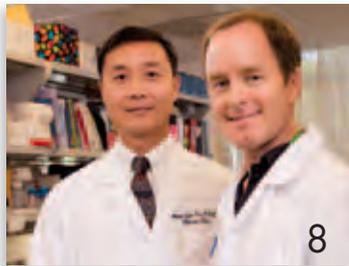
- 20 Grateful ovarian cancer patient gives back

Building on basics

- 24 Researcher seeks refined approach to drug delivery

News briefs

- 27 Protein made by breast cancer gene purified, Larry Kushi joins cancer center's health disparities research team, UC Davis researcher examines popularity of unproven mammography tool, and more



UCDAVIS
CANCER CENTER

*A National Cancer Institute-
designated cancer center*



An expansion for the future

Cancer center marks Cancer Survivors Day with groundbreaking ceremony

It was a day for hope, a celebration of survivorship and renewal, both for those affected by cancer and for the men and women at UC Davis Cancer Center dedicated to taking care of them.

More than 300 people gathered on the center's lawn and pathways on that warm Saturday morning in June to mark National Cancer Survivors Day and to break ground on the long-awaited cancer center expansion.

Men, women and children proudly sported blue-and-gold buttons proclaiming their number of cancer-free years. Women threw bright pink feather boas around their shoulders in honor of breast cancer survivorship. Advocacy and support group members passed out fliers, trinkets and treats. Guests took refuge from the sun in the art gallery to view inspirational artwork by Survivors Day attendee SaEeda Sharon King and others, or to create Japanese origami cranes for good luck and

healing. National Football League Hall of Famer and cancer survivor Jim Otto spoke eloquently about the role the cancer center played in his treatment and recovery from prostate cancer. At lunchtime, tables with red-and-white-checkered tablecloths and white umbrellas offered views of the stage where Native American storyteller Cheewa James told a tale of healing.

The cancer center – one of only 66 designated by the National Cancer Institute – cares for more than 9,000 adults and children each year, from as far south as Fresno and as far north as the Oregon border. But outpatient visits have grown by 50 percent during the past five years, with growth projected to increase by at least 6 percent each year. And with an additional strain on resources due to the closure of some community cancer clinics in the region, the expansion is a critical component in the health system's ability to continue performing integrated and comprehensive cancer care.

"We have made great strides in improving outcomes for our patients," says Ralph deVere White, cancer center director. "But our facility must be able to meet the increasing demand for care."

The 46,000-square-foot expansion, to be completed in 2012, will connect to the existing cancer center via a second-floor bridge on the northern side that overlooks a courtyard. The project also will include remodeling about 9,000 square feet of the existing building. Eventually, another 40,000-square-foot addition will be built to accommodate more clinical trials and to house the radiation oncology department.



Tura Jenkins

Tura Jenkins was already emotionally shaken from a family death when she was diagnosed with Stage III endometrial cancer. Treatment was aggressive and included chemotherapy, external and internal radiation treatments, and blood transfusions (and an extra treatment for an allergic reaction to one of the chemotherapy drugs).

Jenkins admits she mentally broke down twice during her year-long treatment. The first time was when she learned she would lose her hair to chemotherapy. The other time was when she had to have a port inserted in her chest.

"I don't like having stuff under my skin that isn't supposed to be there!" she says, able to laugh about it now. Other emotional hurdles came with the loss of another family member, and with early menopause (she's in her 40s) due to treatment.

But Jenkins became a pro at finding ways to keep her spirits up, such as painting her face green before radiation treatment (her "radioactive zone" look, she calls it). And she found comfort in her aesthetic surroundings.

"The building you come to is more important than you think, and the cancer center is radiant," she says. "You need positive, bright things. It can give you hope."

She also found solace in her health-care team. "I can't stress enough how wonderful every single individual in the facility is, from top to bottom," she says. "The staff is loving and compassionate, and my doctors – John Dalrymple, Wiley Fowler and Jyoti Mayadev – and all the nurses were fantastic. I really would not have done as well without them. I consider them all family, which may seem kind of weird since you're only around for a year. But when people save your life, it makes a huge difference."



National Cancer Survivors Day, held on a Saturday morning in June, was **a joyful demonstration** that life after a cancer diagnosis can be **meaningful, productive and full of hope.**

National renown and construction aside, the intent of the cancer center is always to provide a smoother, more soothing path for the patients who travel its corridors and visit its exam and treatment rooms.

Young patients now are seen at various locations around the medical campus. For example, 10-year-old Parmina Valentine, another Survivors Day attendee, would begin her chemotherapy cycles at the infusion center in one building, then had to linger until transportation was available to take her to the main hospital nearly three blocks away, then sometimes had to wait for a pediatric room to become available.

The new addition will smooth the geographic transition for Parmina and other young patients. By housing both pediatric and adult oncology services, the expansion will ensure more seamless access to physicians, nurses and treatment options for all patients – particularly vital for adolescents who are undergoing the transition from pediatric to adult care.

“We need room to see everyone in one place,” deVere White says. “Pediatric cancers are devastating.



Anne Elbrecht

Anne Elbrecht was on vacation, on her way to Syria, when the gynecologic problems that she had been experiencing worsened. She made a medical pit stop in Istanbul, where doctors diagnosed Fallopian tube cancer. Elbrecht returned home immediately.

Fallopian tube cancer is rare, accounting for only about 1 to 2 percent of all gynecologic cancers. Although she considered gathering second opinions, she already had a UC Davis Medical Center primary-care physician, and had confidence in the health system and the cancer center. She underwent surgery, then six weeks of chemotherapy. Fortunately, she says, “I never had nausea, never got sick.”

The care she received at the cancer center, she says, was exemplary. She loved her surgeon, Anne Rodriguez, whom she called “a sweetheart.” She says that the staff at the infusion center was always upbeat, cheerful and skilled.

“I felt very fortunate, very well cared for,” she says.

Afterward, Elbrecht set to work on recovering her full physical and mental strength, which was naturally compromised by treatment. She was planning another vacation, this time to England, when she learned that her cancer had returned. But she is facing a new round of treatment with her natural aplomb, once she returns home. She’s taking her vacation first.



Mikel Nalley

Mikel Nalley, a self-employed artist and actor, first found a softball-sized lump under his right arm, which he nicknamed “Charlie.” Nalley recalls with amusement that the nurse who

first saw his lump at his primary-care clinic said, “that’s impressive!” She sent him to the emergency department at UC Davis Medical Center for diagnosis and treatment.

Numerous biopsies later, UC Davis Cancer Center oncologist Mrinal Dutia confirmed that the lump was plasma-blastic non-Hodgkin’s lymphoma. Under Dutia’s care, Nalley began a regimen of chemotherapy with radiation.

The treatment was made easier under Dutia’s care, Nalley says. He regards her 1950s, house-calling-doctor demeanor – for example, calling him at night to check up – as a blessing.

“She’s got that great gene for compassion and concern that you’ve got to have in this field,” he says. “You don’t want to see anyone go through pain so you do everything you can to work out a plan, a procedure, a treatment.” When Nalley said he was experiencing a little bit of nausea after his first bouts of chemotherapy, Dutia said firmly, “No – we don’t want any nausea!” She found the right medication to ease his discomfort.

Nalley says “Charlie” began disappearing immediately – and he means

immediately – after treatment began.

“I could literally feel it going down as I walked out of my first session,” Nalley says.

Six months later, smaller tumors began to appear on his other side. This time, treatment included a bone marrow transplant. Dutia moved aggressively to get Nalley approved for the procedure he needed. Nalley was the first patient with HIV to have high-dose chemotherapy with an autologous stem cell transplant at UC Davis Medical Center.

First-class treatment extended from all corners of the cancer center, from the stem cell transplant team – whom he calls “brilliant” – to the cheerful and upbeat day staff he encountered during his stay.

Nalley’s partner, Avi Sharma, was so inspired by Nalley’s interactions with UC Davis health-care staff members that he is now pursuing his medical assistant degree.

“Some good things do come out of this whole mess,” Nalley says cheerfully. In the meantime, his numbers are good, as is his health. “They say I’m at 80 percent, but I feel like 100 percent!”

By co-locating children and adult services, we hope that pediatric oncology can leverage the more vast resources available for adult cancers. It’s more economical for us, but it’s also of greater benefit to the patient.”

DeVere White believes that putting children and adult services together also can benefit the emotional well-being of patients.

“Having adults and children interact helps keep a sense of perspective, and can provide inspiration and hope to older patients,” he says.

At the same time, children also will have their own comfortable space. The pediatric hematology-oncology and infusion clinics will have play areas, isolation rooms,

“We have made great strides in improving outcomes for our patients. But our facility must be able to meet the increasing demand for care.”

~ Ralph deVere White

DVD players and other features to make the visits of young patients as pleasant as possible.

On a more practical note, co-locating resources also will benefit clinical researchers, basic scientists and physicians by helping them keep pace with the growth of much-needed clinical trials and research

programs. The cancer center integrates the work of 179 scientists in 317 research projects dedicated to cancer treatment, including external research partnerships with the Lawrence Livermore National Laboratory, the California Department of Health Services, different departments and colleges

of UC Davis, and other entities.

Historically lacking sufficient resources, clinical research is now much more complex than ever.

“Trials have become far more complicated, and we have to develop a cadre of people who have the expertise to conduct them,” deVere White says. “To be able to quicken the pace by which we make discoveries in the lab and get them to the patients, we need dedicated physician-scientists – and we need the space. If we are to truly bring our resources and expertise to the population of Northern California, it’s important that our whole base be as strong as possible.”



The cancer experience is a journey, at once frightening and illuminating, that millions take every year. The UC Davis Cancer Center expansion project, which continues its fundraising efforts to reach \$35 million, will help support all members of the UC Davis Cancer Center family: those who came out on Cancer Survivors Day, those who will attend in the future, and those who endeavor to provide the best care and outcomes possible for each one of them.

“To be able to **quicken the pace** by which we make discoveries in the lab and **get them to the patients**, we need dedicated physician-scientists – and **we need the space.**”

~ Ralph deVere White



Parmina Valentine

Pauline Marie considers the H1N1 flu to be a blessing. It hampered the breathing ability of her granddaughter Parmina so much that she needed

a chest X-ray. If not for that, the mediastinal embryonal germ cell tumor attached to Parmina’s thymus wouldn’t have been discovered before advancing to Stage IV cancer.

Parmina’s cancer is particularly “special” because her type of germ cell tumor is most typically found in older men and testicular cancer. Her doctors – Theodore Zwerdling, Janet Yoon and Gary Raff – removed “Booger” (Parmina’s name for her tumor) and helped her through surgery and chemotherapy, although she will be monitored for the next several years. Chemotherapy side effects included some permanent hearing loss, lung damage and cognitive difficulties, as well as potential kidney problems.

But the irrepressible fifth-grader – “definitely a preteen,” laughs her grandmother – has faced down adversity since

birth, when she had an enlarged heart and water on the lungs due to her mother’s undiagnosed gestational diabetes.

Today, that perseverance keeps Parmina going. She helps take care of her two younger sisters, both of whom have special needs, and she has started training with a local couple to pursue her dream of being a magician. In August 2010, she performed her magic at the KNCI Radiothon for the Make-A-Wish Foundation.

She also wants to spend time volunteering on the hematology-oncology ward, cheering up inpatient kids.

“She knows that some kids feel really blue when they’re in the hospital, and she’d like to help them feel a little better if she can,” Pauline says of her granddaughter with admiration. “She is just amazingly upbeat, a happy kid.”



SaEeda Sharon King

Having endured cystic breasts for years, SaEeda King was tired of having them so frequently aspirated – so she stopped going to the doctor.

“I didn’t get checked for a few years,” she admits. Then she found a painful lump under her arm. It was stage III breast cancer.

King thought, “I can take care of it myself.” She followed a macrobiotic diet and underwent cleanses. The lump went down, and the pain stopped. But then she developed a new cancer – an aggressive, inflammatory cancer.

Around that time, King, who calls herself multireligious, had a spiritual experience. A friend from her old home in Hawaii had recently died of breast cancer. King built an altar and prayed for her friend: “And her spirit came. She said, ‘By the time I turned to medicine, it was too late. You need to do both.’”

Taking that advice, she began treatment at UC Davis Cancer Center. She underwent chemotherapy, a full mastectomy, radiation, and then a year

on the drug Herceptin, which targeted her specific type of breast cancer. Her spirituality never flailed.

“I did Buddhist chants and visualizations,” she says. “I would picture the chemo and radiation as bursts of gold-colored light, knocking out the cancer.” Before her operation, she also buried two rose quartz heart-shaped crystals in the earth as a ceremonial goodbye to her breasts.

King has nothing but praise for the health-care professionals who helped her.

“I felt comfortable with their spirits,” she says. “You have to decide whether to trust your physician and trust what they have planned for you.”

She is now three years cancer-free, but she doesn’t use the word “remission.”

“I prefer to think it’s not coming back,” she says. “It’s gone forever, in this lifetime and in any others!”

The cancer center – one of only 66 designated by the National Cancer Institute – cares for more than 9,000 adults and children each year, from as far south as Fresno and as far north as the Oregon border.



Taking on a formidable foe

Researchers explore new cellular avenues to improve bladder cancer survival

Doctors may be winning some fights against cancer, but have been losing the battle against invasive bladder tumors. Bladder cancer is not only becoming more common, but the mortality rate for patients is increasing as well. During the past five years, the number of deaths associated with bladder cancer each year has increased from 11,200 to 14,370.

“We should have done much better,” says Ralph deVere White, director of the UC Davis Cancer Center. “Bladder cancer should be among the most treatable of malignancies. The bladder itself is readily accessible to inspection and biopsy, making both diagnosis and treatment monitoring relatively simple.”

The primary problem, says deVere White: a lack of funding. In 2008, the National Cancer Institute allocated \$24.1 million for bladder cancer research, compared to \$285.4 million for prostate cancer and \$572.6 million for breast cancer. Yet the lifetime cost of treating bladder cancers is higher than for any other cancers. Its daunting 50 percent recurrence rate means years of follow-up surveillance and continuing treatment.

The majority of those who die from the disease have malignancies that have invaded the bladder muscle.

“If we want to lower mortality from this bladder cancer, we need to improve the survival of people with muscle-invasive and metastatic disease,” deVere White says.

DeVere White and other urological oncologists developed a national clinical trial for patients with muscle-invasive tumors. They found that 40 percent of patients who received chemotherapy prior to bladder-removal surgery had no signs of tumor in their bladder after the surgery. The survival rate among these patients was 85 percent.

Their doctors aren't ignoring the standard of care. Rather, they are all too aware of another grim fact: that half of all bladder tumors do not respond to drugs. Uncertainty about whether preoperative chemotherapy will help has made doctors reluctant to prescribe it, lest they subject patients to needless discomfort,



Ken Turtletaub and Paul Henderson

expense and delays in tumor removal.

If deVere White and colleagues at UC Davis Cancer Center have their way, such treatment dilemmas will become a thing of the past. They are developing ways to predict which tumors will be most responsive to chemotherapy. Patients will benefit from treatments personalized to the susceptibilities of their particular tumor, and will be more likely to avoid ineffective treatments. These same techniques also will spotlight types of tumors that require additional research into new therapies. And what scientists learn from these studies will be applicable to other types of cancers as well.

A drop of treatment

More is not always better, goes the old adage. This could be the motto of UC Davis toxicologist Paul Henderson and molecular oncologist

Chong-xian Pan. The two scientists are applying microdoses of drugs – amounts too small to cure or injure a patient, but enough to interact with tissues – to guide chemotherapy choices for individual patients.

For their proof-of-concept study, Pan and Henderson are studying how the chemotherapy agent carboplatin penetrates bladder cancer cells. Carboplatin binds to DNA at sites called adducts. This DNA damage triggers cells to self-destruct. Cells that are proliferating, such as those in malignant tumors, are the most likely to die.

For the study, the researchers have synthesized clinical-grade carboplatin from scratch using a heavy isotope of carbon. Bladder cancer patients will receive the drug a few hours before their bladders are removed in surgery. The amount of carboplatin they receive will be 1/100th of the dose used for cancer

treatment. Toxicologist Ken Turtletaub of Lawrence Livermore National Laboratory will analyze the tumor DNA using an accelerator mass spectrometer. The instrument can count every heavy carbon atom bound to the DNA and, by extension, the amount of bound carboplatin.

“The higher the levels of adducts in a tumor, and the longer they last, the more likely the tumor is going to respond to chemotherapy,” Henderson says.

All patients will then receive a therapeutic course of platinum-based chemotherapy. A database will track both their outcomes and their adduct numbers. Once data from all 85 patients in the study are collected, researchers will be able to determine which patients are most likely to benefit from the chemotherapy. The result: clearer guidelines for personalized bladder cancer treatment.

“This technology has the potential to identify resistant cancer before patients receive toxic chemotherapy,” Pan says. “Furthermore, it may guide medical oncologists to design personalized chemotherapy to overcome chemoresistance.”

Henderson, who also founded a company seeking to commercialize clinical microdosing studies with carboplatin, is enthusiastic about the new approach.

“It’s a whole new way to do cancer research,” says Henderson. “In addition to carboplatin, we will be able to apply this technique to plenty of other drugs and cancers.”

Already, Henderson and Pan are using the approach to improve veterinary care. Carlos Rodriguez of the UC Davis School of Veterinary Medicine is replicating the microdosing study with 20 canine bladder cancer patients.

MicroRNA markers

Cells become cancerous because they are expressing genes that encourage unchecked growth. Scientists have been comparing the gene expression patterns in healthy and cancerous cells for years, with only limited results. More recently, researchers have discovered another mechanism involved in gene control: microRNAs. Each of these short snippets of nucleic acid can derail the production of hundreds of different proteins.

UC Davis Cancer Center researchers Clifford Tepper and Ruth

Vinall are comparing microRNA patterns in bladder tumors. They hope to use these molecular markers to identify tumors susceptible to chemotherapy. Previous work by UC Davis researchers and other scientists have identified microRNA signatures involved in prostate and breast cancer.

For their study, the scientists purified the microRNA from 30 bladder tumors and analyzed them with microarrays printed on glass slides. These microarrays can identify which of the 866 known microRNAs

are present or lost in each tumor. Based on the microarray results, Tepper has been able to divide the samples into responder and nonresponder groups with approximately 72 percent accuracy. A number of the microRNAs in these profiles affect pathways controlled by tumor suppressor genes and oncogenes.

The scientists are now developing a set of microRNA markers that clinicians can use to identify patients who would benefit from chemotherapy. Eventually, these markers will help determine alternative treatment regimens for patients whose tumors don't respond to current cancer drugs.

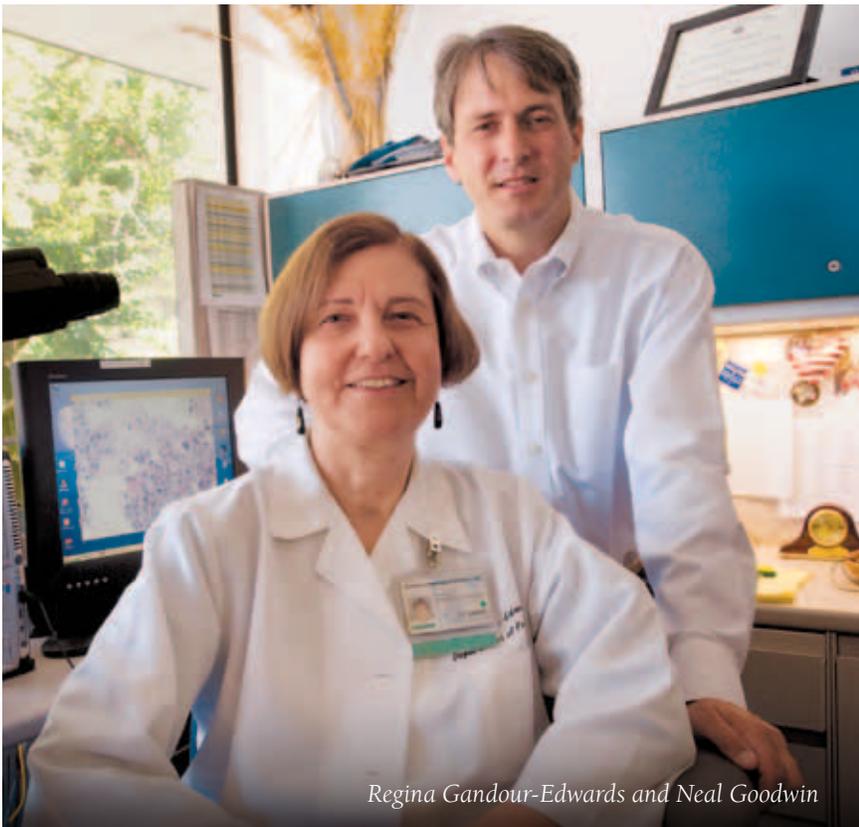
"This study is not just profiling of samples; its ultimate goal is to translate to a direct impact on patient care," Tepper says.

In a related study, the scientists are profiling microRNAs from tumors that already have resisted chemotherapy treatment. These tumors have their own unique set of microRNA signatures. By linking these microRNAs to gene expression, the researchers should be able to explain the mechanism responsible for resistance and to reveal new targets for chemotherapy.

The researchers plan to refine their marker system by increasing the number of samples in both studies. New technology is playing a pivotal role in their research. Both next-generation sequencing techniques and new computational methods are enabling them to better analyze microRNA levels and their influence on cancer gene expression.

A better mouse model

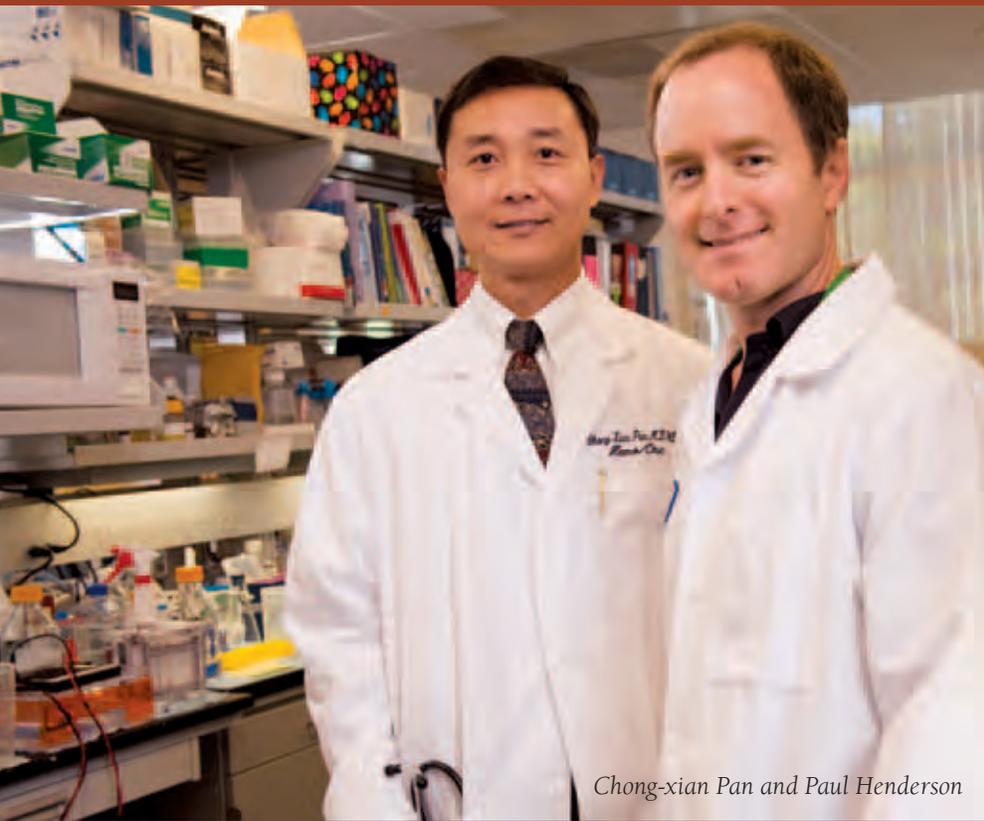
A major factor limiting development of new cancer therapies is the availability of good animal models. While scientists can now grow tumor cells with ease in incubators, in vitro cultures lose many of their original cellular characteristics as well as



Regina Gandour-Edwards and Neal Goodwin

"It gives you the **most humanlike lab tool** to **preserve and study** these tumors."

~ Neal Goodwin



Chong-xian Pan and Paul Henderson

“It’s a whole new way to do cancer research. In addition to carboplatin, we will be able to apply this technique to plenty of other drugs and cancers.”

~ Paul Henderson

the environment that encourages their growth.

UC Davis researchers are collaborating with JAX-West, a division of the nonprofit Jackson Laboratory, on a co-clinical trial of bladder cancer therapies. The research revolves around a rodent called the NSG mouse, which lacks major immune system components.

“For the first time ever we can engraft and study a tumor in the presence of the human extracellular matrix, which provides the cells and factors that help propagate this tumor in the human being,” says JAX-West

scientist Neal Goodwin. “It gives you the most humanlike lab tool to preserve and study these tumors.”

UC Davis urological oncologists, together with pathologist Regina Gandour-Edwards, supply Jackson with tumor tissues from patients undergoing bladder removal at UC Davis Medical Center. The lentil-sized fragments are injected beneath the skin of multiple mice within an hour of their removal in the operating room.

“It’s a living bank of these patients’ disease that can be used for the foreseeable future,” Goodwin says.

The researchers are treating the mice with chemotherapy agents to identify promising new drugs.

“For cancers that do not respond in the mice, we will bring them back into the laboratory and try to work out why they are not responding – to find their targets, treat them in the mice, and hopefully develop new treatments,” deVere White says.

Goodwin also is analyzing gene expression patterns to identify salient markers for each type of tumor. Eventually, clinicians might be able to use this information to predict outcomes and identify the best treatment regimen for each person’s cancer – enabling doctors to turn the tide of the battle against cancer one healthy patient at a time.

Early work on new pathways

Theresa Koppie, UC Davis assistant professor of urology, hopes her research will lead to better long-term results for bladder cancer patients. She has begun preliminary research into finding bladder cancer biomarkers in urine.

Working with Oliver Fiehn, professor at the UC Davis Genome Center and a renowned expert in the field of metabolomics, and Robert Weiss, professor of nephrology, Koppie is collecting urine specimens from patients without bladder cancer, and from those with bladder cancer in various stages of the disease.

They are looking for small molecule biomarkers called “metabolites” secreted into the urine during the metabolic process that may indicate the metabolic pathways involved in the behavior of advanced tumors.

“All the processes we have now for detection are invasive,” she says. “If we could detect cancer or its progression with a simple urine test, we could potentially detect progression of disease earlier, while decreasing the morbidity of bladder cancer care.”



Healing words

Writing group inspires patients, loved ones affected by cancer

“Something challenged me to the depth of my soul and made me question the existence and function of the universe.”

– Joanne Greer, *writing as part of UC Davis Cancer Center’s Writing as Healing group*

That something to which Greer is referring is cancer, and she is determined to prevent it from defining or breaking her.

So every week, Greer and about eight other people affected by the disease meet at UC Davis Cancer Center. They gather not for chemotherapy, radiation or any other medical treatment related to cancer. They gather to write. And as they write, they heal.

"We show up **at the table as writers**. Our role as **patient, survivor or caretaker is irrelevant**. We are all there to **express something**."

~ Terri Wolf



"We show up at the table as writers. Our role as patient, survivor or caretaker is irrelevant. We are all there to express something," says Terri Wolf, a radiation oncology nurse at the cancer center and one of two volunteer group facilitators.

"People open their hearts and spill their emotions on the page, and there is a sense that we're all one We are sharing at the deepest level," adds Christine Holmstrom, a writing group member who is a cancer survivor.

During the past six years, UC Davis Cancer Center has offered writing groups for people affected by cancer. Called Writing as Healing, the groups allow people a safe environment to write whatever they are feeling as they grapple with cancer in some form in their lives.

The writing groups are modeled after the Amherst Writers and Artists method, which embraces a free-form approach to writing. The method asks writers to respond to various prompts and write in a stream-of-

MAGIC, PATIENCE, KISS and LOVE were the four word prompts

Writing sample by J. Maurice Williams

MAGIC is everywhere. I see it in the skies, nature, animals and people. I don't understand how it all comes together but somehow it does.

PATIENCE is my love. I don't always acknowledge how she is able to be still and centered and count to three but somehow she does it.

KISS – Wow, does she know how to kiss. My heart still flutters every time our lips meet. She is a fabulous kisser. Wow!

LOVE – I had to learn the hard way; until I learned to love myself, I was incapable of loving anyone else. Now I see and feel love in so many people, even my five at-risk juveniles. My work with them is my greatest challenge ever, and I've been working with troubled kids for 40 years.

consciousness style for a set period of time. The prompts may be a poem, a picture, a postcard, a line from a book – anything.

"You want to be evocative somehow, to tap into something that may already be wanting to be written," says Sarah Wenstrand, another writing-group facilitator. "It's very freeing."

The idea behind the method is to unlock whatever is lying within the writer that needs to get out. Sometimes it is anger at the disease. Sometimes it is fear. It may be a random memory from childhood that surfaces, seemingly of its own accord.

"Sometimes we write about cancer. Sometimes we don't," says Rhoda McKnight, a member of the writing group. "It gives you the opportunity, if you hang in there, to let all of your guard down and say whatever it is that needs to be said."

McKnight, 70, a retired

director of communications for the UC Davis College of Agricultural and Environmental Sciences, says she has written throughout her professional life, but was reluctant to join the writing group.

“I thought the last thing I wanted to do was sit in a room and write about cancer,” she says. “Cancer had been my whole life for the past year.”

But McKnight says she had never before written from the depths of her soul, as she says she and others in the writing group do now.

“Some of the **things we thought** were god-awful and painful **turn out to be kind of quirky and funny, too.**”

~ Beverly Williams

“Cancer is a physical thing, but the other portion is psychological,” she says. “You can’t be the same person after doing this kind of work.”

Beverly Williams, 69, says her writing within the group gave her

courage to marry her husband, John Williams, 69. Both are cancer survivors. She says she felt empowered through the whole writing process.

“It’s important to have the courage to live your life,” says Beverly. “Do not live in fear of what the next disaster will bring.”

She adds that the writing has illustrated for her that humor can be found even in difficulty.

“Some of the things we thought were god-awful and painful turn out to be kind of quirky and funny, too,” she says.

Beverly Williams’ most recent cancer recurrence is in her mouth. She recently underwent surgery in which bone from her leg replaced her lower jawbone, and leg tissue replaced tissue that had been removed from her mouth.

“I’ve got my leg in my mouth,” she jokes.

John Williams, who uses the pen name J. Maurice Williams, believes that writing releases endorphins that soothe the writer. A study of breast cancer survivors found sleep improved after participants took part in writing groups.

“A lot of the scars and bad experiences get released in some way through the writing,” he says. Williams adds that he thinks the writing discipline used in the groups is especially helpful to men, whom he believes are typically reluctant to express emotion.

“Sometimes we write about cancer. Sometimes we don’t. It **gives you the opportunity**, if you hang in there, to **let all of your guard down** and **say whatever it is that needs to be said.**”

~ Rhoda McKnight



“All I can say to men is you are missing something so valuable to yourself,” he says.

The Writing as Healing groups are designed to create a sense of safety. Writers may choose to read their writing aloud – or not. Other writers are asked not to criticize the reading, but rather to point out its strengths and emotions it evoked.

“It’s not really time to critique and edit and point out a run-on sentence,” says Wenstrand. “We want to create a supportive community where everyone is recognized as a writer by the simple fact that they write.”

Participants are told that the writing is to be viewed as fiction, not based on the writer’s life. The idea is that treating the work as fiction provides the writer more freedom in writing and separation for the story. It keeps the focus on the writing and prevents the gathering from becoming a support group.

“This is a writing group, not a support group,” says Wenstrand. “We hear each other’s stories, but we are not accountable to try to fix each other.”

Wenstrand started with a writing group in the weeks after her husband died following a 12-year battle with cancer.

“I really started writing as a brand-new widow,” she says. She developed a regular routine of writing and eventually became trained in the Amherst method.

Wolf, the other facilitator, says people in the groups often are amazed at what appears on the page as they write. She, too, is stunned by the depth and beauty of the writing.

“It is truly amazing when you totally let your pen flow, and write whatever comes to your mind, that you get to the place you need to write about,” says Wolf.



Rhoda McKnight, second from left, works on a writing exercise with other members of Writing as Healing.

Hair today, gone tomorrow

Writing sample by Rhoda McKnight

Silly me.
If I lost my hair,
which, of course, I didn’t think I would,
I’d look like G.I. Jane – Demi Moore –
young, tan, fit and fearless.

I waited as long as I could to cut off my hair.
My poor scalp had been hurting for 10 days.
As each hair died, deep in the follicle,
it broke off at the scalp and then drifted down
onto my t-shirt, my toothbrush, my turkey sandwich.

If I stayed alert and vigilant,
I could remove these hairs before anyone could see them.
I was shedding for four or five days;
then, I started molting.
My scalp hurt beyond belief.

Itch.
Itch.
Itch.

It was painful to touch my head
or to lie down on my pillow at night.

Some people I’ve known who’ve had cancer and gone through chemo
lost their hair –
but not everyone.
Of those who did,
some may have talked about the cosmetics of not having hair (being bald)
or the mechanics of looking ‘un-bald’ (a wig),
but I don’t remember anyone ever talking about how it felt
to “lose” all your hair –
to have it come out in handfuls each time you touch it –
or to find that, once it is gone,
you don’t look like G.I. Jane at all.

I looked in the mirror and cried.
Not because I have cancer.
Not because I’m hairless.
But I cried because I looked like Mickey Rooney.
Not the young Mickey Rooney, but the old Mickey Rooney.

If you could see me now!
If they could see me now!
G.I. Jane would smile.
Mickey Rooney would laugh.
But when I saw myself in the mirror,
I just stood there and wept.



Jyoti Mayadev and Carol Foscarini

Motivated and moving forward

Radiation oncology department assembles world-class team

When Carol Foscarini developed bleeding last year, she knew that with menopause behind her, it was unusual. But neither she, nor her primary-care doctor or gynecologist expected the diagnosis her biopsy revealed: a very rare form of vaginal cancer.



“My patients are my inspiration. It is very motivating to try to find ways to extend survival and **offer a better quality of life** for some of these devastating diseases.”

~ Ruben Fragoso

Because the medical community has so little experience with this cancer, a UC Davis team immediately formed to conceive the best course of action. Jyoti Mayadev, assistant professor in the UC Davis Department of Radiation Oncology, came on board to oversee the radiation therapy component of the treatment plan.

“There are no standard guidelines to follow for such an unusual cancer,” says Mayadev. “Mrs. Foscarini’s gynecologist, Anne Rodriguez, and I started to plan her treatment course very early, before her surgery and before I even met Mrs. Foscarini.”

Mayadev was recruited last year to the Department of Radiation Oncology for her expertise in the management of women with gynecological and breast cancers. She believed that the best course for Foscarini after surgery would encompass externally delivered radiation – the ordinary path followed when getting an X-ray – as well as brachytherapy, in which a source of radiation is placed inside the body. Brachytherapy enables more direct delivery of rays to a targeted tumor.

Mayadev is one of several radiation oncologists who have joined the department in recent years. Modernized with new state-of-the-art equipment, the department has burgeoned under the leadership of Richard Valicenti, hired in 2009 as chair. Valicenti quickly set about assembling a professional team

composed of some of the best young minds in the country, as well as acquiring the newest and most powerful tools available in radiation oncology.

“My goal has been to form a department with subspecialists in the major areas of cancer – doctors who are at the forefront of their specialty and who are able to deliver innovations and the highest standard of care to our patients,” he says.

Valicenti’s efforts have paid off. The UC Davis Medical Center radiation oncology department has become one of the premier facilities in the country, with a dynamic staff and modernized quarters that could double for a space-age Hollywood set. The busy department serves 60 to 80 patients a day, and has three dedicated radiation machines capable of



New treatment planning suite uses soothing sights and sounds to calm patients.

New members of the UC Davis Radiation Oncology Department

Jyoti Mayadev, M.D. (*far left*) A leader in managing breast and gynecological cancers, Mayadev is pioneering the use of brachytherapy in these areas. This technique, in which a source of radiation is placed inside the body, allows delivery of high doses of radiation close to the tumor. Her research examines the use of brachytherapy to improve the “therapeutic ratio” – maximizing destruction of the tumor while sparing healthy tissue. “Managing therapy and harm is a constant balancing act in radiation therapy,” says Mayadev. “We closely follow all our patients after radiation treatment. If a cancer recurs, we can utilize our tools to deal with it.”

Ruben Fragoso, M.D., Ph.D.

Specializing in brain and central nervous system cancers, Fragoso is particularly excited about exploring therapies that may eliminate the need for surgery. He is an expert in the use of the gamma knife, which precisely delivers high-dose radiation and can allow the destruction of tumors deep in the brain that would otherwise be inoperable. Fragoso is conducting research on glioblastoma multiforme, an aggressive brain cancer with few treatment options. “My patients are my inspiration,” says Fragoso. “It is very motivating to try to find ways to extend survival and offer a better quality of life for some of these devastating diseases.”

Connections >>



With cheering fans in the wings, 8-year-old Muntadhar “Tony” Aljoher lit up the radiation oncology waiting room in July as he took on – and handily outplayed – Ruben Fragoso, assistant professor of radiation oncology, in a Guitar Hero contest. The young rock ‘n roll wizard was celebrating the end of a 30-visit series of radiation treatments for medulloblastoma, a brain tumor, diagnosed in May.

Computer-controlled linear accelerators deliver varying radiation doses to multiple points, “sculpting” the radiation three-dimensionally to fit the tumor. High-intensity radiation beams can be delivered to small areas with little scatter, allowing for knife-like precision in destroying a tumor and avoiding damage to surrounding healthy tissue.

delivering high-precision radiotherapy.

Valicenti has emphasized creating a team that takes a multidisciplinary approach to patient care. The remodeled department contains a large work space where doctors and technicians can meet together at computer stations to plan therapy. According to Valicenti, everyone in the department works closely together to develop treatment plans, which can be incredibly complex.

“For every hour we spend face-to-face with a patient, we probably spend 20 to 30 hours planning his

or her therapy,” he says.

The field of radiation oncology has developed exponentially in recent decades as technological advances in imaging, mapping and radiation delivery have spurred each other’s progress. Using sophisticated computer modeling programs, doctors can map and shape the delivery of radiation so that a tumor’s location can be precisely identified, accounting for changes of tumor size and shape during the course of therapy and even taking into account changes of position during breathing.

“The capabilities of radiation oncology today are phenomenal,” Valicenti says. “Garnering a team with each member having a specialized expertise in a certain area has been critical to maximizing use of the important innovations now available in cancer treatment.”

Research is another important component of the department. Each specialist has a particular research interest, and being a part of an academic center constantly promotes innovation.



“Garnering **a team** with **each member having expertise** in a certain speciality area has been critical to **maximizing** use of the **important innovations now available** in cancer treatment.”

~ Richard Valicenti



Allen Chen and Sun Yi

New team members

continued

Allen M. Chen, M.D. (*this page, far left*)

An expert in head and neck anatomy, Chen has developed an “atlas” for radiologists to better plan therapy. His nerve maps of the head and neck, which help radiologists avoid damaging critical nerves, have been adopted into standard guidelines issued by the national Radiation Therapy Oncology Group. Chen is skilled in using stereotactic body radiation therapy (SBRT), which delivers a single high dose of radiation from multiple beam angles using a coordinate system to precisely locate the tumor. SBRT is an alternative to surgery in early-stage lung cancers. “Radiation oncology is an exciting field because it is used in so many settings,” says Chen. “Radiation now plays an important role in primary treatment, postoperative therapy and palliation for pain control.”

Richard Valicenti, M.D., M.A. (*far left, bottom*)

Specializing in prostate and other urologic cancers, Valicenti uses intensity-modulated radiation therapy (IMRT), an advanced high-precision radiation method. The accuracy of IMRT results from the use of computer-controlled linear accelerators to sculpt a three-dimensional radiation dose map to deliver precisely targeted radiation doses to a tumor. As chair of the department, Valicenti takes special pride in creation of a group of specialists who subscribe to a team approach. “Not only do we regularly consult with one another, but we call in experts from other departments and work closely with the patient’s primary-care physician and other members of the treatment team,” Valicenti says. “Multidisciplinary approaches are critical to solving complex medical problems today.”

“The large patient volume and the opportunity to treat unusual tumors such as Mrs. Foscarini’s puts us in a unique position to conduct innovative clinical trials, especially ones that have the potential to lead to rapid clinical applications,” says Valicenti, who is involved in a trial studying treatment of bone metastases from prostate cancer. “Participation in clinical trials also offers our patients access to promising therapies that are not available otherwise.”

Despite the high-tech, ultra-modern feel to the facility – or maybe because of it – staff members pay particular attention to making patients feel comfortable. One treatment planning room has a wall and ceiling lined with screens hooked up to a selection of relaxation videos geared toward children or adults. Patients can watch Alpine scenery, waving palm trees or cartoon fairylands while they undergo a radiation therapy planning session, typically 30 to 40 minutes long.

“The videos were very helpful,” says Foscarini, who also appreciated the background music. “I once told the technician that I’m of the age that enjoys Elvis, and the next day they had Elvis playing for me!”

Foscarini required daily intensive radiation treatment for six weeks, followed by a few more weeks of twice-weekly treatment.

“Everyone – from Dr. Mayadev and the other doctors to the technicians and receptionists – made me feel like family,” she adds. “Although the reason I was getting treatment was certainly not positive, I actually looked forward to coming in.”

Valicenti, who is rightfully proud of the transformed radiation oncology department, concurs that many components are essential to building a successful treatment facility – state-of-the-art equipment, expertise in different specialties, teamwork, and caring for patients’ needs.

“We never lose sight of our primary goal,” says Valicenti,

“to provide innovative cancer therapy with optimal care, maximizing longevity with the highest possible quality of life.”



One woman, one cause

Grateful ovarian cancer patient gives back

When the ovarian cancer came, Pattie Laubhan made no plans to fight it beyond surgery. She had watched her aunt and mother struggle through their treatments for breast cancer, and it was not a journey she wanted to take.



Passport to Discovery is the backdrop for **emotional reunions** between patients and nurses, **moving testimonials by cancer survivors** and **research updates from doctors** that take place **amid some lively rounds of golf.**

But John Dalrymple, the hematologist-oncologist at UC Davis Cancer Center who had seen her through the successful operation, emphatically urged her to additionally have chemotherapy.

During that meeting and a long follow-up phone call, Dalrymple patiently answered her questions, eased her fears and, Laubhan recalls, “convinced me to go for it.”

That was seven years ago, and today Laubhan is not only an inspiring cancer survivor, but also a one-woman fundraising machine for the cancer center that helped restore her health.

For the past five years, Laubhan has organized an annual golf tournament and dinner to raise money for ovarian cancer research. This year’s event, dubbed Passport to Discovery, was held in June at the Granite Bay Golf Club. The event is the backdrop for emotional reunions between patients and nurses, moving testimonials by cancer survivors and research updates from doctors that take place amid some lively rounds of golf.

All told, the tournaments have yielded more than \$80,000 for the cancer center. The funds have been used to support ovarian cancer clinical trials as well as biomarker studies led by UC Davis researchers, said Gary Leiserowitz, the center’s chief of gynecologic oncology.

Laubhan and her husband, Randy, own and operate a commercial property rental business in Roseville. Even though she did not have a fundraising background, her hands-on approach in encouraging philanthropy vividly symbolizes how patients can become some of the cancer center’s most passionate – and important – advocates.

“There are few motivators more powerful than having a disease or having a family member with a disease,” says Leiserowitz. “Pattie’s creativity in finding ways to generate dollars for research, and her commitment to help those afflicted with cancer, are just remarkable.”

Laubhan says two forces spawned her desire to raise money for the cancer center and, through that charitable effort, increase awareness

“Pattie is a truly **inspiring and passionate person** who **works tirelessly to inform others** about ovarian cancer. She lights up when she speaks about the care she was given at UC Davis, and that **makes me very proud to be an employee here.**”

~ Christine McGuire



“Pattie’s creativity in finding ways to generate dollars for research, and her commitment to help those afflicted with cancer, are just remarkable.”

~ Gary Leiserowitz

of the center’s achievements. The first motivator was simply her gratitude that “such a phenomenal facility staffed by such compassionate people was right here in my backyard. Cancer runs in my family, so I’ve had a lot of experience with doctors and institutions,” says Laubhan, 59. “Given that, I know how amazing UC Davis truly is. They don’t just treat the disease – they treat the person.”

Laubhan also was spurred to action by the uncommon nature of her cancer – and the fact that it receives far less attention than breast cancer or other, more prevalent cancers.

While breast cancer affects more women – 200,000 new cases are reported in the United States each year, compared with 22,000 new cases of ovarian cancer – the prognosis for patients with ovarian cancer is much bleaker.

When ovarian cancer is diagnosed at its earliest stage, the five-year disease-free survival rate is about 90 percent — meaning about nine in 10 patients will be alive in five years with no evidence of disease. But because its early symptoms are so subtle and nonspecific, two-thirds of women with the illness aren’t diagnosed until their disease is in

an advanced stage. At that point, the five-year survival rate is 30 to 40 percent.

“Given the grim prognosis for those with ovarian cancer, I think it’s important to support research because the competition for dollars is so intense,” Laubhan said. “But beyond that, my goal is to remind people that those buildings you see when you’re driving down the freeway aren’t just some random medical campus, but an amazing asset that we need to recognize and appreciate.”

Laubhan’s connection with UC Davis was forged by an odd twist

of fate. After feeling ill for several days in the summer of 2003, she tried to see her regular physician but could not get an appointment. Unwilling to wait, she elected to see another doctor outside her insurance network.

The physician who ordered an ultrasound test that revealed ovarian cancer then referred Laubhan to UC Davis – instead of to the hospital that Laubhan normally would have visited through her insurance plan.

“It was definitely a lucky turn of events,” Laubhan recalled. “And I often say the best thing about getting sick was the opportunity to meet so many wonderful people

Laubhan also was **spurred to action** by the **uncommon nature of her cancer** – and the fact that **it receives far less attention** than breast cancer or other, more prevalent cancers.



who have enriched my life.”

After her visit with Dalrymple, she also met with hematologist-oncologist Sidney Scudder, who corroborated Dalrymple’s opinion that she should proceed with treatment. Laubhan subsequently underwent chemotherapy under Scudder’s care. A year later, she was ready to give back.

After considering an endowment and other, more traditional forms of charitable giving, the Laubhans decided that an annual golf tournament would be an ideal way to draw a diverse group of people and create a flock of new donors.

While the economic downturn has thinned tournament turnout and profits, the Laubhans’ energy and determination to carry the torch for years to come have not wavered.

“Cancer runs in my family, so I’ve had **a lot of experience** with doctors and institutions. Given that, **I know how amazing** UC Davis truly is. They **don’t just treat the disease** – they treat the person.”

~ Pattie Laubhan

That spirit has left an enduring mark in the halls of the UC Davis Health System.

“Pattie is a truly inspiring and passionate person who works tirelessly to inform others about ovarian cancer,” said Christine McGuire, the

health system’s senior donor relations officer who has worked with the Laubhans for four years.

“Pattie lights up when she speaks about the care she was given at UC Davis, and that makes me very proud to be an employee here.”

Nanoparticles with a punch

Researcher seeks refined approach to drug delivery

Chemotherapy has saved countless lives, but it's a brutal, all-out assault that can take a terrible toll on cancer patients. They may lose their hair, lose their appetites, and suffer a multitude of other side effects. Some will be minor, many miserable, and a few may be life-threatening. Most will resolve when the chemotherapy ceases, but some serious problems – heart damage, lung damage, infertility – may last a lifetime.

Patients undergoing chemotherapy are sometimes counseled to think of the toxic drugs as an army that's helping them fight for their lives. Unfortunately this army uses its force indiscriminately, attacking the entire body in an attempt to wipe out the cancer cells lurking within it.

"Chemotherapy doesn't just go where you want it, it goes everywhere," says Lorenzo Berti, an assistant research chemist in the Department of Internal Medicine. Berti is researching a more refined approach to attacking cancer, for which he's been awarded a \$450,000 grant from Susan G. Komen for the Cure.

"We've made huge progress in 30 years, and I'm always very gratified when I meet women who are surviving breast cancer for many years," said Ambassador Nancy G. Brinker, founder and CEO of Susan G. Komen for the Cure. "Research like this at UC Davis may help people with breast cancer take charge of their health by giving them a more aggressive and ambitious method of fighting their tumors."



Lorenzo Berti and student researcher Ying Zhou

Berti is exploring how nanoparticles might be used to deliver localized chemotherapy to tumors. He wants to arm infinitesimally small magnetic crystals of iron oxide – a nontoxic and inexpensive material – with drugs and deploy them in the body to invade and destroy cancerous tissue. The nanoparticles would travel benignly through the bloodstream until reaching enemy territory – a tumor – where they’d let loose their cancer-fighting arsenal.

Berti’s battle plan takes advantage of a peculiarity of the blood vessels that grow within malignant tumors to supply the rapidly growing and dividing cancer cells with nutrients and oxygen. The walls of these blood vessels, unlike those in healthy tissue, are pockmarked by holes. Berti plans

to use these holes as a point of entry for cancer-fighting nanoparticles to invade tumors. The nanoparticles that Berti is using in his research are 50 to 200 nm (nanometers) in diameter – about the size of viruses.

“They’re big enough that they can’t squeeze through the walls of normal blood vessels, but when they get to the cancerous blood vessels and find these big holes, they fall through them. Tumors tend to retain

nanoparticles in this size range. These particles are the scaffolds onto which we’ll load drugs.”

Berti plans to attach two cancer-fighting agents to the iron oxide nanoparticles. One, doxorubicin, is a commonly used chemotherapy agent. The other, Berti says, “is essentially a DNA sequence designed to weaken cancer cells,” making them more susceptible to attack by the chemotherapy drug.

“The advantage of this approach is that it’s a platform. You can switch out the components.”

~ Lorenzo Berti

Building on basics>>

“It’s a one-two punch,” he says.

Making the drugs adhere to the nanoparticles is difficult, Berti adds, but he intends to do that by first coating the particles in a polymer that imparts a positive charge. The DNA drug, which has a negative charge, will then stick to the nanoparticles. The chemotherapy drug – doxorubicin – has a strong affinity for the DNA drug, so it will in turn latch on.

“It’s like a little Russian doll, with everything nested in there,” Berti says.

Once these drug-toting nanoparticles have accumulated within a tumor, application of a magnetic field could trigger them to break down and release their therapeutic attack.

There’s even more to Berti’s battle strategy, though. The temperature of iron oxide nanoparticles increases when they’re exposed to a magnetic field – one that’s otherwise harmless to the body. Prompting the nanoparticles to heat up once they’ve invaded a tumor could provoke further weakening of the cancer cells, thereby making malignancies even more susceptible to the chemotherapy drug.

Because the iron oxide nanoparticles are magnetic, their distribution could be monitored using magnetic resonance imaging (MRI), allowing clinicians to see the particles accumulated in a tumor, and to monitor a patient’s progress by comparing the patterns of accumulation over the course of cancer treatment.

Berti plans to test his localized chemotherapy technique on animal models of breast cancer initially. He says that if it’s successful, similar nanoparticles could be used to fight many different kinds of cancer.

“The advantage of this approach is that it’s a platform,” Berti says. “You can switch out the components.



Once these **drug-toting nanoparticles** have accumulated within a tumor, application of a **magnetic field could trigger** them to break down and **release their anti-cancer arsenal**.

You can try different combinations of drugs.”

Berti says that iron oxide nanoparticles, which are used as an ingredient in some MRI contrast agents, pose no danger to patients.

“In terms of safety, the real thing you have to worry about is the drug, not the particle,” Berti says. If his method works, far fewer of those toxic chemotherapy agents will be needed to triumph over cancer.

Protein made by breast cancer gene purified

A key step in understanding the origins of familial breast cancer has been made by two researchers at UC Davis. The researchers have purified, for the first time, the protein produced by the breast cancer susceptibility gene BRCA2 and used it to study the oncogene's role in DNA repair.

The results were published online in the journals *Nature*, and *Nature Structural and Molecular Biology*. They open new possibilities for understanding, diagnosing and perhaps treating breast cancer.

BRCA2 is known to be involved in repairing damaged DNA, but exactly how it works with other molecules to repair DNA has been unclear, says Stephen Kowalczykowski, distinguished professor of microbiology in the College of Biological Sciences, Cancer Center member and senior author of the *Nature* paper.



Wolf-Dietrich Heyer

"Having the purified protein makes possible far more detailed studies of how it works," Kowalczykowski says.

Kowalczykowski's group has purified the protein from human cells; another group led by Professor Wolf-Dietrich Heyer, also in the UC Davis Department of Microbiology and co-leader of the Cancer Center's molecular oncology program, used genetic engineering techniques to manufacture the human protein in yeast. That work is published in *Nature Structural and Molecular Biology*.

The two approaches are complementary, Heyer says, and the two teams have been talking and cooperating throughout.

"It's nice to be able to compare the two and see no disagreements between the results," says Heyer.

One application of the purified protein would be to make antibodies to BRCA2 that could be used in test kits as a supplement to existing genetic tests, Kowalczykowski says.

Cancer center grant boosts prostate cancer research

Cancer Center researchers have received a new, four-year federal grant to investigate molecular pathways involved in the failure of drugs aimed at slowing prostate cancer.

The \$1.1 million grant from the National Cancer Institute will be used to advance research into how certain molecules work to make cancer cells resistant to treatments that

work initially by blocking the cancer-promoting action of the male hormone androgen. In advanced prostate cancers, even anti-androgen drugs can't prevent reactivation of the androgen receptor, leading to disease progression.

Investigators hope their findings provide insights into how prostate cancer becomes resistant to androgen withdrawal therapies and lead to more effective treatments for the disease.

The grant is one of 21 currently funded projects at the UC Davis Cancer Center tackling the problem of so-called "castration-resistant" prostate cancer, which does not respond to withdrawal of male hormones. Prostate cancer is the most common cancer in American men, and is the second leading cause of cancer death in men. Median survival for men with castration-resistant prostate cancer that has spread to other parts of the body is one to two years.

The new grant, awarded to UC Davis Cancer Center Director and urology professor Ralph deVere White, expands earlier research into the role of tiny strands of genetic material called microRNA in the progression of prostate cancer.

"This is a novel hypothesis," says DeVere White. "If we can understand the functions of microRNA in prostate cancer, and determine whether it can be used as a potential biomarker or drug target for the disease, we can make tremendous progress against this devastating disease."

Larry Kushi joins cancer center's health disparities research team

Lawrence "Larry" Kushi, an internationally renowned cancer epidemiologist with Kaiser Permanente Northern California, has joined UC Davis as adjunct professor.

Kushi, who maintains his Kaiser affiliation as Associate Director for Etiology and Prevention Research for Kaiser's Division of Research, serves as co-leader of Population Sciences and Health Disparities, one of the cancer center's key programs, with Moon S. Chen Jr., UC Davis professor and Associate Director for Cancer Control.

The partnership benefits Kushi's continued epidemiological research at Kaiser as well as bolsters the research being done at UC Davis to study cancer patterns in populations and to reduce cancer health disparities.

"We already have really outstanding work in cancer health disparities led by Moon Chen, and we are excited about building and expanding our program," says Ralph deVere White, cancer center director. "With Larry Kushi we will also have a world-class cancer epidemiologist and comparative effectiveness researcher."

Kushi is a prolific researcher with more than 150 peer-reviewed publications and is principal investigator of multiple grants funded by the National Institutes of Health. He is internationally recognized for his expertise in nutritional epidemiology, and his research interests focus on the role of diet and nutrition in the etiology of breast and other cancers.

Kushi said he looks forward to having access to the research talent in UC Davis fellows, graduate students, residents and junior faculty. They can assist in the analysis of significant stores of data, including genetic information, to help answer important questions about cancer diagnosis, treatment, prevention and control.

Among Kushi's current research projects: an examination of lifestyle factors such as diet, physical activity and use of alternative therapies on risk of recurrence and survival in women who have had breast cancer; comparative effectiveness studies of genomic tests in colorectal cancer care and screening; and a cohort study of 444 girls to examine environmental and other predictors of early sexual maturation.

UC Davis researcher examines popularity of unproven mammography tool

In a study illustrating the potentially powerful influence of political pressure on medical practice, UC Davis physician-researcher Joshua Fenton found that use of a largely unproven mammography screening device has surged since Medicare began covering its cost.

Fenton, assistant professor in the UC Davis Department of Family and Community Medicine, with colleagues from the University of Washington and University of Minnesota, examined the use of computer-aided detection (CAD), a medical device designed to help radiologists interpret mammograms, since Congress mandated that Medicare pay for it 10 years ago.



Joshua Fenton

He found that the prevalence of CAD jumped from 5 percent in 2001 when Medicare began covering it, to 27 percent in 2003, the most recent year for which data was available. Extra mammography fees for CAD use cost Medicare an estimated \$19.5 million in 2003 alone. But actual costs are probably greater because the device has been associated with higher recall rates and greater use of diagnostic tests such as breast biopsy.

The increase in computer-aided detection use occurred even though "systemic reviews point to uncertainty regarding whether CAD has a clinically important impact on key breast cancer outcomes," Fenton wrote in a June issue of the *Archives of Internal Medicine*.

"This illustrates how industry and government interact to determine the course of health-care practice, and it's not really guided by science," Fenton said. "This is a case in which expensive technology gets widely adopted in clinical practice before it is proven effective."

Smoking during radiation therapy for head and neck cancer associated with poor outcomes

Smokers who don't quit before radiation therapy for throat, mouth and other head and neck cancers fair significantly worse than those who do, a UC Davis Cancer Center researcher has found.

Allen Chen, an assistant professor in the Department of Radiation Oncology at the UC Davis Cancer Center, found that head- and neck-cancer patients who continue to smoke during radiation therapy have poorer 5-year overall survival and higher rates of disease recurrence than those who quit smoking prior to treatment.

Chen's study, published online in the *International Journal of Radiation Oncology, Biology and Physics*, should help oncologists counsel patients about the benefits of quitting smoking after a diagnosis of head and neck cancer, says Chen, lead author of the study.

"I always tell patients, 'You should really stop smoking,' but I had no tangible evidence to use to convince them that they would be worse off if they continued to smoke," Chen says. "I wanted concrete data to see if smoking was detrimental in terms of curability, overall survival and tolerability of treatment. We showed continued tobacco smoking contributed to negative outcomes with regard to all of those."

The researchers found that 55 percent of patients who had quit smoking prior to treatment were still alive five years later, compared with 23 percent of those who continued to smoke. The poorer outcomes for persistent smokers were reported for both patients who had surgery prior to radiation therapy and patients who had radiation therapy alone.



Chen says additional research will be needed to explain these differences in outcomes for patients with head and neck cancers. One theory suggests that smoking deprives the body of much-needed oxygen. "Radiation therapy requires oxygenation for the production of free radicals, which attack cancer cells," he said.

Elisa Tong awarded grant to study Chinese-American smokers and nonsmokers

Elisa Tong, assistant professor of general internal medicine, has received an \$890,000 Research Scholar Grant from the American Cancer Society to conduct a novel smoking-cessation study focused on Chinese-American smokers and nonsmokers who live in the same residence.

Tong has begun targeting approximately 300 San Francisco households in which a smoker lives with a nonsmoker. She and her research team plan to educate participants about the dangers of tobacco-smoke exposure using information from scientific studies. They then will counsel the pairs about the benefits of living together in a smoke-free residence.



Elisa Tong

The Research Scholar Grants are designed to support studies in basic, preclinical, clinical and epidemiologic research to advance health. Tong's research aims to translate the known benefits of smoke-free policies and recommendations into actual clinical interventions to benefit smokers and nonsmokers. It also will encourage ongoing social support to establish smoke-free environments in the home.

"The Chinese may be particularly responsive to smoke-free messages when they are linked to certain social group norms," says Tong, whose previous tobacco-related studies include an analysis of smoke-free rules in the home and indoor work areas among Chinese- and Korean-American women. Tong is conducting similar work in the general English-speaking population with a study funded by the UC Davis Clinical and Translational Science Center.

Collaborators on the Research Scholar Grant include Debora Paterniti, associate adjunct professor of internal medicine and sociology; Chin-Shang Li, associate professor of biostatistics; and Janice Tsoh, associate adjunct professor of psychiatry at UC San Francisco. Community advisory groups for study assistance and dissemination include the San Francisco-based Chinese Council, Asian American Network for Cancer Awareness, Research and Training and the American Cancer Society's New York-based Asian Initiatives program.

Synthesis is published twice each year by UC Davis Cancer Center.

If you receive multiple copies of this publication, please share them. To add your name to the mailing list or change your address, please call (916) 734-9450.

Ralph deVere White
Director, UC Davis Cancer Center

EXECUTIVE EDITOR
Carole Gan

EDITOR
Dorsey Griffith

ART DIRECTOR
Jodi Adkins

GRAPHIC DESIGN
Page Design Group

PHOTOGRAPHERS
Robert Durell
José Luis Villegas
Keith Sutter

WRITERS
Ana Cotham
Anna Davison
Andy Fell
Dorsey Griffith
Pamela Martineau
Nora Steiner Mealy
Jenifer Warren
Kathleen Wong

UC DAVIS **CANCER CENTER**

The University of California does not discriminate on the basis of race, color, national origin, religion, sex, sexual orientation, disability, age, veteran's status, medical condition, ancestry or marital status. The University of California is an affirmative action/equal opportunity employer. Call (530) 752-2071 for more information. Speech or hearing impaired persons may call (530) 752-7320 (TDD).

**UC DAVIS
CANCER CENTER**

4501 X STREET
SACRAMENTO, CA
95817-2230

ADDRESS SERVICE
REQUESTED

NON-PROFIT ORG.
U.S. POSTAGE
PAID
UC DAVIS



Team Will, a group of cyclists from around the region, rode 3,400 miles from San Francisco to Kittyhawk, N.C. to raise funds and awareness for childhood cancer. At the outset of their cross-country adventure, the group stopped at UC Davis Cancer Center to visit with pediatric patients. The money raised went to the Foundation for Children with Cancer for financial assistance to families of children with cancer.

**UCDAVIS
CANCER CENTER**

Designated by the National Cancer Institute

www.ucdmc.ucdavis.edu/cancer

Synthesis

Synthesis – the art of bringing together distinct elements in a way that makes them whole – is a particularly relevant name for the magazine of UC Davis Cancer Center, which is distinct in its commitment to team science. Our research program unites clinical physicians, laboratory scientists, population specialists and public-health experts from throughout UC Davis and Lawrence Livermore National Laboratory with the goals of making cancer discoveries and delivering these advances to patients as quickly as possible. We are also dedicated to sharing our expertise throughout the region, eliminating cancer disparities and ensuring all Californians have access to high-quality cancer care. *Synthesis* – linking the best in cancer science toward the united goal of improving lives – is the name of our magazine, and our promise as your National Cancer Institute-designated cancer center.