SYNTHESIS

THE MAGAZINE OF **UC DAVIS CANCER CENTER**

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Miraculous gifts

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A custom fit for lung cancer treatment
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Leveling the playing field for Latinos
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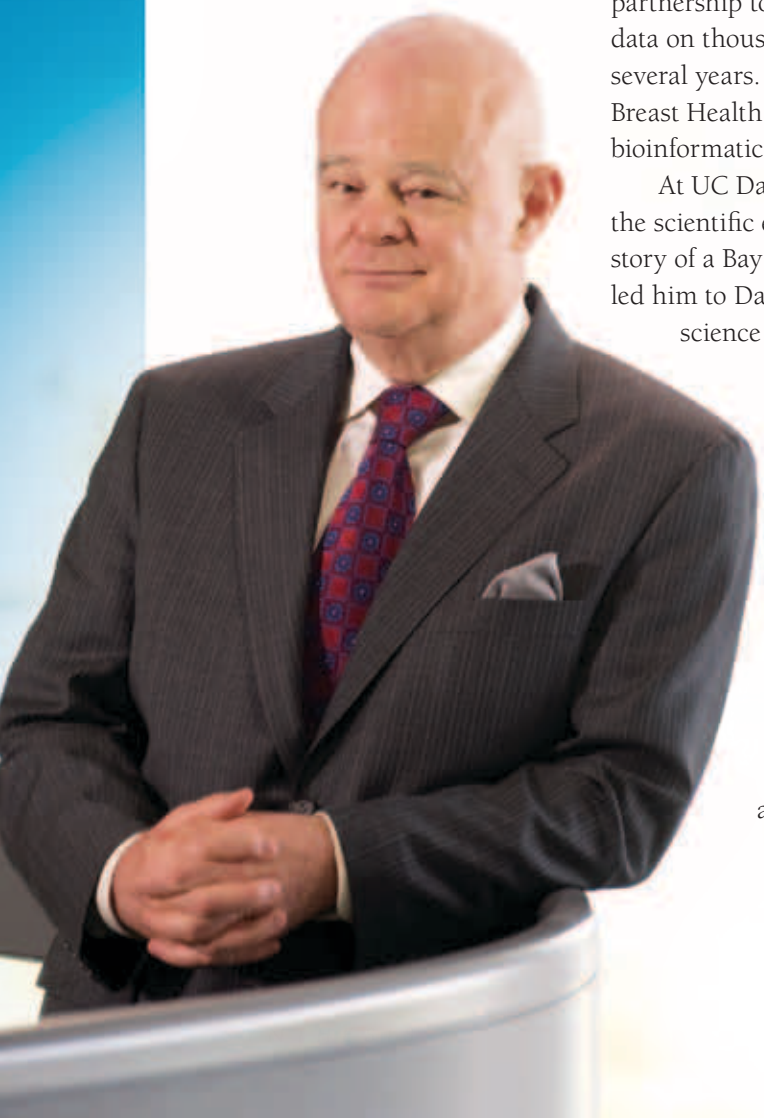

Dear Reader,

I am inspired by the ambitious goals set out by UC Davis Chancellor Linda Katehi, who wants to see our university move in just four years from 11th to fifth in the nation for research funding. At the UC Davis Cancer Center, we look forward to doing our part to reach this exciting milestone.

In these challenging economic times, we are moving in the right direction. By combining individual innovation with team science our researchers are making important advances against this vexing disease.

In this issue of *Synthesis*, we explore several of these, from basic laboratory work to discern and kill cancer stem cells to the creation of interactive software to help Latinos understand the importance of colorectal screening — and reduce disparities in colon cancer incidence among Latinos.

It is only when traditional barriers to collaboration are dismantled that scientific discovery can thrive. At UC Davis, we have forged a unique collaboration with the School of Veterinary Medicine that allows us to bridge the gap between animal and human medicine, particularly in the understanding and treatment of certain types of cancer. In this edition of *Synthesis*, you will read how a young veterinary oncologist, Michael Kent, is helping build that bridge.

Similarly, we have joined the other UC cancer centers in an unprecedented partnership to improve outcomes for women with breast cancer by collecting data on thousands of patients throughout the state and following them over several years. Our breast cancer program team will help lead the ATHENA Breast Health Network, contributing our cross-campus expertise in pathology, bioinformatics and biospecimen collection.

At UC Davis Cancer Center, patients benefit from and are participants in the scientific endeavors that improve care for all. We are excited to share the story of a Bay Area lung cancer doctor, whose own experience with the disease led him to David Gandara and Phillip Mack, UC Davis experts using team science to develop a personalized approach to lung cancer treatment.

Pregnancy is a major event in any woman's life. For patient Tracy Hartman, that good news was complicated by a cancer diagnosis. A team of UC Davis oncology experts have completed numerous studies on patients like Hartman, working to ensure that when cancer strikes during pregnancy both mother and baby are survivors.

UC Davis Cancer Center relies on other kinds of teams as well. Support from the Children's Miracle Network, which teams with researchers, has allowed our pediatric oncologists to make new discoveries in the treatment of childhood cancer.

We hope you enjoy this issue of *Synthesis* from the UC Davis Cancer Center, where we are breaking barriers and building bridges to beat cancer.

Ralph deVere White

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

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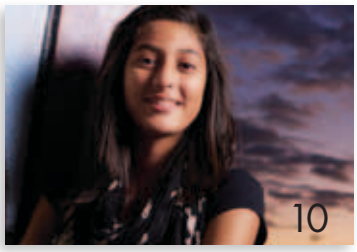

UC DAVIS CANCER CENTER

A National Cancer Institute-designated cancer center

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The other stem cells

Jian-Jian "JJ" Li

Finding, destroying cancer stem cells may lead to cures

Not too long ago, the idea that stem cells could give rise to tumors was only a theory. The hypothesis was that cancer stem cells had the unique ability to evade the lethal effects of radiation and chemotherapy because those treatments target rapidly dividing cells.

Cancer stem cells, however, could lay dormant, recur and spread, making the cancer difficult to cure. Today, mounting evidence supports that theory. UC Davis researchers are among those looking for cancer stem cells and working on ways to destroy them. Their work offers new hope for curing some of the deadliest forms of the disease, says Jan Nolta, director of the UC Davis Stem Cell Program.

"We now have clear evidence that some types of tumors arise from a stem cell that has gone awry," Nolta says. Scientists are starting to view cancer as a stem cell differentiation disease, she says. "Until we understand the nature of cancer stem cells, we can't stop the recurrence."

Since scientists discovered leukemia cancer stem cells in 1997, cancer stem cells have been found in brain, breast, colon, ovarian, pancreatic and prostate cancers.

Normal stem cells have the capacity to self-renew and differentiate into a number of cell types. Self-renewal means dividing into two daughter cells: one identical to itself and one that will differentiate into a specific tissue. With cancer stem cells, this process is not well understood, and normal differentiation may be blocked. Those that self-renew may be the cells that spread to different sites, a process called metastasis.

Nolta's lab acts as a clearinghouse for many UC Davis cancer researchers. She and her colleagues isolate stem cells from tumors and other tissue samples, providing them to different groups on campus. "These groups have state-of-the-art tools for asking the important questions about cancer stem cells that will one day let us wipe them out," she says.

"We think a lot of cancers come from **mutations in stem cells**, and bladder cancer is likely one of them."

~ Eric Kurzrock

Bladder cancer

The questions UC Davis researchers are asking depend on what type of cancer they are studying and how well its basic biology is understood. Eric Kurzrock is an associate professor of urology and pediatrics who treats children in the clinic and operating room, but studies bladder stem cells in the lab. He says that about 10 to 20 percent of bladder cancers are aggressive, possibly due to dormant bladder cancer stem cells that are able to evade otherwise effective treatment.

Kurzrock not only is searching for those cells, but also is studying human embryonic stem cells. He hopes to prod human embryonic stem cells into differentiating into the cells that line the bladder, called urothelial cells, because they are the ones that eventually become cancerous.

"Once we understand normal differentiation, then we can understand abnormal differentiation — which is the definition of cancer," says Kurzrock, one of a few researchers in the country looking for bladder cancer stem cells. "We think a lot of cancers come from mutations in stem cells, and bladder cancer is likely one of them."

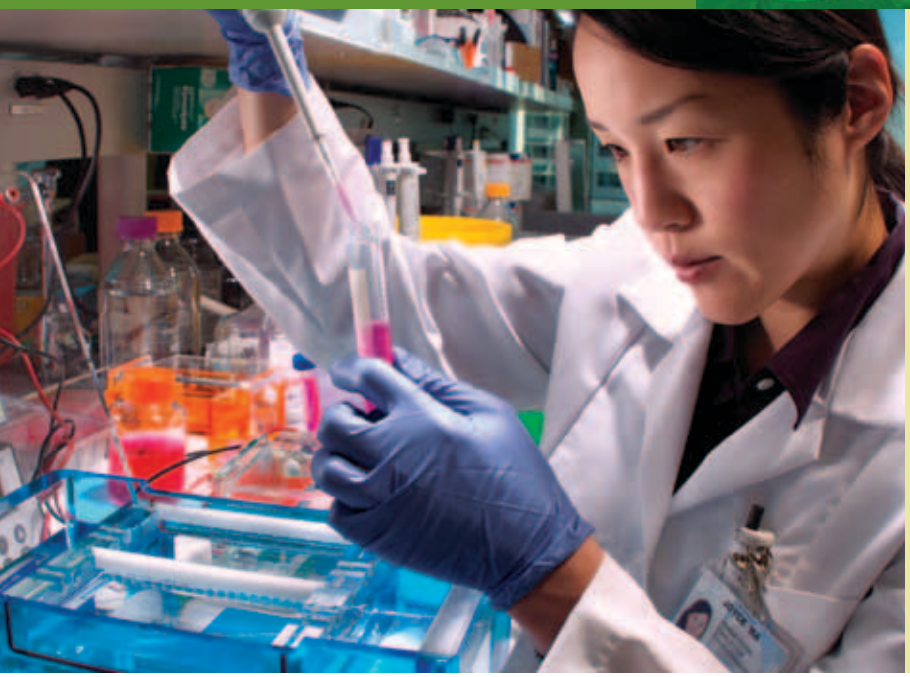
Brain cancer

Mutated stem cells are now thought to be behind one of the deadliest cancers, a form of brain cancer called glioblastoma multiforme. According to the National Cancer Institute, the five-year survival rate for glioblastoma is only 3 percent. Removal of the tumor in most cases does little to improve prognosis as the tumors readily grow again.

In 2007, a team of UC Davis researchers led by assistant professor of neurosurgery Rudolph Schrot was the first to identify the specific location of cancer stem cells within human brain tissues from a glioblastoma patient. Their findings were published in the *Journal of Neuro-Oncology*. Since then, Joyce Ma, an M.D.-Ph.D. student and co-author of the paper, has developed a new therapeutic agent that targets these brain cancer stem cells while sparing normal cells. She is working with Nolta to test the treatment in the lab.

"Chemotherapy and radiation cannot tell the difference between cancer cells and normal cells," Ma

Building on basics>>



Joyce Ma, an M.D.–Ph.D. student, has developed **a new therapeutic agent** that **targets brain cancer stem cells** while **sparing normal cells**. She is working with leading stem cell experts to test the treatment in the lab.

explains. "Our therapeutic agent seeks out cancer stem cells and causes them to die in a way that doesn't injure the surrounding tissue." Ma hopes to prevent tumor recurrence while reducing the side effects associated with current cancer treatments.

Breast cancer

Scientists discovered breast cancer stem cells in invasive cancer in 2003. UC Davis professor of radiation oncology Jian-Jian "JJ" Li is working to understand how invasive breast cancer stem cells become resistant to radiation therapy.

"We are the first to show that breast cancer cells that are initially susceptible to radiation undergo changes during treatment so that they become resistant to treatment," explains Li, who also is director of translational research for the Department of Radiation Oncology.

Li's work focuses on a particular kind of invasive cancer called HER2-negative breast cancer. HER2 stands for human epidermal growth factor receptor-2. Approximately 15 to 20 percent of breast cancer tumors test positive for this cell-surface protein. It is associated with increased disease recurrence and worse prognoses, and is treated with a drug (trastuzumab, marketed as Herceptin) that targets those cells.

Li's work showed that HER2-negative breast cancers can become HER2-positive during radiation treatment. He is focused on targeting these radiotherapy-resistant cells. "If we can do that, we can tremendously improve the efficacy of breast cancer treatment," he says.

Cells that cause invasive breast cancer in humans most likely arise as precancerous stem cells found in milk ducts, a team led by Alexander Borowsky reported in *Breast Cancer Research* last year. "Our work shows that programmed cancer stem cells are already present at the earliest stage of breast cancer," says Borowsky, an associate professor of pathology and laboratory medicine, who holds a joint appointment at the UC Davis Center for Comparative Medicine.

This early form of breast cancer is called DCIS, or ductal carcinoma in situ. In DCIS, abnormal cells multiply and form a growth within a milk duct of the breast. DCIS is noninvasive and is usually easily treated with breast-conserving surgery and radiation. If it is not completely treated, however, it may give rise to potentially lethal invasive breast cancer, which infiltrates surrounding breast tissue and can metastasize to other parts of the body.

Borowsky did his work in mice, first by developing the mouse model of human DCIS. The mice reveal that breast cancer outcomes can be programmed in the pre-cancer stem cells. He is now working to use breast

Cells that cause **invasive breast cancer** in humans most likely arise **as precancerous stem cells** found in **milk ducts**.

cancer stem cells collected from DCIS biopsies as diagnostic tools to predict cancer behavior and eventually to tailor therapies to improve patient outcomes.

"Detection of DCIS by improved imaging technology is rapidly increasing," he says. "Some of these women whose breast cancer is caught in this earliest stage may be better treated with drug or hormonal therapy, whereas others may need more aggressive surgical and radiation treatment."

Leukemia

Leukemia cancer stem cells were the first cells to be studied, yet the science to target them is almost futuristic in nature. Chong-Xian Pan and his colleagues are developing tiny guided missiles that seek out and destroy leukemia stem cells. The work involves creating ligands, which are molecules that recognize and bind to proteins on leukemia stem cells. These ligands are attached to nanoparticles, man-made objects tiny enough to enter a cell, carrying lethal chemotherapy drugs.

"Inside the nanoparticles we can load chemotherapy drugs, allowing us to deliver high concentrations of the drugs directly to the cancer stem cells," Pan says. Researchers already know these drugs work and, at the highest doses, they work even better. Those high doses, however, are quite toxic to patients.

"These nanoparticles will allow us to use those high doses on just the cancer stem cells, sparing the patient of severe side effects and eliminating the cancer." Pan and his colleagues are testing these therapies on animal models and human leukemia cancer cells in culture.

Pan believes most researchers no longer question the existence of cancer stem cells. "We think cancer stem cells are possibly a universal phenomenon for most cancer types," he says.

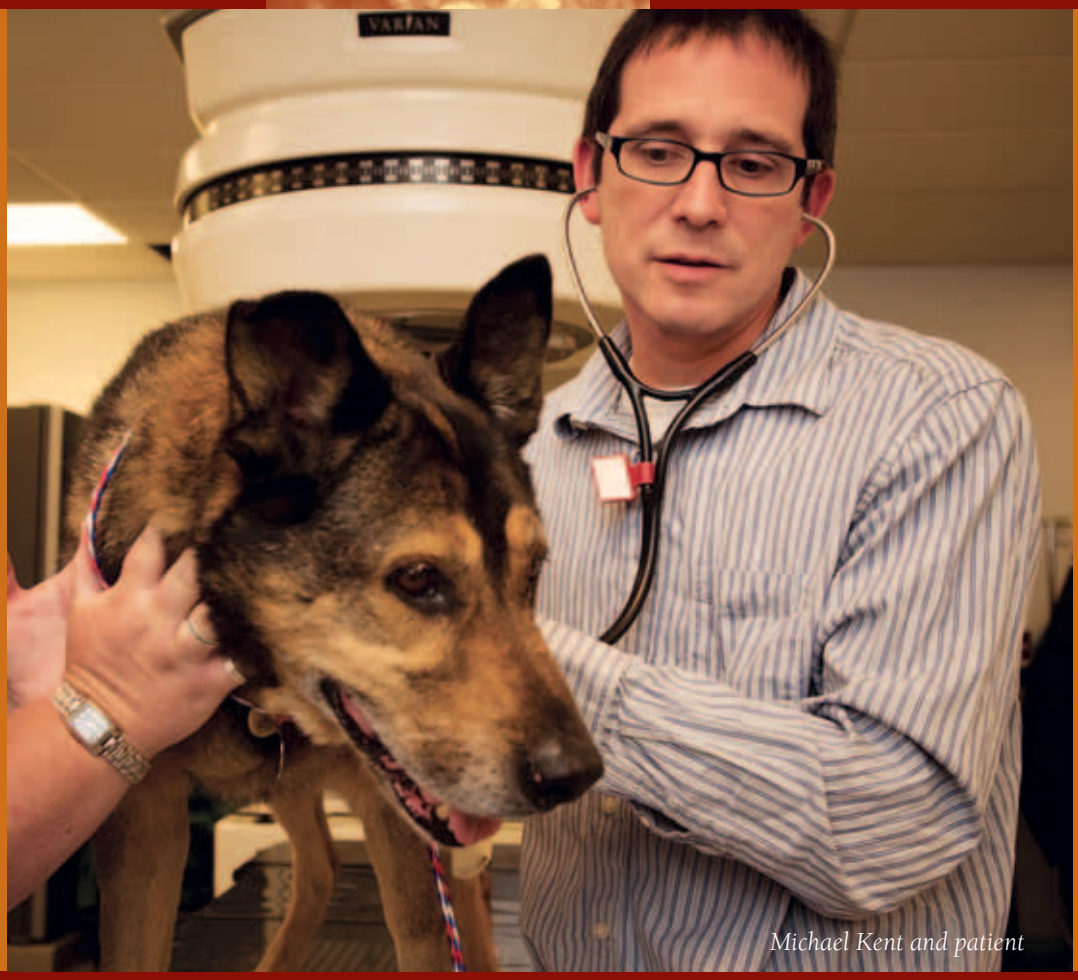
Definition debate

Controversy remains, however, on how to define them. According to Borowsky, a cancer stem cell must have the self-renewal and differentiation properties of normal stem cells and the ability to reconstitute a cancer when transplanted from one animal to another in the lab. Some researchers are using markers found on other cancer stem cells for identification purposes, but only animal transplant studies offer definitive proof.

"Markers are only surrogates," Borowsky says, adding that it's more likely that some cancers would have stem cells with a different array of markers, as he has found in mice. "I think it's safe to say that defining the markers still remains a challenge."

Still, Borowsky says, the effectiveness of new cancer therapies will be measured by how well they kill stem cells. "All treatments probably affect cancer stem cells to some extent, but identifying the rate of cancer stem cell death is going to be an important thing to know."

Jan Nolta's lab acts as a clearing-house **for many UC Davis cancer researchers**. She and her colleagues **isolate stem cells from tumors** and other tissue samples, providing them to different research groups on campus.



Michael Kent and patient

Man's best friend, and then some

Collaboration bridges gap in animal-human medicine

Outside the UC Davis Center for Companion Animal Health lies a memorial walk honoring beloved dogs and cats that have battled cancer under the care of veterinarians at the state-of-the-art pet hospital. One inlaid brick dedicated to Marley by his owner, Kirk Fornoff, reads: **"At first they need us, and then we need them."**

"Dr. Kent is highly competent by himself, but he also possesses the **interpersonal skills** and **willingness to work with people** of other backgrounds and disciplines to **form new teams** that will advance science a lot faster than it otherwise would."

~ Fred Meyers

The affectionate pit bull terrier had succumbed to an aggressive form of lymphoma, one of several cancer types shared by dogs and humans. Fornoff's words fittingly describe the sentiment among a team of UC Davis clinicians who believe our four-legged companions deserve the best available care, and also champion the idea that advances in cancer treatment for pets will ultimately benefit human patients, as well.

The roots of this homegrown, progressive approach toward translational medicine were laid down by the collaborative environment fostered between two of UC Davis' renowned resources – its National Cancer Institute-designated cancer center and the School of Veterinary Medicine. It was this strong interdisciplinary culture that allowed Michael Kent, an expert in radiation and medical oncology at the Center for Companion Animal Health, to put that sentiment into practice.

"I think that dogs can become a more important model in trying to unlock different treatments and cures for cancer," says Kent. "We're hoping that by using the dog as a model first, we're able to come up with more rational therapeutic trials that can then go on to people."

Spontaneous tumors that arise in pets mimic human cancers much more closely than the transplanted human tumors typically studied in laboratory mice. With a more natural and genetically similar model to follow, Kent argues, potential breakthrough therapies backed by pets are then more likely to work in people.

A practicing veterinarian at UC Davis since 1999, Kent completed the Mentored Clinical Research Training Program a few years ago through the Clinical Translational Science Center. The National Institutes of Health-supported initiative was designed to foster innovative and collaborative research across the UC Davis campus. There, he picked up the skills he needed to translate the most promising research from the bench-top to his patients' "cage side" through clinical trials. But he could not do it alone.

"We try to nurture the skills, attitudes and behaviors that promote team science," says program director Fred Meyers, executive associate dean of the UC Davis School of Medicine. "The major advances in cancer research have really happened because of people working collaboratively, but it's been a relatively rare occurrence, and we're trying to accelerate that."

Meyers says Kent was one of the program's star pupils embodying the principles for successfully bridging the gap between animal and human medicine.

"Dr. Kent is highly competent by himself, but he also possesses the interpersonal skills and willingness to work with people of other backgrounds and disciplines to form new teams that will advance science a lot faster than it otherwise would," he adds.

During his training, Kent connected with several UC Davis Cancer Center clinicians over shared research interests. One of the budding relationships was with

professor and Chief of Hematology and Oncology Kit Lam, an expert in targeted drug therapies for cancer.

Kent is now bringing a novel drug delivery approach developed by Lam to canine patients suffering from lymphoma, an often lethal cancer in pets for which chemotherapy is the preferred, life-extending treatment.

Lam and his group have packaged chemotherapeutic drugs into nanoparticles that can easily pass through the leaky blood vessels that nourish many solid tumors to deliver a powerful, toxic blow.

Lam and his group have packaged chemotherapeutic **drugs** into nanoparticles that can **easily pass** through the **leaky blood vessels** that nourish many solid tumors to **deliver a powerful, toxic blow**.

"You can potentially increase the amount of drug delivered to the tumor site and less to normal organs," Lam says, adding that the treatment can be tailored to deliver other drugs for many cancer types. "In that way, the drug will be more effective and there will be fewer side effects."

Kent and his colleagues at the Center for Companion Animal Health have just closed their first clinical trial in dogs using a nanoparticle formulation of paclitaxel, a drug used to treat lung, ovarian and breast cancer in humans. While their main goal was to identify safe guidelines for delivering the new therapeutic agent, Kent believes the project shows a lot of promise in benefiting his patients.

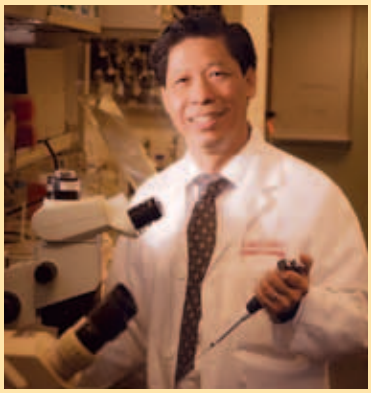
"For dogs, we've never actually been able to use paclitaxel before because they often get allergic reactions," he said. "In this new formulation, we may have found a less toxic form of the drug."

Kent looks forward to starting the next run of clinical testing, this time with an enhanced concoction of the nanoparticle vehicle coated with a peptide — named by Lam "LLP2A" — that singles out and binds specifically to the surface of both human and canine lymphoma cells rather than healthy ones.

"These canine trials will provide a basis for helping decide if this is worth going on to human trials," Kent adds.

Ralph deVere White, director of the UC Davis Cancer Center and a urology professor, says that Kent's work is especially valuable in an environment where working both as a clinician and researcher is a very demanding challenge.

"We are very lucky that Michael possesses both qualities," he says. "However, in Michael's case his work benefits both his patients and our patients. We hope our work will equally benefit his patients and keep our four-legged companions safe."



"Michael is a **wonderful collaborator**. The companion dog with cancer is an excellent model for human cancer. The result of this study will provide **crucial data** for the development of this drug in humans."

~Kit Lam

While **genetic similarities** between the two species are evident, Kent and other researchers are finding that **many of the important pathways** that are mutated or changed in **human cancers are similarly altered in dog cancers**.

Along with veterinary radiologists Allison Zwingenberger and Erik Wisner, Kent also has started using the targeting agent LLP2A to image and locate lymphomas in dogs. If proven successful, doctors could use the approach to improve tumor staging and devise better customized treatments for their patients.

Kent's own research strongly reflects his view that spontaneous cancers in dogs offer an excellent model for studying human cancers and devising improved, safer treatments that will benefit both. While genetic similarities between the two species are evident, Kent and other researchers are finding that many of the important pathways that are mutated or changed in human cancers—such as the p53 tumor suppressor—are similarly altered in dog cancers.

Kent recently found that a common cancer survival pathway in humans also is activated in canine osteosarcoma and melanoma. Drugs called mTOR inhibitors that target this pathway have gained traction through clinical trials in the past few years as promising treatments for human sarcomas. As part of the NCI-headed Comparative Oncology Trials Consortium, Kent helped UC Davis complete one of the first nationwide clinical trials to deliver mTOR inhibitors in dogs with osteosarcoma. He is now looking at the drug's efficacy for treating melanoma and as a potential agent for sensitizing canine tumors to radiation therapy.

With deVere White and his colleagues, Kent has started a new project to compare molecular signatures in an invasive form of bladder cancer that is hard to detect in dogs and difficult to treat in both dogs and humans.

DeVere White explains that standard therapy for patients with cancer that has invaded the bladder wall muscle is chemotherapy followed by bladder removal. "The problem is that only 50 percent of patients benefit from the chemotherapy, and we cannot tell prior to administering the chemotherapy which patient will or will not benefit," he says.

The hope is that before chemotherapy treatment, tumors can be removed and genetically analyzed to distinguish the responders from the non-responders.

"It seems like the course of this disease can be very similar between dogs and people," says Kent, "so if we can find a good model for the disease, my patients can benefit, and then hopefully down the road people can benefit, too."

Miraculous gifts

Children's philanthropy supports pediatric patients, inspires research

Nina Garcia can't hold back tears as she recounts what happened the day Yaya, her 10-year-old daughter, was taken by ambulance to UC Davis Children's Hospital.

The Woodland fifth grader had been feeling sick on and off for almost a month. Thinking it was growing pains, her mother had kept Yaya comfortable with Tylenol, but her temperature had reached 104.3 degrees.

"The doctors didn't have any answers at first – they just knew something was wrong," Garcia recalls of that day in March 2007. After doctors had run a series of tests, Garcia spotted a note on Yaya's chart about leukemia. The next day, the diagnosis was confirmed: acute lymphoblastic leukemia, a common and fast-growing cancer of the white blood cells.

"It was almost like it wasn't real," Garcia says. "I didn't know what would be ahead of us."

What lay ahead was two and a half years of cancer treatment for Yaya provided by a pediatric cancer team at UC Davis Children's Hospital, a group that included a "child-life specialist" to help guide Yaya through her ordeal.

The contributions of child-life specialist Amber Hall were made possible with a grant from the Children's Miracle Network, a philanthropy with a mission to improve the health and well-being of hospitalized children by supporting patient care, research and education for patients, providers and the public.

UC Davis Children's Hospital is one of nine Children's Miracle Network hospitals in California. The organization adds needed funds to power the arsenal of hope that inspires researchers at UC Davis to find new and better cancer treatments for children such as Yaya.

It also supports an extraordinary variety of programs that make UC Davis a key resource in Northern California for young cancer patients. At UC Davis Cancer Center, pediatric hematology and oncology physicians diagnose and treat more than 400 children with all types of malignancies, including leukemia, every year.

After completing several rounds of chemotherapy, Yaya is now cancer

Yaya Garcia underwent several rounds of chemotherapy, her supportive family and friends at her side.

Yaya and Nina Garcia

free and thriving at school with her peers.

Nina Garcia says the people at Children's Hospital were so friendly, they seemed like family. "Any time we had questions we got answers, and if I had doubts, the staff would give me peace of mind," she says. "I can't tell you how much that helped out."

The Cancer Center has used CMN funding to staff pediatric art therapy programs for young cancer patients as well as for the child-life specialists who teach children coping strategies before and during treatment procedures.

Hall, the specialist who worked with Yaya, helped ease her anxiety during her leukemia treatment, which included lumbar punctures and bone marrow aspiration.

"Every time Yaya had a procedure, Amber would help Yaya deal with her emotions," Garcia recalls. "Yaya might hold things in and say everything was okay, and Amber would help her express what she was feeling."

Yaya's diagnosis was devastating for the Garcia family, but fortunately her disease was very curable, Hall says. "They've shown by their example that no matter the tragedy of a dreadful illness, you can battle emotionally and spiritually through it and beat the cancer."

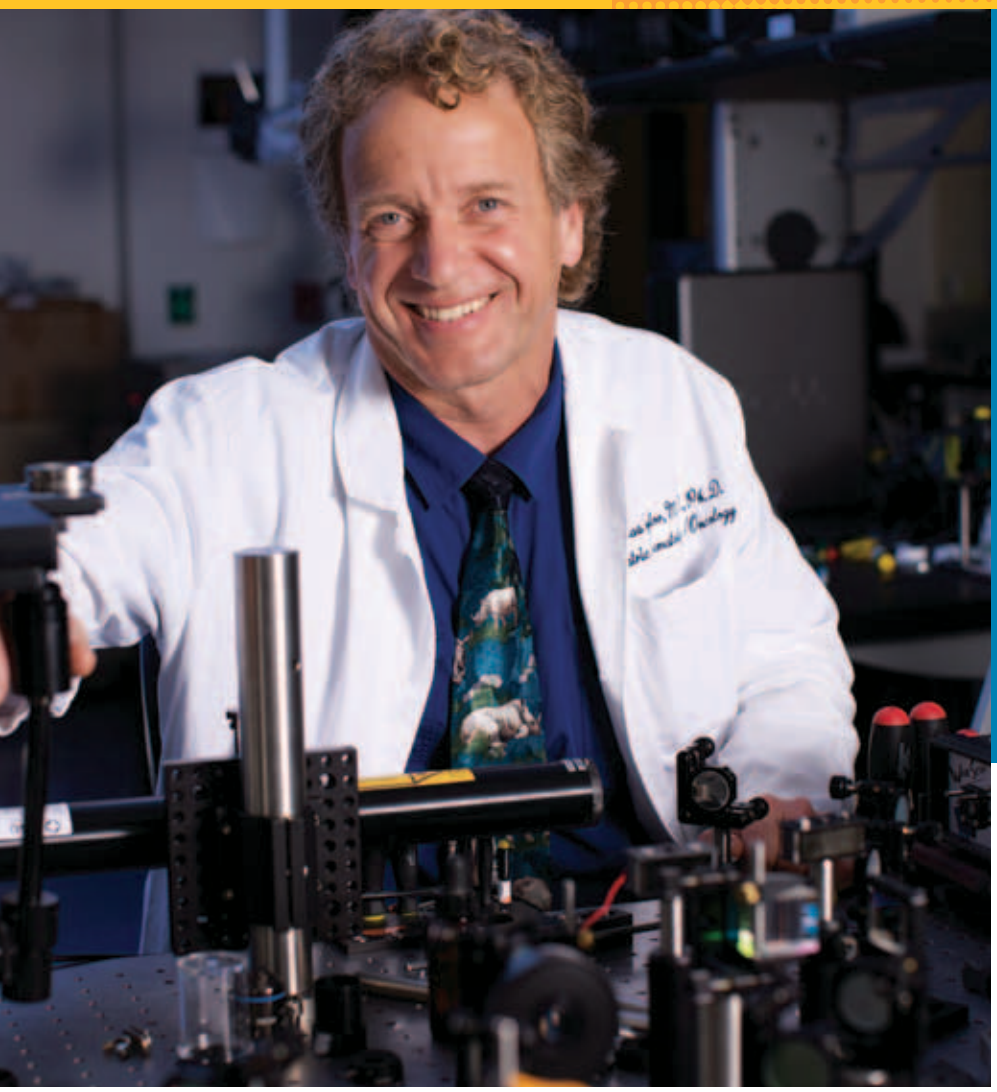
Hall says her young patient possesses "a beautiful, vibrant personality" and left a lasting impression. "I was invited into her life," she says, "but I was the one who was touched by having the opportunity to work with her."

Children's Miracle Network also supports research.

One beneficiary is Douglas Taylor,

"Any time we had questions **we got answers**, and if I had doubts, the **staff would give me peace of mind**. I can't tell you how much that helped out."

~ Nina Garcia



In a laboratory near UC Davis Cancer Center, Taylor and physicists Thomas Huser and James Chan are working to develop a **quick and reliable diagnostic** technique to **identify cancer types**.

director of the Pediatric Stem Cell Transplant Program and an associate professor of pediatrics, who has won grants totaling $200,000 to investigate novel tools for identifying and analyzing cancer cells.

In a laboratory near UC Davis Cancer Center, Taylor and physicists Thomas Huser and James Chan are working to develop a quick and reliable diagnostic technique to identify cancer types. The technique utilizes Raman spectroscopy, a laser-based approach that allows scientists to identify cell and tissue type by characterizing biological molecules within a cell, or tissue samples. Raman spectroscopy overcomes many limitations of current technologies used to detect, identify, quantify and sort both normal and cancer cells. Taylor hopes his research eventually will help doctors diagnose cancer using less invasive methods, choose the most suitable drug for a particular cancer and quickly assess the effectiveness of treatment.

Because the key ingredients for a dynamic research program in pediatric cancer at UC Davis are well within reach, CMN also has granted $430,000 to support an endowed chair in pediatric cancer, which would fuel recruitment of a dedicated physician-researcher to lead pediatric cancer research at UC Davis.

"The all-encompassing care required to look after pediatric cancer patients and their families makes finding time for research very difficult for our pediatric oncology colleagues," said cancer center director Ralph deVere White. "That they are able to accomplish both speaks greatly to their dedication. It also speaks to the support that they have received from CMN, and to the organization's generous commitment toward the recruitment of a dedicated pediatric cancer researcher."

The endowment is critically important for the future of the cancer center, which hopes to bring its pediatric program under the roof of an expanded cancer center facility within the next few years. UC Davis pediatric oncologists now see more than 50 newly diagnosed children each year, and their clinics log in excess of 2,500 patient visits.

For the Garcia family, visits to the cancer center are far less frequent these days. Now 13, she wears her newly regrown hair to her shoulders, and is an unabashed fan of pop music stars Rhianna and Beyonce.

"I'm glad to be back in school with everyone," she says. "My energy

is good, but sometimes I still get tired. This year I want to play soccer again really bad. I'm going to try out for the team in February."

And although Yaya focuses on her future, she hasn't forgotten her experience as a cancer patient. She is helping organize a holiday bake sale and crafts sale to raise funds for the family of another child she met during her chemotherapy treatment, who recently passed away.

It's part of giving back, said Garcia, grateful for the return of the color to her daughter's cheeks. "The main thing is we have her here with us," she says. "You don't know until you face something like this that there are hundreds of people out there who are willing to lend a hand when you are in need."

"You don't know until you face something like this that there are **hundreds of people** out there who are **willing to lend a hand** when you are in need."

~ Nina Garcia

Children's Miracle Network: Helping children for 26 years

Children's Miracle Network (CMN) is an international non-profit organization dedicated to saving and improving the lives of children by raising funds for children's hospitals across North America since 1983.

UC Davis Children's Hospital was **one of the first 22 hospitals** to join the CMN team, making it the exclusive CMN hospital serving children in our community.

Today, CMN hospitals treat **17 million children each year** for every disease and injury imaginable. CMN hospitals provide state-of-the-art medical care, life-saving research and preventative education for children 24 hours a day, 365 days a year.

Through its year-round efforts to help hospitalized kids, CMN has raised more than $3.4 billion to date, most of which is donated a dollar or two at a time by caring individuals across North America. CMN's founding pledge to keep **100 percent of donations in the area in which they were raised** and to put children first in all it does remains at the core of its philosophy.

Keeping with the CMN tradition, all funds raised locally benefit the sick and injured children who visit UC Davis Children's Hospital, which is the Sacramento region's only comprehensive hospital for children. From primary care offices to specialty and intensive care clinics, pediatric experts provide compassionate care to more than 100,000 children each year and conduct research on causes and improved treatments for conditions such as autism, asthma, obesity, birth defects and cancer.

Children's Miracle Network®

Survival, times two

When cancer strikes during pregnancy, improving the odds demands teamwork

Only six weeks after discovering she was pregnant with her second child, a doctor gave Tracy Hartman more big news.

"I could just tell from the look in her eyes that something was wrong," she recalls.

Hartman had cervical cancer, a diagnosis that in many cases demands a radical hysterectomy, chemotherapy and radiation treatment.

"My first thought was, what about the baby?" she says.

From that moment forward, Hartman's hope for an uneventful pregnancy became an ongoing struggle to decide how best to improve the chances both for herself – and her growing fetus.

Radiation treatment is not recommended during pregnancy, and some chemotherapy drugs may harm a fetus. Chemotherapy treatment

A study based on data from the California Cancer Registry found about **one in a thousand women** have cancer when they give birth, and most **don't know** it until **after they've delivered**, says Lloyd Smith, an author of the study and chair of obstetrics and gynecology at UC Davis.

during pregnancy also can result in low birth weight and increase the risk of the child developing cancer. Anesthesia required for surgery can increase the chance of premature birth, and in some cases surgery can effectively terminate a pregnancy altogether.

Fortunately, Hartman's agonizing scenario is rare. A study based on data from the California Cancer Registry found about one in a thousand women have cancer when they give birth, and most don't know it until after they've delivered, says Lloyd Smith, an author of the study and chair of obstetrics and gynecology at UC Davis.

"They're very complex and challenging cases," Smith says, "for both the doctors and the patient."

Pregnant women aren't any more likely to get cancer than others their age, and the malignancies most common in mothers-to-be — cancers of the breast, thyroid and cervix, melanoma and Hodgkin's disease — tend to be the most common cancers among young women.

Gary Leiserowitz, a specialist in gynecologic oncology at UC Davis, puts it this way: "Pregnancy happens to women who also sometimes get cancer."

And when it does, malignancies can be missed because pregnancy may obscure the diagnosis. Leiserowitz says that's because some symptoms of cancer, such as rectal bleeding, also are common during pregnancy.

Or doctors may miss signs of cancer for other reasons. "Doctors don't want to believe that a pregnant woman may have a life-threatening malignancy, and they often overlook symptoms or findings that they should be following up on," says Smith. "Doctors don't want to think about cancer in a young woman who's pregnant."

As pregnant women with cancer go, Hartman was lucky. Symptoms surfaced even before she knew she was pregnant. After two abnormal Pap smears, a vaginal ultrasound and two biopsies, she learned she had an early-stage cervical cancer. Exams uncovered a golf ball-sized lesion covering her cervix, which raised concerns about spread to her lymph nodes.

Hartman was being seen by doctors in San Ramon, who recommended she undergo a radical hysterectomy — an option that would have given Hartman the best chance for a cure, but would have ended the pregnancy.

"If I hadn't been pregnant, it would have been a pretty easy decision," says Hartman, who now lives in El Dorado Hills. "But I really wanted to do whatever I could to have the child."

To better understand the risks and options for women like Hartman, UC Davis researchers have carried out a series of studies in recent years on cancer in mothers-to-be. They've looked at breast, thyroid, cervical,

ovarian and colorectal cancers, as well as melanoma, gathering data about when pregnancy-associated cancer is diagnosed and how patients fare.

What they've learned is that there are a lot of options for effectively fighting cancer in a pregnant woman without harming her baby, and that such cases require a multidisciplinary approach, with input from high-risk pregnancy and cancer specialists.

The best way to treat cancer diagnosed during pregnancy depends on the kind of cancer, how advanced it is, and how far along the patient is in her pregnancy, says Anne Rodriguez, a specialist in gynecologic oncology at UC Davis.

"It's really important that a pregnant woman in this situation does not make the decision to terminate because she thinks she can't have treatment. She may be able to," Rodriguez says, adding, however, that some women do choose to end a pregnancy in order to maximize their options for treatment, and increase their chance of survival.

If the disease is not very advanced, it may be possible to postpone treatment without affecting the mother's prognosis – either until she gives birth at the end of a full-term pregnancy, or until the baby is old enough to survive a planned early delivery that will allow the mother to begin treatment as soon as possible.

Pregnant women also can undergo surgery with little risk to the fetus, Rodriguez says, ideally early in the second trimester to minimize risks associated with anesthesia.

Hartman decided against a radical hysterectomy, instead opting for a lymphadenectomy – surgical removal of lymph nodes suspected of being cancerous.

The young mother knew going into surgery that her now 3½-month-old fetus still could be in jeopardy. "The oncologist asked me, 'If we find a lot of positive lymph nodes, do I have permission to go ahead with the complete hysterectomy?'"

"I said, 'I really want this baby.' She said, 'We'll do the best we can.'"

When she awoke from surgery, Hartman searched frantically for a nurse to ask if she was still pregnant. Indeed, she was.

Back home, and with an eight-inch abdominal incision, Hartman again was faced with life-and-death decisions, after her doctor called to say that two of the nodes removed were positive for cancer. Again, the oncologist recommended the hysterectomy – and said it should be done quickly.

"They're very **complex** and **challenging** cases, for both the doctors and the patient."

~ Lloyd Smith

After a night of intense prayer, Hartman told her doctor she would not have a procedure that would end the pregnancy. Her husband, Tom, supported the decision. Instead, she agreed to undergo chemotherapy treatment, and to have an early, planned surgical delivery.

Some chemotherapeutic drugs can be used in expectant women, although the timing is important.

"Generally we don't give anything during the first trimester," says Helen Chew, who heads the clinical breast cancer program at UC Davis. The first three months of pregnancy are crucial to the development of a baby's organs, and women are advised to steer clear of even common, over-the-counter medications, Chew says.

Hartman had three courses of chemotherapy later in her second trimester, and took steroids because of concerns that the baby might not be growing adequately.

Doctors had warned Hartman that her newborn might be small, because of everything she'd gone through. Just before the planned delivery, tests revealed that her baby's lungs weren't sufficiently developed, so they waited a few more weeks.

Morgan arrived a healthy 6 pounds by Caesarean section, nearly at term, in a room crowded with some 25 doctors, nurses and technicians. In addition to the delivery, doctors took out her cervix and uterus and repaired a hernia. Because she was only 35 years old, they spared her ovaries. Six weeks later, Hartman had more chemotherapy

"If I hadn't been pregnant, it would have been a pretty easy decision. But I really wanted to do whatever I could to have the child."

~ Tracy Hartman

and also radiation treatments.

The prognosis for women like Hartman who have cancer while pregnant is the subject of considerable debate, and research findings vary in terms of how well pregnant women fare compared with cancer patients who aren't expecting.

One UC Davis study on breast cancer found that women who had the disease when they were pregnant were slightly more likely to die of it than women who weren't pregnant, and not only because pregnant patients tended to have more advanced disease at diagnosis — another of the study's findings.

"That is an interesting finding," says Leiserowitz. "However, most studies on cancer in pregnancy show that a patient's prognosis is usually dependent on the stage of the cancer and the response to treatment."

Hartman, who now sees UC Davis gynecological oncologist John Dalrymple for follow-up care, is in remission, and free to focus on raising her children.

Morgan is now 8. She has long known that her Mom had been sick when she was a baby. But it was only recently, after the family participated in a bike ride to raise money for pediatric cancer research, that Hartman revealed to Morgan that it had been cancer.

"We both teared up," Hartman says. "She said, 'Mommy, could you have died?' I said, 'What kept me going was that I really wanted you. I wanted you so badly.'"

Faced with the same situation today, Hartman says, she'd do it again. "I can't imagine my life without her."

A custom fit for lung cancer treatment

Bay Area physician, patient chooses UC Davis care

Fred Marcus

Fred Marcus knew exactly what to do when he was diagnosed with lung cancer.

That's because the 62-year-old physician had been treating patients with the disease in his Silicon Valley practice for nearly 30 years.

"It was a surreal experience," says Marcus, who lives in the town of Nipomo, about 25 miles south of San Luis Obispo. "I never smoked, and I had never been sick."

First, Marcus had his tumor analyzed at the genetic level. Then he turned to UC Davis Cancer Center's David Gandara for treatment.

"I have known David Gandara professionally for many years," says Marcus, who was diagnosed in 2006. "He's also the best lung cancer doctor in our area."

Gandara is associate director of clinical research and director of the center's Thoracic Oncology Program, and an international leader in the treatment of lung cancer.

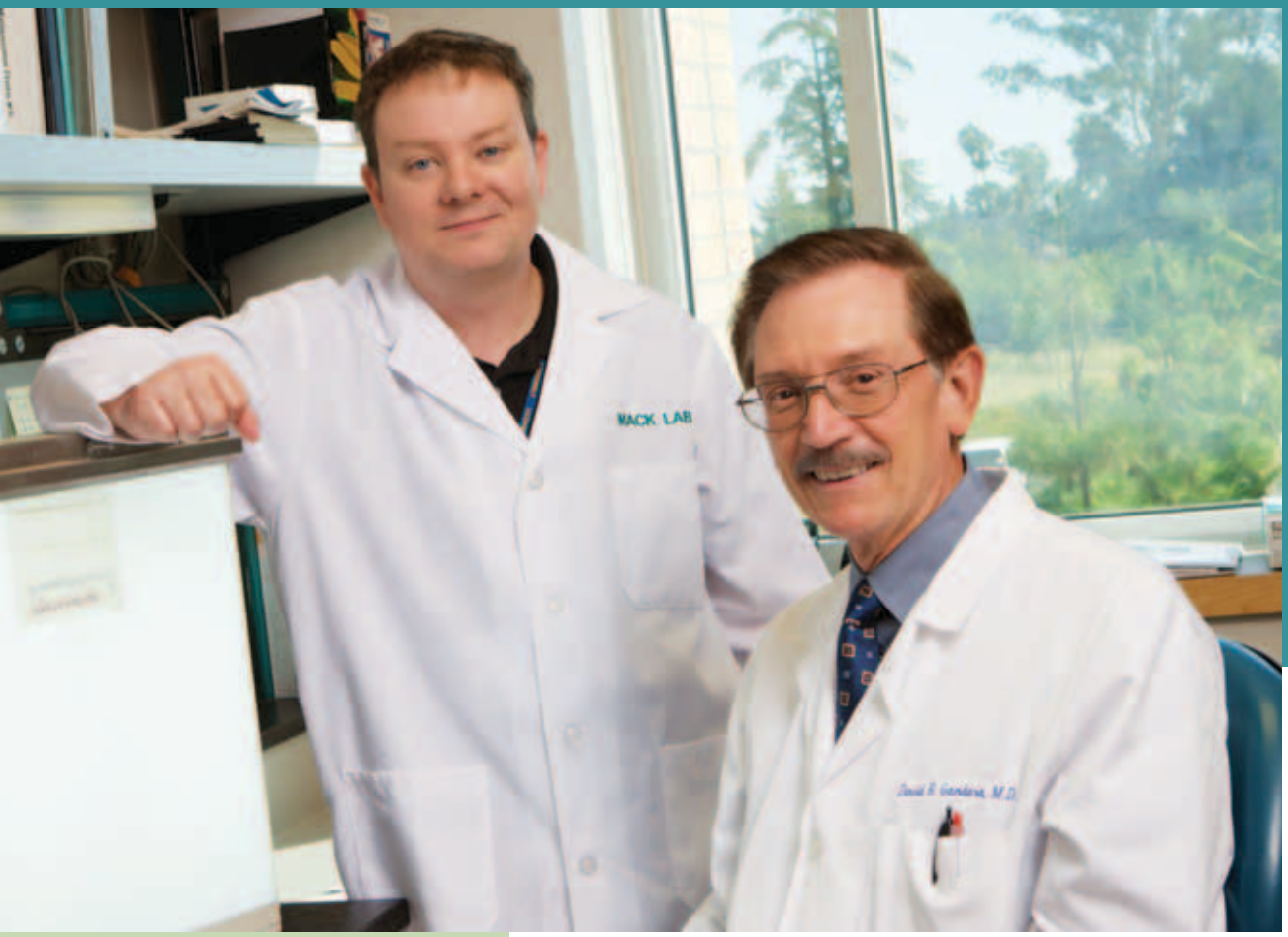
Marcus knew that Gandara and his colleagues could provide personalized treatment for lung cancer, care he could find only at a National Cancer Institute-designated Cancer Center like UC Davis.

In treating all of his patients, Gandara takes into account a host of factors such as age, gender and stage of disease, which oncologists have relied upon for years. But he also evaluates the patient's genetic makeup to select chemotherapy drugs that will have the fewest side effects. And he conducts genetic tests of the tumor to determine which therapies most likely will kill the cancer.

This integrated approach has worked for Marcus, who continues to benefit from Gandara's efforts to optimize his treatment regimen. "There is no question in my mind that this personalized approach is the answer," Marcus says.

Gandara agrees. "Personalized medicine is having a profound impact on the way physicians approach making the best treatment choices for their patients with lung cancer," says Gandara, who also is a UC Davis professor of medicine.

Marcus knew that Gandara and his colleagues could provide **personalized treatment** for lung cancer, **care he could find only** at a National Cancer Institute-designated Cancer Center like UC Davis.



LEFT TO RIGHT:
Phil Mack and David Gandara

Gandara is on a mission to **educate fellow physicians** about the importance of **personalized treatment** for lung cancer and the availability of **diagnostic tests** that make it possible.

Gandara likes to use a shopping analogy to describe how personalized cancer therapy will work. "It is becoming increasingly apparent that one size does not fit all when it comes to cancer therapy. Instead of buying your new clothes off the rack, the tailor – the oncologist – will be able to custom-fit your selection."

Even before his treatment, Marcus encouraged colleagues in his practice and in the oncology community to use the personalized approach. "I was doing the cutting-edge genomic testing before it was very popular," he recalls.

Gandara says Marcus is an exception among lung cancer physicians, many of whom do not realize how important genetic differences are in how our bodies handle drugs. "We don't treat on the basis of these individual differences," he says. "For some of these cancer drugs, we may need to do that."

Gandara is on a mission to educate fellow physicians about the importance of personalized treatment for lung cancer and the availability of diagnostic tests that make it possible. As incoming president for the International Association for the Study of Lung Cancer, he works toward that goal, including serving as co-chair of the association's 13th World Conference on Lung Cancer in San Francisco, which was held in late July.

"Physicians need to know that we can already use predictive biomarkers to choose lung cancer treatments," Gandara says. Tests for those markers are covered by Medicare and by most insurance companies, he adds.

In addition to caring for patients and educating physicians, Gandara is conducting clinical trials research in the emerging field of pharmacogenomics. This area of science aims

to tailor drug regimens to patients' genetic profiles.

Gandara notes that he is on the board of directors of Response Genetics Inc., a Los Angeles-based company that offers genetic testing for lung and colon cancer patients.

In May, Gandara and a team of U.S. and Japanese researchers published a groundbreaking pharmacogenomics study that used a new model, called the common-arm clinical trial, to look at the differences in effectiveness of cancer therapies between ethnic groups.

In a common-arm study, clinical trials conducted in different countries use a standardized design that included similar study designs, eligibility criteria and treatment regimens. "We're the only ones taking this approach to cancer therapy," Gandara says.

Gandara is a member of the Southwest Oncology Group (SWOG), the largest federally funded U.S. cancer trials network. The common-arm study was a huge undertaking that took years of collaboration between SWOG and the Japanese equivalent of the U.S. Food and Drug Administration.

In addition to caring for patients and educating physicians, Gandara is conducting **clinical trials** research in the emerging field of **pharmacogenomics**. This area of science aims to **tailor drug regimens** to patients' genetic profiles.

Researchers launched the study in hopes of explaining why clinical trials conducted in different countries involving two commonly used chemotherapy agents, paclitaxel and carboplatin, resulted in different outcomes for patients with non-small-cell lung cancer.

The results confirmed those of previous studies, explains molecular biologist Philip Mack, a UC Davis Cancer Center researcher, one of the study authors and also a member of SWOG. "The Japanese experienced more toxicity, but a better one-year survival rate," Mack says.

The researchers also looked at single-nucleotide polymorphisms, or SNPs (pronounced snips), in six genes associated with drug metabolism. SNPs are portions of genes in which the DNA sequence varies by a single nucleotide — A, T, C or G.

They found differences in genetic variation for four of the genes between the two groups. "We were able to determine that there are significant differences in distributions of these SNPs," says Mack, who also is a UC Davis associate adjunct professor of medicine.

Gandara says the results of the study support the idea that genetics matter when it comes to treating lung cancer. "SNPs account for the differences in how our bodies handle drugs. We don't typically treat on the basis of these individual differences. For some of these cancer drugs, we may need to do that."

He explains that this kind of common-arm study is part of a growing trend toward the globalization of clinical trials. Gandara plans to collaborate with researchers conducting similar studies in the future, including ones from Latin America now planning common-arm clinical trials with SWOG.

Gandara and Mack also are working to personalize lung cancer treatment based on tumor genetics. Mack's lab is responsible for identifying oncogenes in tumor samples of

"We're still in the **information-gathering** stage, but we can already **refine** a patient's **therapeutic course** so that they are **more likely** to receive a drug that will be **successful**."

~ Phillip Mack

Marcus continues to **benefit from Gandara's efforts** to optimize his treatment regimen. "There is no question in my mind that this **personalized approach** is the answer," he says.

cancer center patients. An oncogene is a gene that, when mutated or expressed at high levels, helps turn a normal cell into a cancerous one.

"Two people with the same diagnosis may have radically different compilations of oncogenes that contribute to their disease," Mack explains. The latest cancer therapies target cellular signaling pathways that are abnormally activated by these oncogenes. "We can do a better job of using these tools if we can understand the specific genetic profile of each individual's tumor."

These treatments are more likely to work in the growing number of lung cancer patients who have never smoked, Mack says. That's because non-smokers have fewer oncogenes than smokers do, making it easier to predict which targeted molecular therapy will work. "In the next two years, we should be able to assign never-smokers to optimal initial therapy in 30 to 50 percent of cases," Mack predicts.

On the other hand, personalizing treatment for smokers based on tumor genetics will take longer. "The tumors of smokers often have rampant mutations, and therefore the tumors are generally less responsive to molecular therapies," Mack says.

In both non-smoker and smoker cases, the genetic profiles needed to individualize therapy are sometimes hard to come by. That's because lung cancer tumors are diagnosed from very tiny biopsies, and often there is not enough tissue left over from pathology tests to use to perform molecular analysis. So, recently, Mack and his colleagues instead have begun to look at harvesting tumor cells and DNA from patient plasma.

"Tumor material is shed into the blood, and we can investigate that for the presence of key mutations. It's forensic-type research," Mack explains. "We're looking for small amounts of tumor DNA in the blood."

According to Mack, both pharmacogenomics and tumor genetics are revolutionizing cancer therapy. "We're still in the information-gathering stage, but we can already refine a patient's therapeutic course so that they are more likely to receive a drug that will be successful," he says.

Gandara concurs. Thanks to this two-pronged, personalized approach, cancer treatment is evolving from empirical selection of therapies — choosing drugs based on a person's age, stage of disease and other general factors — to what Gandara calls "molecular selection."

Marcus, however, points out that patients like him still can't access specific drugs for every type of tumor, since drug development has yet to catch up with what's being learned about genomics and tumor biology. But he's hopeful. "Even in the last three years there have been great advances in tailoring therapy to individual needs," he says. "It's the promise of personalized medicine, and it's really coming to fruition."

Attacking breast cancer on all fronts

ATHENA research project could revolutionize treatment

Doctors, scientists and patients are finding many reasons to be hopeful in the fight against breast cancer, as researchers at UC Davis and elsewhere figure out new ways of detecting and fighting the disease, the most common cancer in women.

But moving a promising new treatment or diagnostic technique out of the laboratory and into the clinic where it can help save lives is a long, involved process. For Tianhong Li, who joined the UC Davis Cancer Center in June as an assistant professor of medicine, it is a welcome challenge and one for which she is especially qualified.

"That's what needs to be done now," says Li, a physician-scientist who splits her time between research and clinical care. Li's job is to help spearhead the movement of new therapies and technologies developed at UC Davis into clinical trials. "It feels likes it's the right time, and I'm lucky to be in the right place."

As part of Li's role building a stronger bridge from the bench to the bedside, she is leading UC Davis' efforts in an ambitious new

"It provides a way to **view patients as a whole**, and it enables us to **follow them over time**. The idea is really to **build an infrastructure** so you **monitor the patient** from their screening mammogram through diagnosis, treatment and then **into survivorship**."

~ Tianhong Li

demonstration project – the ATHENA Breast Health Network, a multi-year, multi-center endeavor to provide the kind of boost to advances in breast cancer that the Framingham Heart Study in nurses had for cardiovascular disease.

ATHENA, launched this fall, will gather breast cancer screening, demographic, lifestyle and other information on 150,000 women from the five University of California cancer centers – Davis, Los Angeles, San Francisco, San Diego and Irvine – and will follow the patients for decades. Researchers hope the data will yield a greater understanding of the biology of breast cancer, which can be integrated into clinical care so that doctors better understand who is at risk for the most serious cancers, and how they can be prevented.

"We want to generate a new model of treating patients," Li explains – one that offers a personalized approach based on a more detailed picture of the individual's disease. By demonstrating the effectiveness and efficiency of such a strategy, ATHENA leaders hope to establish a model that could be used to manage other cancer types.

Also, by closely following women in the screening cohort treated for breast cancer, researchers will be able to hone their approach to managing the disease, so that patients with less invasive cancers can forego unnecessary procedures, and those with aggressive disease can get treatments tailored to their needs.

"It provides a way to view patients as a whole, and it enables us to follow them over time," Li says. "The idea is really to build an infrastructure so you monitor the patient from their screening mammogram through diagnosis, treatment, and then into survivorship."

The ATHENA project requires

ATHENA, launched this fall, will **gather breast cancer** screening, demographic, lifestyle and other **information** on **150,000 patients** and will **follow them for decades**.

"lots of layers of groundwork," Li says, and one of the first priorities is setting up standardized systems to gather and manage the wealth of information that will be generated.

A key part of that is creating the informatics architecture for the collection of data on a massive scale. Michael Hogarth, professor of pathology and laboratory medicine at UC Davis, is heading that effort.

Another goal is to establish a biospecimen repository of thousands of samples taken from women diagnosed with breast cancer at UC medical centers. The collection will include both specimens from tumors and from normal tissue adjacent to tumor. At UC Davis, that task will be directed by Regina Gandour-Edwards, professor of pathology.

That is good news to Colleen Sweeney, an associate professor of biochemistry and molecular medicine and co-director of UC Davis' breast cancer research program, who says one of the biggest challenges in her work is access to tumor specimens.

"Tumor specimens tell us if our hypotheses are valid," Sweeney says. "They are the ultimate litmus test."

A specimen can help determine, for example, whether a certain protein in breast tumors is a natural cancer fighter or if it has mutated into an oncogene that has the capacity to cause cancer.

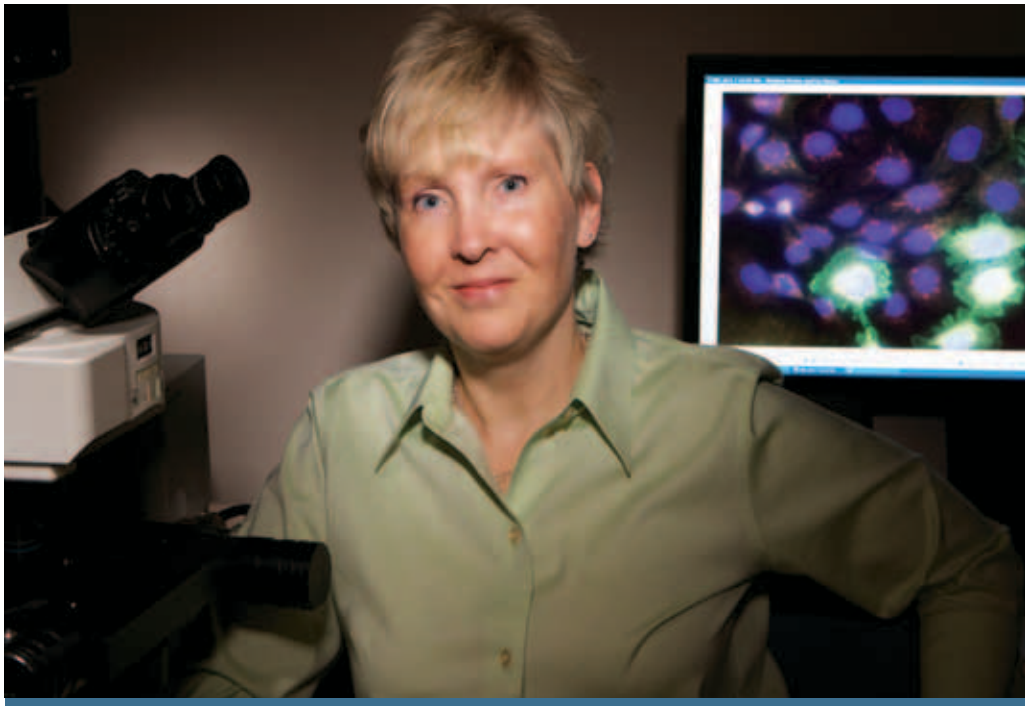
"They're precious, and difficult to acquire," she says. "You need a large number of samples to make sure your results are statistically significant."

Leading ATHENA's pathology and biospecimen repository work-group for all five campuses is Robert Cardiff, director of the Center for Genomic Pathology at UC Davis. He will be responsible for establishing common methods of managing breast tissue specimens, pathology diagnostic procedures and digital imaging of breast tissue.

Alexander Borowsky, an associate professor of pathology and laboratory medicine at UC Davis, is working on innovations for easier access to the specimens.

Tissue samples mounted on slides for examination under a microscope can be converted to digital images and stored in a database. But rather than downloading an entire image from a massive database, Borowsky says satellite image retrieval technology could be used to retrieve pixels on demand, displaying only a particular magnification of part of the specimen. Google uses the same kind of system to offer Web-surfers satellite views of their neighborhoods.

Borowsky also is figuring out



"There's nothing better than getting everybody in the same room, thinking about the same problem. I think ATHENA will **create a structure** for that. Bringing together people from **different disciplines** and **enabling their collaboration** is really what's going to make the difference."

~ Colleen Sweeney

"Any time you have important clinical questions, it's always better to **pull together our heads and resources.**"

~ Helen Chew

how specimens could be collected and prepared not only for standard pathologic testing, but also for gene expression profiling. That could allow for personally tailored therapies, potentially revolutionizing treatment.

"Ultimately we might be able to say each patient's breast cancer is unique," Borowsky says.

The ATHENA biospecimen bank will be linked with various patient details, including whether their cancer went into remission, they developed resistance to a certain drug or their cancer recurred, for example.

"We need all this information so we can understand the impact of what we're studying on overall patient prognosis." Sweeney explains.

The ATHENA network also will include a databank of mammograms and other imaging data from tens of thousands of patients.

Karen Lindfors, chief of breast imaging for the Department of Radiology, says that by correlating breast imaging results with other data, imaging specialists will better understand the implications of what they see.

Currently, breast cancer doctors don't have good data on what types of lesions may have a high likelihood of being benign and do not require aggressive treatment. In those cases, patients can be safely followed using surveillance imaging alone.

"It would be helpful for us to know what we need to worry about, and what we can ignore," Lindfors says. "The information gathered through ATHENA will allow us to come up with standards on such lesions like we have for mammography."

The ATHENA network also will create common systems integrating data collection, management and research across the UC campuses to advance every aspect of breast cancer science.

"Any time you have important clinical questions, it's always better to pull together our heads and resources," says Helen Chew, who leads the clinical breast cancer program at UC Davis. Dealing with breast cancer requires "a multimodality approach," she adds, in which medical oncologists work closely with surgeons, radiation oncologists and imaging specialists.

"There's nothing better than getting everybody in the same room, thinking about the same problem," Sweeney adds. "I think ATHENA will create a structure for that. Bringing together people from different disciplines and enabling their collaboration is really what's going to make the difference."

The ATHENA network also will **create common systems** integrating data collection, management and research across the UC campuses to **advance every aspect of breast cancer science**.

Leveling the playing field for Latinos

Software program aims to boost colorectal cancer screening rates

Colon cancer is a silent killer. Its symptoms appear only after it has reached an advanced stage. But when caught early, the disease is highly curable.

Latinos in the United States are among the groups **more likely to be diagnosed** with colon **cancer at advanced stages** and, as a consequence, are **more likely to die from the disease**.

Unfortunately, some groups are less likely to get screened for colon cancer, a disparity that makes the disease a disproportionate killer, as well.

Latinos in the United States are among the groups more likely to be diagnosed with colon cancer at advanced stages and, as a consequence, are more likely to die from the disease.

"Latinos nationally have half the rate of colon cancer screenings as non-Latinos," says Anthony Jerant, associate professor of family and community medicine at UC Davis. "So far traditional educational approaches such as pamphlets and public service announcements have failed to narrow that gap."

Jerant is tackling the problem as the principal investigator on a study that begins in January. With a grant from the National Cancer Institute, Jerant hopes to find out if an interactive multimedia computer software program that personalizes the educational information can boost colon cancer screening rates among Hispanic patients.

"There have been no studies to my knowledge looking at whether by tailoring to people's baseline knowledge, needs and perceptions, we can help level the playing field and reduce health-care disparities," he says. "If that pans out, it would be important, because there's very little evidence so far that health-care interventions can lessen disparities."

The project adapts an earlier version of the software piloted at UC Davis in 2005. The new study will evaluate its impact in the primary-care offices of physicians in the UC Davis Medical Group, as well as in several federally qualified community health centers in New York City and Rochester, N.Y.

"Our initial outcomes with an English-language version of the software were very promising," Jerant says. "Now we can use it and the Spanish-language version at

"Latinos nationally have **half the rate of colon cancer screenings** as non-Latinos."

~ Anthony Jerant

more sites and truly put it to the test in determining whether or not it can improve screening among both English- and Spanish-speaking Latinos."

Jerant and colleague Peter Franks, professor of family and community medicine, were inspired to develop the program after finding disparities in colon cancer screening and a failure of traditional methods of communication to reach patients about its importance.

In one study published last year in the *Archives of Internal Medicine*, the two UC Davis researchers revealed that blacks, Asians and Latinos were less likely to undergo colorectal cancer screening than whites. Their findings suggested that improved access to care and, for Latinos, providing care and information in their preferred language, could greatly increase screening rates.

In another study published in the *Journal of General Internal Medicine*, the UC Davis researchers suggested a need for different methods to increase screening among Latino subgroups. They concluded that personally tailored interventions, provided within a culturally salient framework in the patient's preferred language, could mitigate screening rate disparities.

"You can improve some patients' knowledge by giving them a pamphlet or CD, but it tends not to change their behavior," Jerant explains. "What is more likely to change their behavior is making sure the information they get is relevant to what their concerns are."

The interactive software program

The program is **interactive** in that its messages are **tailored** to address the **patients' responses** to questions.

"You can **improve some patients' knowledge** by giving them a pamphlet or CD, but it tends not to change their behavior. What is more likely to **change their behavior** is making sure the information they get is **relevant to what their concerns are**."

~ Anthony Jerant

uses a combination of text, narration, video clips and animation in English and Spanish to address perceived barriers to screening.

The program is interactive in that its messages are tailored to address the patients' responses to questions. For example, if a patient indicates fear that screening is painful, the program responds with information about the procedure to address the concerns. The program explains that some people may experience pain, but that for most it is minimal and that sedatives are used to alleviate discomfort.

"One of the major differences in this software program is that it is offered right in the patients' own doctors' offices, when they may already be thinking about their health and have time to talk with their physicians," Jerant says.

The study, co-managed by Christina Slee and Dionne Evans Dean, will collect data from at least 1,344 patients ages 50 and older in California and New York over an 18-month period.

Information from Latino patients will be compared with information from non-Latino patients to determine if the software helps improve participation in screening overall and, specifically, if it helps reduce or eliminate disparities between these groups. If shown to be effective, the software eventually could be made available widely in physicians' offices.

Kurt Slapnik, medical director of UC Davis' Primary Care Network, sees the project as a tremendous opportunity for both physicians and patients.

Unfortunately, **some groups are less likely** to get screened for colon cancer, a disparity that makes **the disease a disproportionate killer**, as well.

"This allows the Primary Care Network to be exposed to the research and teaching components of UC Davis Health System," says Slapnik, who also sees patients in UC Davis' Medical Group office in Folsom. "Patients will be brought in a little early for their regular appointment and will be educated about colorectal cancer screening, with the idea that it will break down the barriers to getting this screening done. By the time they see their primary-care physician, they will be more ready to discuss screening, and it will make the whole process much easier for everyone."

News briefs>>

Holistic approach best to spur Native Americans to get mammograms

Low breast cancer screening and survival rates for American Indian and Alaska Native women have more to do with cultural beliefs than with barriers such as access to health care, a UC Davis study has found.

Linda Navarro

Researchers with UC Davis and the Turtle Health Foundation, Inc. also found that more holistic educational interventions designed by American Indian and Alaska Native women prompted women in those communities to seek mammograms and to change unhealthy eating and sedentary lifestyles.

"The results highlight the significance of cultural beliefs and attitudes when designing effective cancer risk-reduction and cancer control interventions," says Marlene von Friederichs-Fitzwater, an oncology professor and director of the UC Davis Outreach and Education Program. "Access to mammography screening and quality follow-up care are critical, but we learned that access is not the only barrier to improving breast cancer screening rates among American Indian/Alaska Native women."

Breast cancer is now the second leading cause of cancer-related deaths among American Indian and Alaska Native women, with mortality rates that could be cut by more than 30 percent if screening were increased to recommended levels.

The UC Davis and community researchers identified several important cultural and tribal issues that affect cancer control strategies. For example, in some native languages, the literal translation for cancer is "the sore that never heals," reflecting a belief that cancer is incurable. Among some groups, cancer carries a stigma, which can impede the effectiveness of cancer screening educational programs and interventions to reduce risk.

"My experience with people who did not survive their cancer is that many of them didn't tell anyone except for those very, very close to them," says Linda Navarro, co-chair of the project and a member of the Torres Martinez Desert Cahuilla tribe. "One of the reasons is they didn't want to be a burden to anyone."

The study, funded with a grant from the California Breast Cancer Research Program, resulted in a more culturally appealing breast cancer morbidity and mortality reduction approach called the "Mother's Wisdom Breast Health Program." The program, delivered in a DVD format, was disseminated using traditional storytelling, talking circles and other Indian communication methods.

Cervical cancer study findings may guide physicians and patients in follow-up treatment decisions

Research from the UC Davis Center for Healthcare Policy and Research has found that women treated for cervical intraepithelial neoplasia (abnormal cervical cell growth) are at higher risk for a recurrence of the disease or invasive cervical cancer.

The large population-based study, which appeared online in the *Journal of the National Cancer Institute*, **sheds new light on the long-term risks of subsequent abnormal cell growth or invasive cancer,** and should help in the development of follow-up treatment guidelines for women with a history of treatment for abnormal cells.

"We now have a much more clear idea of the risks of recurrent abnormal cells and invasive cervical cancer over time after treatment of these cells," says Joy Melnikow, professor of family and community medicine and director of the UC Davis Center for Healthcare Policy and Research, who led the study. "Recurrence risk depends on the grade of abnormal cells that were initially treated, what treatment was used, and the woman's age."

Joy Melnikow

The study, which used data from the British Columbia Cancer Agency cytology database and was funded by a National Cancer Institute grant, looked at 37,142 women treated for abnormal cells from Jan. 1, 1986, through Dec. 31, 2000, and compared them with a group of 71,213 women with no previous diagnosis of abnormal cells.

They found that risk of subsequent abnormal cells or cervical cancer was associated with the type of treatment they received, their age and the initial grade of diagnosis. At later stages, the type of treatment depends on several variables, including the grade and distribution of abnormal cells, and whether the patient has been treated previously.

Melnikow says the findings could help guide physicians in making recommendations about the intensity of follow up needed after treatment for abnormal cells. In addition, she said the findings may help physicians and patients in deciding which type of treatment for abnormal cells to choose.

Socio-economic status key to disparities in tobacco exposure among Asian Americans

Smoke-free policies are not always effective among Asian American women, a majority of whom don't smoke but may be at risk for secondhand smoke exposure, a recent study has found.

UC Davis researcher Elisa Tong, an assistant professor of medicine, found that while California has a longstanding history of smoke-free social norms and regulations, their effectiveness in Asian-American communities depends largely upon socioeconomic status.

Tong's study, "Smoke-Free Policies Among Asian-American Women: Comparisons by Education Status," was published recently in a special supplement of the *American Journal of Preventive Medicine*. The supplement, funded by the National Cancer Institute and American Legacy Foundation, was dedicated to the unintended consequences of tobacco control policies in women of low socio-economic status.

Elisa Tong

In her work, Tong acknowledged that California has significantly decreased racial, ethnic and educational disparities in its smoke-free home and indoor work policies. But she wanted to know specifically how Asian-American women were faring.

"Asians are half of the world's smokers," she says. "But this is a population that hasn't been looked at traditionally in the U.S. because it is difficult to study."

Tong and her colleagues used the California Tobacco Use Surveys for Chinese Americans and Korean Americans, which were conducted in 2003 by senior author Moon Chen, UC Davis professor of medicine and principal investigator of the Asian American Network for Cancer Awareness, Research and Training. Tong analyzed the data in 2008 to compare women with lower and higher education status in terms of their adoption and enforcement of smoke-free policies.

Tong found that regardless of educational status, most respondents reported that they prohibit smoking in their homes and indoor workplaces, and understand the dangers of exposure to secondhand smoke. But lower-educated women were more likely than their higher-educated counterparts to report someone smoking in their home or having recently been exposed to smoke at their indoor workplace.

Tong concluded that an unintended consequence of the success in California's tobacco-control efforts is that disparities exist in how they are enforced among Asian-American women due to educational status. Lower-educated women, she said, may need assistance with empowerment in enforcing rules around exposure to secondhand smoke.

"We learned that almost all women know secondhand smoke is bad for you, so that means that having policies is not enough," Tong says. "There has to be an additional component. Maybe this is where a health-care provider can step in and be an advocate for these women."

Roseville activist leads breast cancer fundraising efforts

Carol Garcia's roots reach deep into the city of Roseville – five generations' worth. That might explain why, after getting her college degree at Sacramento State University, she returned home to raise her family and launch her career.

It's lucky for Roseville – and the greater Sacramento area – that she did.

Today, the community recognizes her work as a city council member, tenure leading the Roseville Chamber of Commerce and job as senior vice president of Granite Community Bank.

But they may not be aware of her contribution toward finding cures for breast cancer through the Placer Breast Cancer Endowment that she co-established. The group aims to raise $1.5 million for an endowed chair at UC Davis Cancer Center.

Garcia's dedication was evident this fall in the roster of events she helped plan to boost the endowment. Among them: a party co-hosted by United Auburn Indian Community, Thunder Valley Casino and Austins Steakhouse; the Hot Pink 5K through Historic Old Town Roseville; and the Pink & White Ball at the Granite Bay Golf Club.

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News briefs>>

Diagnosed with breast cancer in 1998 at age 39, Garcia has taken on the cause with the same kind of energy and enthusiasm she has for her other civic priorities.

"I had five surgeries – removal of the tumor, of the breasts, of the lymph nodes and reconstruction," she says. "After going through that, I thought we have to do something to find a cure."

Teri Munger, co-founder of the fund, called her friend "a tireless crusader" for the endowment – which, like many in a challenging economy, has struggled to meet its ambitious fund-raising goals.

Carol Garcia

"She has kept focused on this cause for the last five years," Munger says. "Without her dedication and perseverance, this nonprofit would not exist. She just keeps charging forward. She sets a goal and demands that there is no turning back."

Garcia credits a cadre of fellow volunteers, many of them also breast cancer survivors, for the group's accomplishments so far: $800,000 in the bank for the endowed chair.

"I firmly believe that when we have someone solely focused on breast cancer research at UC Davis, they will be successful in finding the cure," she says. "That is our goal, and that is our hope."

Dixon girls' creations benefit melanoma research

Sometimes, as they say, the greatest gifts come in the smallest packages. That is certainly true in the case of Ireland and Maren McGuire, who have given deeply of themselves in an effort to combat the disease that recently claimed the life of their beloved grandmother.

Ireland, 9, and Maren, 6, are on a quest to raise money for melanoma research and to heighten awareness of the deadly form of skin cancer.

The girls' grandmother, 64-year-old Donna Burke of Dixon, died from her disease on Sept. 20, two years after her diagnosis. She received treatment at UC Davis Cancer Center, where the girls' mother also works in the Health Sciences Advancement department.

The girls, who live in Dixon, have been creating and marketing their own beaded jewelry and other small treasures, with the help and guidance of their extended family. Every penny of their profits will go to doctors at UC Davis for melanoma research.

"Ireland is the one who came up with the idea," said their mother, Christine McGuire. "She wanted to do something that she thought would help my mom. My husband, Chris, and I thought it would be a good way to help the girls cope with their grandmother's illness and be a part of the fight against this horrible disease."

The pair's first coup was a sale they called "Two Irish Girls Jewelry Event" that featured some 300 pieces – necklaces, earrings and bracelets – which netted more than $2,000 for UC Davis oncologists Steve Martinez and Scott Christensen.

The young fund-raisers also developed a Web page dedicated to teach young people about the importance of skin cancer and melanoma prevention. The pair also intends to continue selling their creations.

"Prevention is really the key, and the tie-in for what these wonderful little girls are doing to raise awareness of the disease," says Christensen, one of Donna Burke's doctors. "We still continue to look for new options for melanoma [treatment]. That is why their efforts are so greatly appreciated. What we have, while useful, is not as good as we would like it to be."

Christine McGuire said she is proud of her girls for showing such initiative during a very challenging time for everyone.

Ireland and Maren McGuire

In the weeks following her mother's death, Christine McGuire admits that motivation for the jewelry-making waned, so she asked the girls to gear up for the UC Davis Health System holiday bazaar.

"It gave us something to look forward to, and my dad has asked that we please continue our efforts as a legacy to my mom, who would be so proud."

Prostate cancer research thriving at UC Davis

They are relatively few, but the men and women of the UC Davis urology department have created a research powerhouse. Their cutting-edge work, especially in prostate cancer, is leading the way toward better therapies – and outcomes for patients.

A recent analysis of National Institutes of Health funding for schools of medicine found that the UC Davis urology department was ranked third among all urology departments in the nation, with nearly $4 million in research grants in 2008.

Christopher Evans

Major research commitments bolster UC Davis' comprehensive clinical approach to prostate cancer, said Christopher Evans, professor and chair of urology.

"Patients not only have the opportunity to get into clinical trials, but we as clinicians have an insight from our molecular research to help understand what is going on in patients," he says. "We aren't just treating the cancer, we are treating the disease process."

The NIH research data, compiled by the nonprofit Blue Ridge Institute for Medical Research, found that UC Davis has the only urology department in the nation to rank among the top three institutions receiving NIH funding the past three years.

Evans noted that the other top-funded urology departments are much larger than UC Davis' department, and that of the eight urology faculty members at UC Davis, four have funding for basic science research. "That is unparalleled," he says.

Evans points to Ralph deVere White, cancer center director, as the architect of UC Davis' strong urology research team.

"Ralph put prostate cancer investigators together with the goal of translational research," Evans says. "This has facilitated many new projects throughout the UC Davis community."

The major theme of the UC Davis prostate cancer program is the role of the male hormone androgen and androgen receptors in prostate cancer. In early stages, prostate cancer tumors depend on androgen to grow, so treatment with drugs to counter androgen production has long been used to slow their growth. Unfortunately, when the cancer progresses, this treatment stops working, and the disease cannot be cured.

UC Davis urology researchers are working to identify the mechanisms that lead to the development of so-called "androgen-independent prostate cancer." The hope is that understanding the mechanisms will lead to more effective approaches to treatment of advanced disease.

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UC Davis Cancer Center's colorful "garden of hope" booth drew hundreds at the annual Making Strides Against Breast Cancer Walk to benefit the American Cancer Society. Volunteers at the October event also recruited more than 50 cancer survivors interested in becoming "peer navigators" to guide other women newly diagnosed with the disease.

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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.