

# SYNTHESIS

THE MAGAZINE OF UC DAVIS CANCER CENTER VOL 12 • NO 1 • SPRING/SUMMER 2009

## Finding pancreatic cancer's weakness



Beyond hormones

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Helping the  
body fight back

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Navigating the first  
days of breast cancer

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Dear Reader,

Unlocking the mysteries of cancer requires a lot of keys, each of which can open a door that leads to many more gateways of discovery.

Molecular oncology researcher Hongwu Chen, for example, has found that certain proteins that control how often genes are expressed play a much larger role in upsetting normal hormone function – and promoting cancer cell growth – than was previously thought. The discovery may fuel the development of new, more targeted cancer therapies.

A frustration with the lack of effective treatments for pancreatic cancer led surgeon Richard Bold out of the operating room and into the laboratory to better understand pancreatic cancer cells. As you will learn, Bold and his collaborators found that by depriving the cells of the enzyme arginine, cancer-cell proliferation could be cut in half. The finding could help extend the lives of patients with pancreatic cancer.

These opportunities are possible only because of our integrated system, which combines the talents of researchers across the academic spectrum. The newest member of our research program, immunologist William Murphy, broadens our capabilities even further. Murphy is finding ways to kill cancer stem cells, control the immune system's role in tumor growth and boost the efficacy of immunotherapy for various types of cancer.

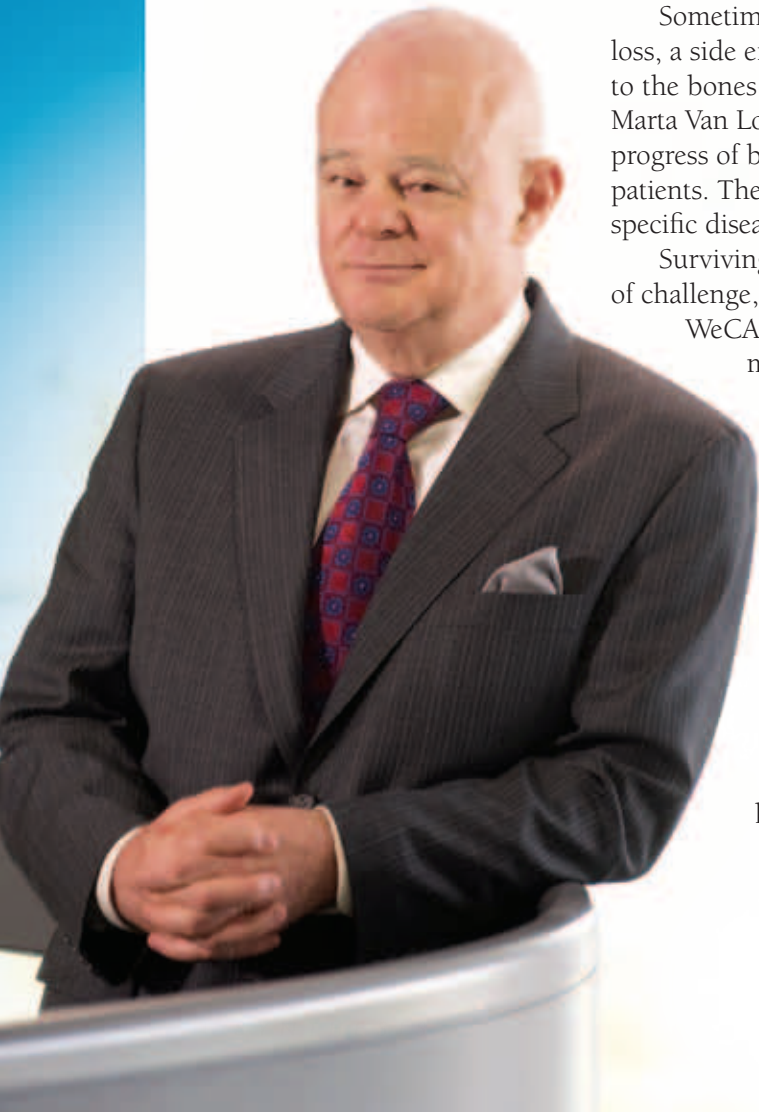
Sometimes, anti-androgen therapy for prostate cancer can cause bone loss, a side effect that can be devastating when the prostate cancer has spread to the bones. UC Davis oncologist Primo Lara and research physiologist Marta Van Loan have developed a blood test to better diagnose and track the progress of bone metastases and predict survival outcomes for prostate cancer patients. Their test may prove useful in tailoring treatments to each patient's specific disease.

Surviving the emotional trauma of a cancer diagnosis is a different kind of challenge, one that cannot be addressed from a research laboratory. The WeCARE Community-Based Breast Cancer Peer Navigator Program matches newly diagnosed breast cancer patients with breast-cancer survivors. The “cancer coaches” can help ease anxiety and provide meaningful guidance for patients.

In Amador County, the connections that support UC Davis Cancer Center are intimate, too. In this scenic community, Cathy Landgraf has focused her efforts on raising funds for UC Davis Cancer Center in memory of her sister, Christine, and mother, Helen. Her efforts are an example of the power of small communities of individuals to make a very big difference.

UC Davis Cancer Center physicians, researchers, volunteers and community fundraisers are determined to find answers to cancer's greatest challenges. Together, their keys are helping open the doors to healing.

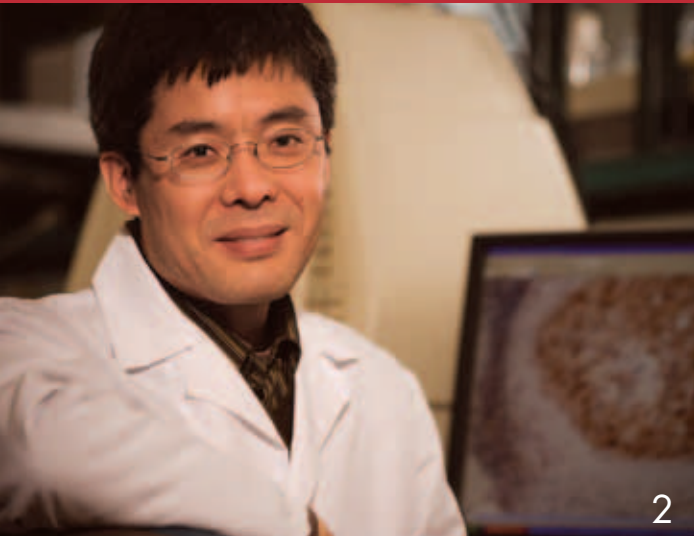
Ralph deVere White  
*Director, UC Davis Cancer Center*  
*Associate Dean for Cancer Programs*  
*Professor, Department of Urology*



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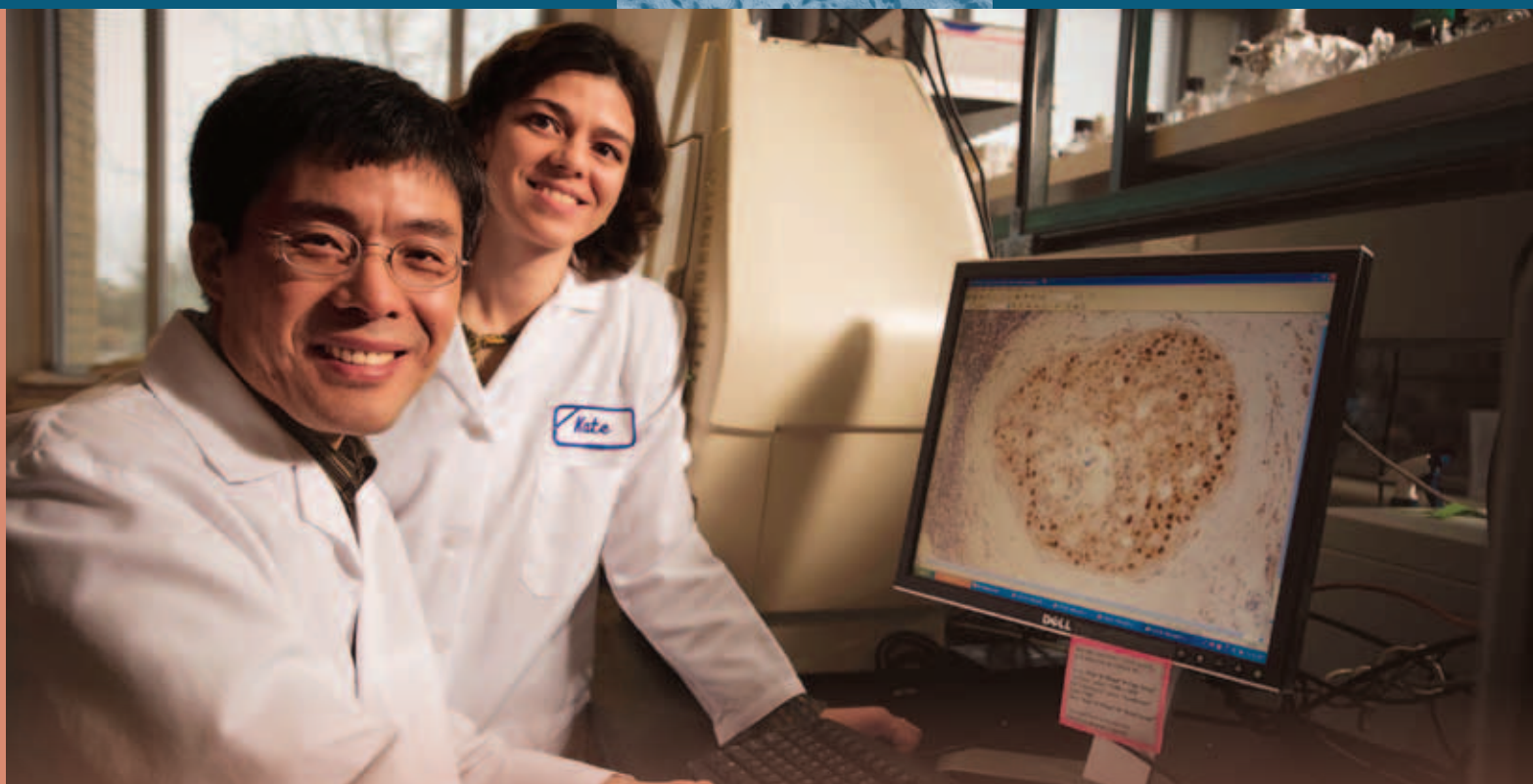
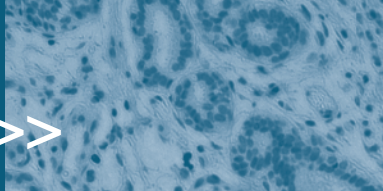
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**UCDAVIS**  
CANCER CENTER

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Building on basics>>



## Beyond hormones

Proteins controlling hormone receptors could be the key to many cancers

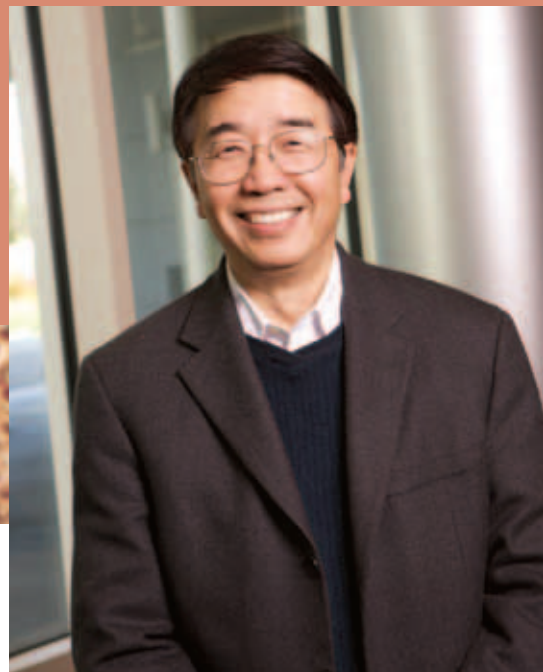
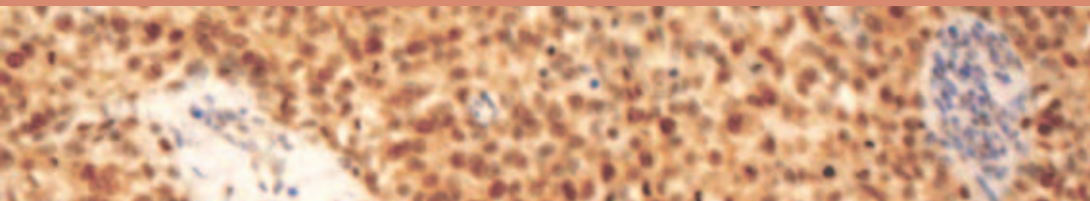
Abnormal hormone functions were once thought to be the major reason for breast and prostate cancers. But Hongwu Chen's research is showing that a much broader network of cellular functions are actually at work.

Sex hormones – androgen and estrogen – are the elixirs that turn girls into women and boys into men. In cancer, however, these chemicals can go horribly awry and drive the formation of tumors in breast and prostate tissues. Cancers of the uterus and ovaries have also been linked to sex hormones and how they interact with other cells.

The role of sex-hormone signaling in cancer is an area of intense interest among scientists seeking a better understanding of the disease and potential targets for new treatments. One of the leaders in this area of research is Hongwu Chen, an associate professor of biochemistry and molecular medicine and co-leader of the molecular oncology research program at UC Davis Cancer Center.

“...we have come to the realization that **coregulatory proteins** can play the **key role** in derailing normal hormone functions.”

~ Hongwu Chen (pictured, left, with Ekatarina Kalashnikova)



“**Dr. Chen has a knack** for identifying important molecules to pursue for new therapies because of **his insights** and the careful, hard work of his lab. His current work **exemplifies** the type of translational research and integrative approaches our cancer center promotes.”

~ Hsing-Jien Kung

A homegrown Aggie – he earned his doctorate in molecular and microbiology at UC Davis in 1995 – Chen has spent years studying the molecular foundations of hormone-related cancers. Recently, however, his research has led him to decipher a mechanism at work in a far wider variety of cancers and yielded promising targets for the next generation of chemotherapy drugs.

### **A molecular siren song**

To better define those new drug targets, Chen is currently investigating a family of proteins that controls how often genes are expressed. Within human cells, DNA is wound in a structure called chromatin, like kite string around “packaging” proteins called histones. This packaged DNA must first be loosened up and made accessible before the information it encodes can be read.

The protein molecules in charge of unwinding and flagging a segment of DNA for expression are known as coregulators. These proteins can land on packaged DNA/chromatin and modify the

chromatin structure, and they may also bind to one another to form complex, DNA transcription-controlling molecular devices. Chen is finding that coregulatory proteins constitute a major means of controlling gene expression.

“People used to think coregulatory proteins didn’t really belong at the forefront of cancer biology, that they just played an accessory role,” Chen says. “But we have come to the realization that coregulatory proteins can play the key role in derailing normal hormone functions.”

Chen’s interest in coregulatory proteins arose during his studies of hormones in breast and prostate cancers. He was particularly interested in a protein elevated in some breast cancers called ACTR. Previous researchers had found that ACTR interacts with estrogen receptors to trigger endless cell division and, thus, cancer.

Chen, expecting ACTR to operate only via hormone receptors, found the protein also caused proliferation among cells lacking estrogen receptors. In other words, ACTR didn’t need a hormone receptor to do its dirty work.



“They don’t function through the hormone receptor, but through one of the core cell circuits crucial for cancer development,” Chen says.

Through further analysis, Chen found ACTR operates like the molecular version of a mermaid. Rather than enticing sailors to a briny death, ACTR lures away a molecule that keeps a tight lid on DNA transcription. Once this check on cell division is removed, a cell can begin the endless replications that cause cancer.

## **A new culprit in many cancers**

Intrigued, Chen and his team dug deeper into how ACTR wreaked its havoc. They looked to see which genes ACTR activated. One of these – ANCCA – caught their attention.

Just by examining ANCCA’s sequence, Chen could tell the protein encoded by ANCCA was worth a closer look. First, it contained an adaptor called a bromodomain that enabled it to bind to DNA-wrapping histones, making it a coregulatory protein. ANCCA also contained a structure that can metabolize ATP – the form of energy used in cells. This feature is common to enzymes that modify the shapes of other proteins.

“Based on these two characteristics, we felt this protein might play a very important role in the control of gene expression,” Chen says.

ANCCA turned out to be amazingly similar to ACTR. Both are coregulators of hormone receptors for androgen and estrogen. But both can function in cells lacking hormone receptors too.

“It was like déjà vu,” says Chen.

The discovery meant that ANCCA could be involved in cancers that aren’t hormone-related. Chen and his team went on detecting the protein in cancer tissues, and found it not just in hormone-associated cancers such as prostate, ovarian and breast tumors, but in liver and lung tumors as well. His hunch proved to be correct.

“In each type of cancer cells we examined, we found ANCCA was crucial for their proliferation and survival,” Chen says. “Thus, it may control a mechanism that is fundamental to many different cancers.”

To date, they have analyzed hundreds of tumors for ANCCA. Levels of the protein were elevated in 60 to 70 percent of the breast cancer samples examined – an amazingly high fraction of the tumors. By comparison, the protein targeted by the drug Herceptin,

widely prescribed to treat breast cancer, is elevated in about 30 percent of breast cancers.

“Even within, say, all prostate cancers, different things have gone wrong. So the impact of finding a coregulator like ANCCA that is common to the majority of cancers would be more significant,” Chen says. “It offers a means to subvert a wide range of tumors with one swoop.”

ANCCA also appears to have some value in predicting tumor aggression. Chen is finding that cells expressing ANCCA appear to replicate faster than other tumor cells.

“ANCCA may be a way for cells to overcome the proliferative hurdles that normally keep them under tight growth control,” says Alexander Borowsky, a UC Davis associate professor of pathology and laboratory medicine and one of Chen’s research collaborators.

Borowsky and Chen are studying how tumor cell differentiation affects cell replication rates. Cells that are less differentiated tend to replicate faster. They are also associated with more aggressive cancers with a worse prognosis. The researchers want to know how the interplay of cell differentiation and proliferation, or what Borowsky

“In each type of cancer cells we examined, we found **ANCCA was crucial** for their proliferation and survival. Thus, it may **control a mechanism** that is **fundamental to many different cancers.**”

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“ANCCA may be a way for **cells to overcome** the proliferative hurdles that normally keep them under tight growth control.”

~ Alexander Borowsky

calls “the yin and yang” of cancer growth, influence tumor growth and patient outcomes.

Understanding the relationship between ANCCA and cell division may help doctors tailor cancer treatment regimens, Borowsky adds. Some types of chemotherapy are most effective in tissues that are replicating fast. So if ANCCA does correlate with cell division rates, a test for the protein could identify the tumors that should respond best to cytotoxic chemotherapy. Chen’s team is currently testing this idea in the lab.

ANCCA’s involvement in such a high percentage and wide range of cancers also makes it an alluring target for drug therapy.

In addition to its bromodomain and ATP binding site, the molecule contains a third area that allows it to clump together with other ANCCA molecules into oligomers. This gives scientists at least three

places to target with drugs, which greatly increases the likelihood of finding methods to block ANCCA’s effects.

“There are a lot of ways for small molecules to specifically target its function,” Chen says.

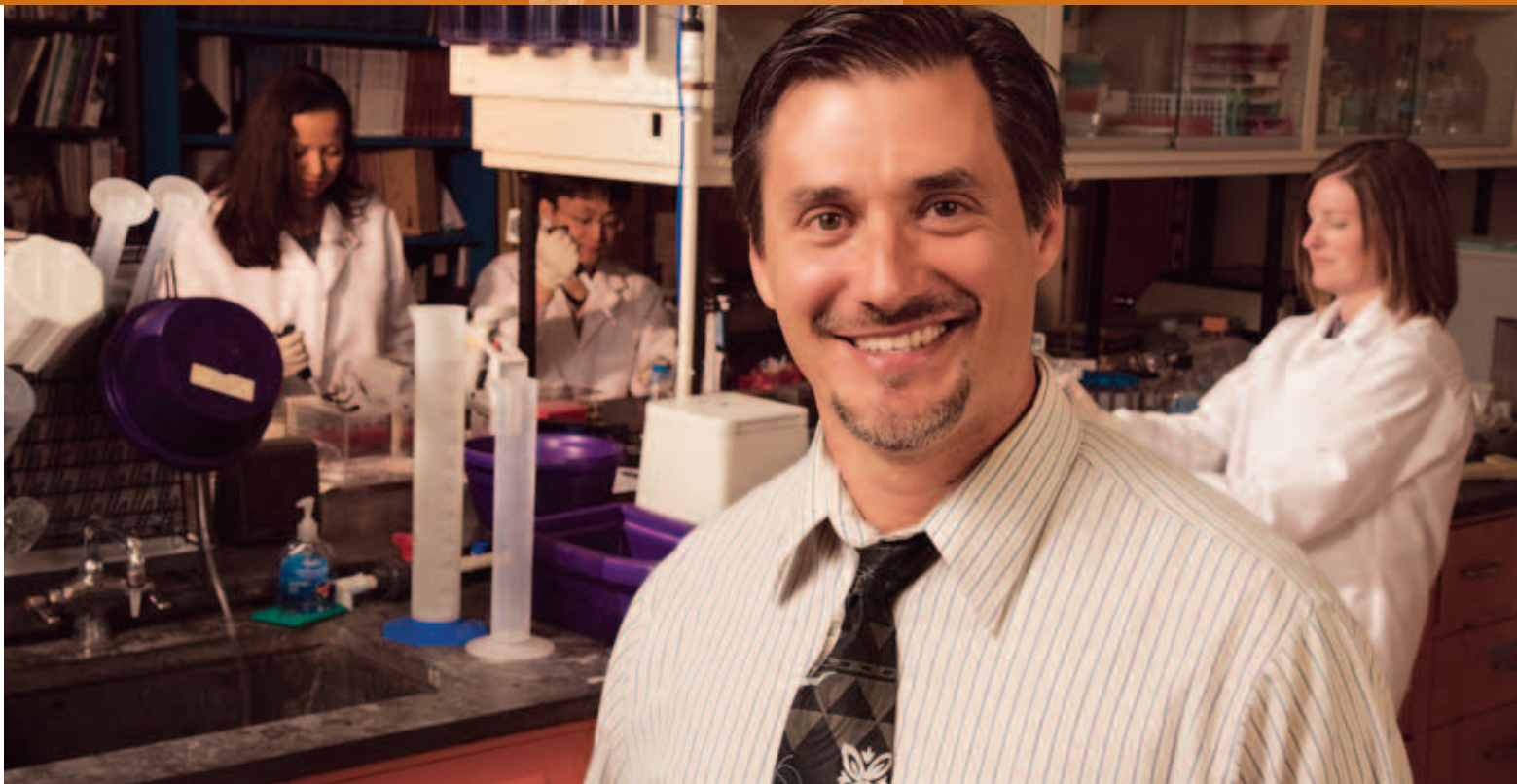
Together with Ph.D. candidate Ekatarina Kalashnikova, Chen plans to publish the ANCCA overexpression in breast cancer results. His ACTR and ANCCA discoveries, however, have already generated a great deal of excitement in the endocrine and cancer research community.

“With such a high frequency of over-expression in cancer specimens and demonstrated potential to stimulate cell growth, ANCCA promises to be a valuable cancer marker,” says Hsing-Jien Kung, professor of biochemistry and molecular medicine and director of basic sciences for UC Davis Cancer Center. “Dr. Chen has a

knack for identifying important molecules to pursue for new therapies because of his insights and the careful, hard work of his lab. His current work exemplifies the type of translational research and integrative approaches our cancer center promotes.”

If researchers can find pharmaceuticals to hijack ANCCA, many cancer patients could potentially benefit. Foremost among these could be breast and prostate cancer patients whose disease becomes hormone refractory. Such cancers rely on the presence of hormones to fuel growth at first, but eventually turn hormone-independent. The vast majority of breast and prostate tumors develop hormone resistance. And once hormone-elimination therapy no longer works on such cancers, relatively few options remain.

For these patients, the discovery of ANCCA could lead to a true lifeline.



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## Helping the body fight back against cancer

**Immune system research promises to boost a variety of developing treatments**

The newest member of the cancer research program focuses on harnessing the power of the immune system to fight disease.

As a college student, William Murphy had two interests: working with children and science. He was a camp counselor and runaway shelter volunteer while earning his teaching certificate and dreaming of becoming a physician. Then he was accepted to graduate school. It was while studying immunology at the University of Texas Southwestern Medical School in Dallas that Murphy became enamored with basic cancer research. He abandoned plans to become a physician.

“You can create anything as a scientist – even a cure for a previously incurable disease,” says Murphy, an expert in the immunology of stem cell transplants who recently joined the UC Davis faculty as a professor of dermatology.



“Understanding the complex immunology of cancer will lead to **better means of preventing** and treating it.”

~ William Murphy (pictured left)

Murphy is inspired by the creativity it takes to do cutting-edge science and finds UC Davis to be the perfect place for his laboratory creations to become fully realized therapies.

“Having top-notch clinician collaborators and world-class facilities like the ones at UC Davis are crucial for advancing the kind of research that will lead to major breakthroughs,” he says.

Murphy spent his postdoctoral years and early career at the National Cancer Institute (NCI) in Bethesda, Md. After 12 years and becoming director of basic research at NCI-Frederick in Maryland, he joined the faculty at the University of Nevada, Reno (UNR) – a cross-country move prompted by his late father-in-law’s poor health.

“We were able to spend nearly three years caring for him,” says the husband and father of four.

Now, the Murphy family – and the Murphy laboratory – are again on the move. Murphy is currently dividing his time between UNR and UC Davis. The move of laboratory personnel will be complete by early summer. The family’s move will wait until his two eldest children graduate from high school.

Murphy’s recruitment fits well with plans to broaden the dermatology research program to tackle a host of health problems related to the immune system, given that the skin is an important defense against immune system invaders and often the first organ to express immune system issues.

“He is a highly respected researcher, and we are thrilled to have him on our team,” says Fu-Tong Liu, chair of the UC Davis



“When you talk to him, he comes up with thoughts and ideas that make your project better. ... **He is a real catalyst**, one of those people with whom you really want to collaborate.”

~ Robert Wiltrott

Department of Dermatology. “We are confident he will strengthen our investigations in the areas of skin diseases, tissue regeneration, cancer and inflammation.”

Because of the broad impact of Murphy’s hire, Liu was joined by leaders from the stem cell program, internal medicine, the cancer center and the dean’s office in working diligently to bring him to UC Davis. For the cancer center, Murphy’s arrival comes at a time when expertise in immunology is needed to help advance today’s most promising cancer treatments.

“The immune system can both fight cancer and promote it during chronic inflammatory conditions. Understanding the complex immunology of cancer will lead to better means of preventing and treating it,” he says.

Jan Nolta, director of the UC Davis Stem Cell Program, agrees.

“Dr. Murphy is a world-renowned immunologist who is already contributing significantly to a broad range of cutting-edge, patient-centered research at UC Davis,” Nolta says. “We are particularly excited about his work to target and kill cancer stem cells, which can remain and metastasize following chemotherapy for some aggressive tumors. It is imperative for our patients that we find new ways to kill these malignant cells, and Bill’s expertise is already helping greatly in that mission.”

### **Pioneering work**

Dan Longo has been a Murphy collaborator for 18 years. Longo, the scientific director of the National Institute on Aging, one of the institutes at the National Institutes of Health, describes Murphy as a world leader on the influence of hormones on the immune system.

From left to right: Jan Nolta, William Murphy and Fu-Tong Liu.

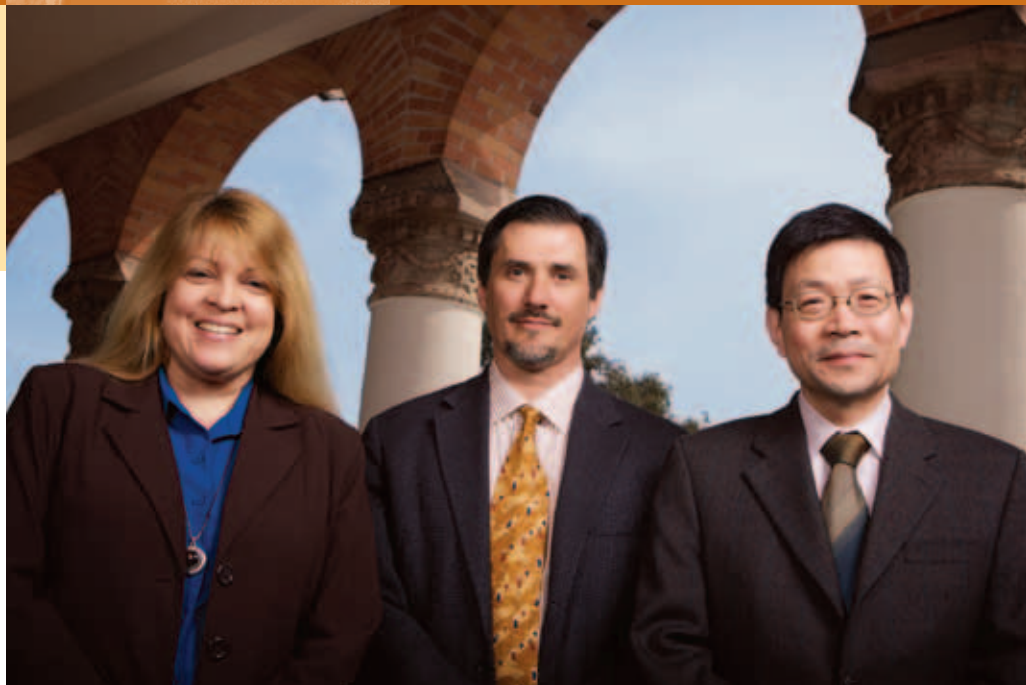
“Although a number of clinical applications are being made from his work, his careful analysis and definition of the cellular basis for certain disease processes has also shed light on basic mechanisms of disease,” he says.

Longo praises Murphy for working to make his laboratory research relevant to the treatment of disease in humans.

“His work is distinctive for its sophisticated use of animal models of disease, which generally mimic clinical situations more closely than purely cell-line studies,” Longo says.

Murphy’s recent work has focused on the role of the immune system in stem cell transplantation, formerly called bone marrow transplantation. First used to treat blood cancers, the procedure is also used today for diseases such as aplastic anemia, immune deficiency disorders and some solid tumors.

The problem is that stem cell transplants don’t always work and, sometimes, cause new diseases. Murphy is credited with discovering the cellular mechanism behind the failure of transplanted stem cells to take up residence in bone cavities and replace immune system functions – a process called engraftment. His work suggested promising ways to enhance engraftment that, Longo says, may make it possible for cord blood to be used in adults as a source of stem cells, making donor – or allogeneic – transplants much safer.



“Dr. Murphy is a **world-renowned immunologist** who is already **contributing significantly** to a broad range of cutting-edge, patient-centered research at UC Davis.”

~ Jan Nolta

## Cancer and immunotherapy

Murphy also pioneered the treatment of cancer using stem cell transplants for immunotherapy.

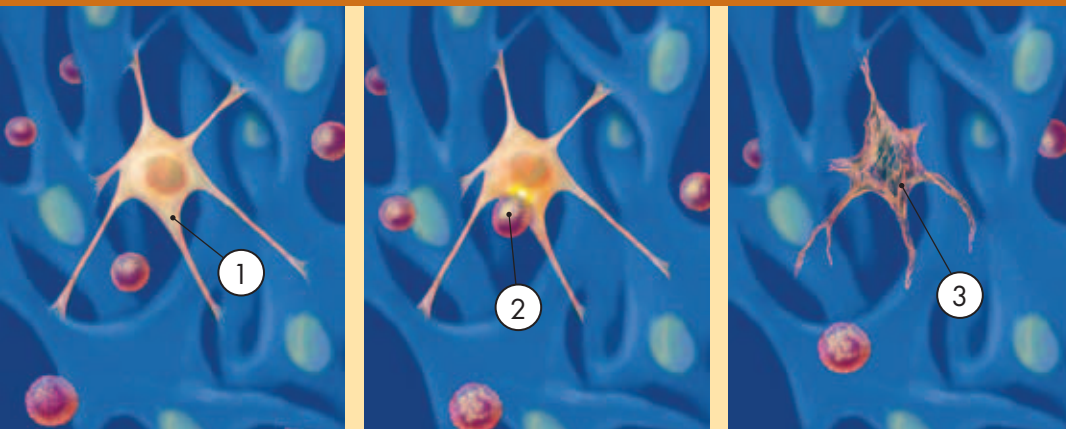
“Tumors have developed elaborate ways of depressing the immune system,” Murphy explains. “The immune system also naturally turns itself on and off. This puts the body at a disadvantage when battling a chronic condition like cancer.”

The goals of cancer immunotherapy, he says, are to inhibit the ability of tumors to depress the immune system, keep the immune system from turning itself off and

stimulating it to destroy tumor cells. Immunotherapy treatments can be used directly or can be combined with existing treatments to improve outcomes.

One area of immunotherapy that Murphy has been working on involves natural-killer cells, which attack tumor cells, virally infected cells and other infectious agents. He has been working on a way to use activated natural-killer cells to improve the results of stem cell transplants.

“We found that transferring natural-killer cells can provide



Murphy and his team are working on ways to better engage the body's own immune-system defenses – like natural-killer cells – to selectively attack tumors. Part of his research focuses on activating natural-killer cell protein receptors to recognize specific proteins on the surface of cancer cells. When the two molecules link, it triggers a signal leading to the death of the cancer cells.

1 – A cancer cell among other cells    2 – Natural-killer cell links to the cancer cell    3 – Cancer cell “skeleton”

significant anti-tumor effects while at the same time reducing the odds of rejecting the grafted cells,” he says.

Natural-killer cells can also reduce the incidence of graft-versus-host-disease, which results when donor cells mount an immunological attack on the recipient's tissues and organs. The condition is one of the biggest hurdles to more widespread use of stem cell transplants. As scientists develop new stem cell-based therapies, preventing graft-versus-host will become increasingly important.

Currently, Murphy has four NIH R01 grants and is on a program project grant with M.D. Anderson Cancer Center looking at ways to improve the efficacy of immunotherapy in a variety of cancers. His team has so far shown that certain drugs sensitize tumors to attack from immune system cells produced by the graft, while another given immediately following a transplant reduces the incidence of graft-versus-host.

“The goal is to decrease graft-versus-host disease while improving graft-versus-tumor effects,” says Lisbeth Welniak, a project scientist who has been with Murphy since his days at the NCI. “We're trying to get better at killing the tumor cells, while at the same time

reducing the attack of the immune system on the host.”

This is one of the first projects Murphy and his lab team will tackle at UC Davis, pending approval of animal-use protocols and renewal of the initial NIH grant. The next step, Welniak says, is to expand and improve on the previous drug findings.

“We've had promising results in mice,” she says. “Now we need to translate those into effective therapies to use in patients.”

### **A new team and community player**

Murphy says UC Davis is the perfect place for the scientific interactions that can bring his basic and preclinical research in graft-versus-host disease and cancer immunotherapy to their full potential for patients. To speed that process for cancer patients, he has launched a cancer inflammation research group together with Reen Wu, professor of cell biology and human anatomy, and Natalie Torok, assistant clinical professor of gastroenterology and hepatology.

“The supportive, collegial environment at UC Davis makes it a real joy to do work,” Murphy says. “That kind of collaborative spirit is essential as science moves away from principal

investigator-centered research to team-based approaches required by the most complex challenges facing science. If you have to do everything yourself in today's science world, you're not going to be competitive.”

According to Robert Wiltout, NCI's director for cancer research, Murphy's new colleagues are bound to benefit from his perspective.

“When you talk to him, he comes up with thoughts and ideas that make your project better. Murphy is also open to suggestions that make his own work better. He is a real catalyst, one of those people with whom you really want to collaborate,” Wiltout says.

One of the ways Murphy brings balance to his scientific work is through his ongoing commitment to kids in need. In Maryland and Reno, he served on a foster care review board and as a court-appointed volunteer investigating cases of abuse and neglect. He plans to volunteer with Sacramento CASA (Court Appointed Special Advocates for Children) once his move is complete.

“It's very rewarding to help those who don't otherwise have a voice,” he says. “At the end of the day, it really puts the ups and downs of academic research into perspective.”

# Finding a cancer's weakness

A metabolic defect may be the key to crippling pancreatic cancer

Cancer surgeon Richard Bold turns to basic science to extend lives.

Richard Bold is motivated by challenge. He specializes in treating one of the deadliest cancers with one of the most difficult surgeries to perform. Yet he is frustrated by the limited treatment options for his patients with pancreatic cancer.

“There have been very few significant advances in years of testing chemotherapies for pancreatic cancer,” he says. “There is a dire need for new options, and we have to turn to basic science to come up with those options.”

Since arriving at UC Davis a decade ago, Bold has performed surgeries on pancreatic cancer patients while simultaneously conducting research to discover better treatments for the disease. That work is now paying off.

Bold and his collaborators recently found that pancreatic cancer cells can lack an important enzyme that helps synthesize arginine – an amino acid with an essential role in cell division, immune function and hormone regulation. In a study published in the October 2008 issue of the *International Journal of Cancer*, they showed that arginine deprivation could cut cancer-cell proliferation in half.

“While our findings do not suggest a cure for pancreatic cancer, they do promise a possible way to extend the life expectancies of those diagnosed with it,” Bold says.

His discovery began when he

learned that arginine deprivation showed promise in laboratory studies of melanoma and liver cancer, two other cancers with limited treatment options. He decided to measure levels of argininosuccinate synthetase – the enzyme required to synthesize arginine – in human pancreatic tumor cells. The enzyme was not detected in 87 percent of 47 tumor specimens, suggesting that most pancreatic cancer cells require arginine to prosper.

“Pancreatic cancer, biologically, has nothing in common with other



**Since arriving at UC Davis a decade ago, Bold has performed surgeries on pancreatic cancer patients while simultaneously conducting research to discover better treatments for the disease. That work is now paying off.**

“Instead of killing cells with typical chemotherapy, **we removed one of the key building blocks** that cancer cells need ... Combining this approach with existing surgical treatment **holds great promise** for increasing survival rates of people with pancreatic cancer.”

~ Richard Bold (pictured, left, with researcher Subbulakshmi Virudachalam)

cancers that lack argininosuccinate synthetase,” Bold explains. “But we still were curious to find out if arginine deprivation could have an effect on pancreatic cancer. We were very lucky. It did.”

The researchers then depleted arginine in pancreatic cell lines by exposing them to arginine deiminase, an enzyme isolated from the organism *Mycoplasma* known to cell biologists as a “nightmare.” Cell cultures exposed to the infectious organism quickly die from a lack of arginine. Using purified recombinant arginine deiminase, Bold’s group showed that pancreatic cancer cell proliferation was reduced by 50 percent.

Next, the team treated mice that had pancreatic tumors with a version of arginine deiminase modified to increase size and circulatory time. There was an identical result: a 50 percent reduction in tumor growth.



## A new kind of cancer treatment

According to Bold, the outcome represented a unique approach to cancer treatment. It was one of the first to identify a metabolic pathway that can be leveraged to interrupt cancer.

“Instead of killing cells with typical chemotherapy, we removed one of the key building blocks that cancer cells need to function and they can’t create on their own,” Bold says. “Combining this approach with existing surgical treatment holds great promise for increasing survival rates of people with pancreatic cancer.”

Bold has since examined whether or not arginine deprivation may be useful in treating other cancers. A study published in January 2009 in *Cancer Research*

showed that 100 percent of the 88 prostate cancer tumors examined lacked the enzyme. Arginine deprivation might therefore be effective in treating prostate cancer as well.

Hsing-Jien Kung, director of basic science at the cancer center and an international leader in cancer biology, was Bold’s collaborator on the pancreatic and prostate cancer studies. Kung – together with Ph.D./M.D. candidate Randie Kim – discovered the mechanism by which arginine deprivation works, a first-ever finding published as part of the prostate cancer paper.

“Most chemotherapeutic agents work by damaging DNA,” Kung explains. “Damage to DNA leads to apoptosis – biochemical changes that eventually destroy the cell. But cancer cells often develop resistance to drugs because mutations help them avoid apoptosis.”

Kung hypothesized that, because arginine deprivation is a form of metabolic stress, a different kind of cell death might be at work. Together with Bold’s group, Kung’s lab discovered that arginine deprivation triggers autophagy – or self-eating – a process in which cellular organelles become encapsulated by digestive enzyme-containing lysosomes.

“The cell literally begins to eat itself. This is the first time we have seen this method of cellular destruction in prostate cancer cells,” Kung says.

For the arginine-deprived prostate cancer cells, autophagy eventually led to apoptosis.

“Our thought is that if you prolong arginine deprivation treatment then you promote both mechanisms of cell death,” Kung says. “Arginine deprivation could be a wonderful adjunctive therapy that would allow us to lower the doses of current drugs that can have debilitating side effects.”

## Taking treatment to patients

Bold and Kung are now conducting laboratory studies on arginine deprivation therapy in conjunction with other agents for treating pancreatic and prostate cancer. They will then look for ways to increase the sensitivity of cancer cells to arginine deprivation.

“This additional research is needed to inform the clinical work and move it forward more quickly,” Bold says.

The researchers have also begun designing human clinical trials in cooperation with the manufacturer of the modified arginine deiminase. They are collaborating on other



**Bold and his collaborators recently found that pancreatic cancer cells can lack an important enzyme that helps synthesize arginine – an amino acid with an essential role in cell division, immune function and hormone regulation.**

(pictured left is resident Diego Muilenburg)



“Arginine deprivation could be a wonderful adjunctive therapy that would allow us to lower the doses of current drugs that can have debilitating side effects.”

~ Hsing-Jien Kung (pictured above, left, with Randie Kim)

arginine deiminase clinical trials, including a phase II study of melanoma, a phase II study for liver cancer and a phase III liver cancer trial. Human trials for prostate and pancreatic cancer will take some time to launch as they involve combined therapies and require additional lab work.

According to Bold, skin, liver, prostate and pancreatic cancers have little in common other than

a lack of argininosuccinate synthetase. So far, no other cancers have shown this metabolic deficiency.

“As far as we can tell, we are not going to be able to use arginine deprivation for all types of cancer,” he says.

Bold knew early in his career that this was the kind of work he wanted to do. As a surgeon-in-training, he saw pancreatic cancer patients who were eligible for but

not getting surgery because of their prognosis. Bold realized the only way he was going to improve his patients’ survival was to find more effective post-surgery treatments.

“This is a terrible disease and few people are trying to find cures,” Bold says. “I took it on as a challenge so that someday we can give people with pancreatic cancer that chance. Now, I can say that that is a real possibility.”



# When cancer is bone deep

## **Bone enzymes point the way to prostate cancer outcomes**

A new blood test could serve as a crystal ball for cancers that have metastasized into bone.

For 29 years, Lee Stram was a production supervisor and avionics operations engineer for an aerospace manufacturer. A family man with two children, Stram was also a product-support engineer on electronic systems for planes, and his company flew him around the world to troubleshoot problems on malfunctioning commercial aircraft.

But in 2004, the then-68-year-old Stram encountered a problem he

couldn't fix alone. A routine visit to the doctor revealed a worrisome jump in his prostate-specific antigen – or PSA – level. A high PSA is a common early warning sign of prostate cancer. A biopsy confirmed Stram's worst suspicions: He had cancer.

Stram is just one of the estimated 200,000 men diagnosed each year in the United States with prostate cancer. The disease is the most





Lara, Van Loan and their colleagues throughout the United States **may have found a better way** to both diagnose bone metastases and predict survival outcomes. Requiring only a blood sample, the new test could offer **a better means to track** bone metastases and tailor treatments to each patient's type of disease.

“We realized that tracking these enzymes could be a way to **increase our ability to detect** and follow prostate cancer cells in bone. They would allow us to get **an early glimpse** of whether or not therapies were actually helping patients.”

~ Primo Lara (pictured far left with Lee Stram)

common cancer among American men, accounting for more new cancer cases than lung, colorectal, pancreas and kidney cancer combined. For Stram, additional diagnostic tests at the time of his diagnosis delivered even more unpleasant news.

“I found out through a bone scan that the cancer had already metastasized to my hip and ribs,” he says.

Several rounds of intermittent anti-androgen therapy administered by his primary oncologist, Ralph deVere White, kept Stram's cancer at bay for years. Most prostate cancers, at least initially, require male hormones such as testosterone in order to grow, and anti-androgen therapy medications slow that process. But in 2008, Stram's PSA levels began rising again – a sign that his cancer was now resisting this line of treatment.

#### **Overcoming treatment resistance**

Stram's story is all too common among prostate cancer patients. After initial treatments involving drugs, surgery, radiation or some combination of these, approximately

a third of patients will eventually relapse. The cancer in most of these patients eventually spreads into bone. Stram was among the 10 percent of prostate cancer patients with skeletal metastases when first diagnosed.

Bone metastases are bad news for any cancer patient. For one thing, they push the body's bone maintenance system out of whack. New bone is constantly formed while old bone is resorbed as part of normal skeletal maintenance. The two processes are normally well-balanced.

“But when cancer enters the bones, the cancer cells destroy other cells, and we find that bone degradation goes on much faster than bone formation,” says Marta Van Loan, a research physiologist at the U.S. Department of Agriculture's Western Human Nutrition Center based at UC Davis and an expert in bone metabolism.

As if that weren't bad enough, says Primo Lara, associate professor of hematology and oncology at UC Davis Cancer Center and an expert in genitourinary cancer, “prostate cancer treatment also contributes to the loss of bone



integrity. Androgen-elimination therapy often causes abnormally low bone density and osteoporosis, which weakens bone.”

Bone pain and even fractures are common among people whose cancers have spread to the skeleton, “things patients don’t need when they’re battling cancer,” Lara says.

But diagnosing cancer in bone can be tricky. Bone scans often fail to detect areas of degradation, and frequently cannot show how well a patient is responding to chemotherapy.

Now Lara, Van Loan and their colleagues throughout the United States may have found a better way to both diagnose bone metastases and predict survival outcomes. Requiring only a blood sample, the new test could offer a better means to track bone metastases and tailor treatments to each patient’s type of disease.

“The test could apply to any cancer in general that has metastasized,” Van Loan says. “It could potentially become a standard of treatment.”

## **A new predictor**

The researchers hit upon the idea unexpectedly. Several years ago, Lara was conducting a small pilot study of a new prostate cancer drug. The drug was also reported to affect bone health. For this reason, Lara took the extra step of monitoring the patients’ bone metabolism. To do this, they measured blood levels of enzymes associated with bone turnover.

Though the drug failed to help the prostate cancer patients, the team stumbled onto something else. Patients with lower levels of bone resorption enzymes tended to survive longer, plus their disease was less likely to progress during the four-month study period. Patients whose enzyme levels dropped over time also had better outcomes. In other words, the test monitored how well patients were responding to therapy and predicted how they would fare on the treatment.

“It was like looking into a crystal ball,” Lara says. “We realized that tracking these enzymes could be

a way to increase our ability to detect and follow prostate cancer cells in bone. They would allow us to get an early glimpse of whether or not therapies were actually helping patients.”

The approach is now being tested as part of a much larger clinical trial on patients whose prostate cancer is resistant to anti-androgen therapy and has spread to bone. More than 900 prostate cancer patients are enrolled in this nationwide double-blind study of a promising new cancer therapy and the bone-enzyme test.

The patients are given docetaxel, a drug that inhibits cell division, and prednisone, a steroid that reduces the pain of cancer in bone. Half of the subjects will also be given atrasentan, an experimental drug for metastatic cancers that inhibits a cancer-advancing protein. All study subjects also will have their bone enzymes monitored to determine if the bone-health measures correlate with patient responses and outcomes.

“We felt this was the opportunity we were looking for – to test the hypothesis that bone markers have potential prognostic value,” says Lara, the study’s principal investigator.

If the bone-enzyme test proves valid, it could mean major improvements in many areas of cancer care, ranging from case monitoring to treatment and counseling. It could also benefit more than just prostate cancer patients.

“Because the test could give doctors a means to track the progression of cancer in bone, it



**“The test could apply to **any cancer in general** that has metastasized. It could potentially become a **standard of treatment.**”**

~ Marta Van Loan (pictured above, right,  
with chemist Erik Gertz conducting a bone marker assay)

could serve as a screening tool for cancer patients as they try different therapies. Those whose test results indicate they are not responding to standard treatments or whose disease is more advanced could be considered eligible for newer, more experimental therapies like atrasentan,” Van Loan says.

### **The path to personalized treatment**

The test could also pave the way toward personalized cancer care.

“Right now, everybody with prostate cancer is treated with the same standard therapy,” Lara says. “This test could help us treat only those most likely to benefit, and we could focus on finding more effective therapies for those who are

not likely to benefit. Patients could avoid having to take drugs unsuited to their particular form of cancer.”

The newfound ability to gauge patient survival could help doctors further tailor the choice of therapies with the goal of longer-term survival.

Stram is enrolled in the study and already feels it is making a difference. Three weeks after his first clinical trial treatment, he visited Lara for a checkup.

“He said, ‘We did it, the cancer stopped growing.’ And I lit up like a Christmas tree,” Stram says, and adds his appreciation for his physicians: “I am so grateful to UC Davis and doctors deVere White and Lara for my health care and well-being.”

# Navigating the first days of breast cancer

**An innovative program helps newly diagnosed women find their way as patients and survivors**

[ A partnership with Safeway broadens support for cancer patients in the Sacramento region.

When Susan Grenda learned she had breast cancer four years ago, the diagnosis left her overwhelmed by a maelstrom of emotions.

There was disbelief.

There was confusion.

There was frustration.

There was sadness.

And, more than anything, there was fear – fear of the malignancy inside her, fear of surgery, fear of complications, fear of the effects on her loved ones, fear of the unknown.

Grenda's experience was by no means unique. Newly diagnosed cancer patients invariably confront an onslaught of worries and questions as they cope with the news, and those with breast cancer face additional concerns about body image, relationships and treatment choices.

A new program at UC Davis Cancer Center aims to make the first few months after diagnosis easier for women.

Known as the WeCARE Community-Based Breast Cancer

Peer Navigator Program, the program matches breast-cancer survivors with newly diagnosed women for up to six months for one-on-one support. It was made possible through a \$128,000 grant from the Safeway Foundation.

Safeway considers breast cancer one of the most significant women's health issues. Last October, the company's Breast Cancer Research and Awareness campaign raised more than \$18.6 million from customers and employees for breast-cancer research, prevention and early detection programs.

"We are committed to working together with our employees, customers and supplier partners to help find a cure for breast cancer," says Karl Schroeder, president of Safeway Northern California Division. "But while we focus on the research, we see an opportunity to benefit from the lessons and experiences of survivors. Their success can be passed on and shared with others. We are pleased

to partner with UC Davis Cancer Center and believe this program will go a long way in helping newly diagnosed women ultimately reach the road to recovery."

The first team of peer navigators, also known as cancer coaches, underwent training in January.

Among the class of 14 recruits was Grenda, a Roseville mother of two.

"I think for most people who have not been through it, a cancer diagnosis just feels like a death sentence," says Grenda. "This program is an awesome idea because it not only gives new patients a resource, but also introduces them to vibrant, positive women who have come through treatment and continue to live fulfilling lives. That is huge."

Marlene von Friederichs-Fitzwater, the program's founder, could not agree more. She is an assistant adjunct professor with the UC Davis School of Medicine as well as director of the cancer center's Outreach Research and Education Program. She is also a cancer survivor.

Recalling her own experience at the time of diagnosis, von Friederichs-Fitzwater says new patients often feel helpless, bewildered and alone – even if they have supportive family and friends.



“When you first hear ‘breast cancer’ everything else becomes a blur, and you can’t focus on anything except ‘I’ve got the big C’ and ‘Am I going to die?’ Next comes, ‘How did I get it’ and ‘Why me?’ And then you just want answers and information.”

~ Mary Pat Kroll

“The idea behind our program is that having an experienced, trained cancer survivor at your side can make a world of difference as you travel this path,” von Friederichs-Fitzwater says. “We don’t want anyone to have to make that journey alone.”

### **A region-wide scope**

More than 1,400 new breast cancer cases are expected in 2009 in the four-county Sacramento region, according to estimates from the American Cancer Society and the California Cancer Registry.

Not wanting to reserve the benefit of peer navigation exclusively for patients at UC Davis, von Friederichs-Fitzwater took pains to give the program a wide scope.

Toward that end, peer navigators are being trained to work with patients at Mercy General Hospital, at other area clinics, and through African-American churches and community organizations targeting Native Americans and other underserved populations. Coaches also are being sought to work with cancer centers in Marysville, Merced, Pleasanton and Truckee,

which are linked through the UC Davis Cancer Care Network and committed to providing first-rate, community-based cancer care.

Mary Pat Kroll is the first peer navigator deployed at Mercy General Hospital. Kroll, who has been cancer-free for nearly eight years, has worked with two patients so far – and hopes to offer her services to many more in the coming years.

“When you first hear ‘breast cancer’ everything else becomes a blur, and you can’t focus on anything except ‘I’ve got the big C’

# Outreach>>

“For some newly diagnosed patients, the idea of waiting six weeks for that first appointment can feel like forever. It’s like this alien monster inside of you, and you want it out now.”

~ John Linder

and ‘Am I going to die?’” Kroll says. “Next comes, ‘How did I get it’ and ‘Why me?’ And then you just want answers and information.”

## Living life to the fullest

Kroll says one element of her coaching approach is to share with patients how many wonderful things have happened to her since that fateful mammogram found a malignant lump in her breast. To wit: Two of her children have married, she has three new grandsons, she celebrated her 40th wedding anniversary, and she has traveled to Alaska and Hawaii.

“I live life to the fullest now, every day, and I think it helps for new patients to see that positive things can happen after a cancer diagnosis,” Kroll says.

Kroll and Grenda also confirm a fringe benefit of the program that came as a pleasant but welcome surprise to von Friederichs-Fitzwater. While intended to support new cancer patients, the WeCARE program also helps the peer navigators.

“I think for women helping other patients there is a great sense of satisfaction and help with their own healing and recovery,” von Friederichs-Fitzwater says. “They’ve been there and now they want to give back.”

The concept of using “navigators” in health care is not new. Nurses or clinical social workers, however, have typically filled the role, and their focus has mostly been on helping patients with insurance and other administrative challenges, von Friederichs-Fitzwater says.

Peer navigators have a much closer relationship with patients and tend to help with a much broader range of needs. Contact begins by telephone but can include face-to-face meetings and even accompanying a patient to chemotherapy and radiation treatments or doctor visits.

“After a patient is referred to us, our volunteers will make contact and let them know this program is available,” von Friederichs-Fitzwater says. “Some aren’t ready right away, but we want them to know that if they need a fellow traveler, we’re available.”

The origins of the WeCARE program date back several years to a time when von Friederichs-Fitzwater and others became aware that the time between diagnosis and a patient’s first appointment with an oncologist or surgeon was creating significant anxiety. At one point, the cancer center offered an orientation to these new patients, but

attendance was poor. After that, a professional patient navigator was hired, but grant funding for that position ran out, says John Linder, a clinical social worker and psychotherapist assigned to the cancer center.

The WeCARE program is the third – and best – response to address the stress that patients feel in the early weeks following diagnosis.

“For some newly diagnosed patients, the idea of waiting six weeks for that first appointment can feel like forever,” Linder says. “Cancer is not like heart disease, which you get from eating too much fettuccini Alfredo. It’s like this alien monster inside of you, and you want it out now.”

Part of the peer navigator’s job would be to reassure those patients that for most cancers the waiting period is not going to make a significant difference either in the staging of the cancer or the proposed treatment.

“Beyond that,” Linder adds, “there is all the practical stuff people



want to know. ‘Tell me about radiation. Does it burn? How sick will I be with chemotherapy? What about a mastectomy?’ You just can’t put a value on the importance of talking with a survivor about all of these issues.”

To qualify as a peer navigator, volunteers must complete a one-day training followed by monthly two-hour sessions led by a variety of medical and community professionals. Among the topics covered are productive communication techniques for talking to the doctor, confidentiality and patient-privacy issues, patient resources at the hospital and in the community, and how to recognize whether a patient needs psychotherapeutic help.

A substantial part of the training also focuses on problem-solving and coping techniques using the COPE model, which stands for Creativity, Optimism, Planning and Expert information (see sidebar).

As of March, about one in four newly diagnosed breast-cancer patients was requesting a peer navigator. Von Friederichs-Fitzwater believes interest will grow as news of the program spreads. She is conducting training for new peer navigators every other month and hopes to have 100 cancer coaches working in the community by the end of the year.

And that’s just the beginning.

“This is a pilot program we are hoping to expand,” says von Friederichs-Fitzwater. “After fully establishing the program in our region, the next step is to share the program throughout the United States. We want to be the national model and standard for cancer support.”

## Becoming a peer navigator

Any breast-cancer survivor who completed treatment at least two years ago, has good interpersonal communication skills, can complete the mandatory training and is available to work with a breast-cancer patient as needed for up to six months is eligible to be a peer navigator. The training involves a one-day session followed by monthly two-hour sessions on the requirements and resources needed to be an effective peer navigator.

Being a successful navigator, however, takes more than training.

“Peer navigating is a particular kind of support with COPE at its core,” says Lea Spencer, project coordinator for the WeCARE Community-Based Breast Cancer Peer Navigator Program and a cancer survivor.

COPE – the model addressed during training – stands for Creativity, Optimism, Planning and Expert information. It is set of interaction tools focused on problem-solving and coping skills that all navigators are expected to learn, use and share with patients.

“Navigating is more than being someone’s buddy,” Spencer says. “It’s an orderly process with the specific goals of helping someone work through obstacles and use information effectively in dealing with a serious medical condition.”

Besides understanding and using COPE, Spencer says the best navigators are those who were strongly proactive during their own treatment. The most motivated also tend to come from one of two camps: survivors who had a lot of support



“Most of all, it’s very important to be a good listener.”

~ Lea Spencer

during treatment and want to make sure others do as well, and those who had little or no support and want to make sure no one else has the same experience.

According to Spencer, there is one quality that is key to all effective navigators.

“Most of all, it’s very important to be a good listener,” she adds. “The training and our team will give navigators everything else it takes to provide the necessary support to a cancer patient.”

Anyone interested in becoming a peer navigator can begin the process by calling Spencer at (916) 734-5786 or e-mailing [lea.spencer@ucdmc.ucdavis.edu](mailto:lea.spencer@ucdmc.ucdavis.edu).

# A community unites to take on cancer

## Amador County residents launch a foundation to fund research

Cathy Landgraf expands her family's commitment to curing cancer by asking her friends to help.

In 1973, John and Helen Landgraf established an endowed cancer research fund at UC Davis in memory of their daughter, Christine. Now their other daughter, Cathy, is broadening the impact of what her parents started by involving her community in the cause.

Amador County, where the Landgraf family spent their summers, is now the base for the Amador Cancer Research Foundation. Since it began in 2007, the organization has become known for energetic fundraising events. Its first "Spaghetti Western" was held at Cooper Vineyards in Plymouth last September. More than 450 people showed up – and seriously kicked up their heels.

"It was truly a great party," says foundation board director Cathy Landgraf about the event, which featured barbecued tri-tip and live country-western music and was emceed by Sacramento television broadcaster Walt Gray.

Aside from providing a good time, the event netted \$18,000 – money the foundation intends to donate to UC Davis Cancer Center. But the foundation plans to give the center far more than that.

"We want to get to \$1 million plus," says Landgraf.

"I am so grateful for the board members. They all have such busy lives but still give their time, talent and money toward this cause."

~ Cathy Landgraf



*Aside from providing a good time, the Spaghetti Western netted \$18,000 – money the foundation intends to donate to UC Davis Cancer Center.*





BOARD OF DIRECTORS left to right, back row: Brenda Ristrom, John Mills, Gary Little, Loren Fasmer; middle row: Jago Landgraf, Hal Jones, Marylou Fasmer; front row: Shirley Jones, Frankie the dog, Cathy Landgraf (not present: Stephen Honeychurch)

## Community-directed fundraising

A million dollars may seem pie in the sky for a small community during tough economic times, but there are reasons for Landgraf's optimism. Their community-directed fundraising model – unique to UC Davis – truly works. A similar group in nearby Placer County, the Auburn Community Cancer Endowment Fund, succeeded in raising \$1.5 million to establish an endowed chair in basic cancer research at UC Davis. Another group in Roseville, called the Placer Breast Cancer Endowment, was formed with the goal of amassing \$1.5 million toward an endowed breast-cancer research chair, and they are already nearly halfway there.

“Even with the strong track record in other communities, I wasn't really sure we could do this,” says Landgraf of her thoughts right before launching the foundation. She changed her mind at their first meeting.

“We have such a good group and so many good ideas,” she says.

“And we got great inspiration from Dr. deVere White (director of the cancer center) and Dr. Meyers (UC Davis executive associate dean). It was at that point that I knew we could have a big impact, and I haven't doubted that since. That initial big thinking and incentive is still with us today.”

The Amador foundation is further along in making an impact than the \$41,000 raised to date suggests. That's because of its connection to the Christine and Helen S. Landgraf Memorial Research Fund, which is named for Christine and her mother, who also had cancer.

Nearly 40 UC Davis researchers so far have received \$5,000 awards for promising projects, including the search for molecular-targeted anti-cancer drugs, genetic abnormalities in pancreatic cancer, improved prevention outreach for women and the role of the immune system in leukemia and lymphoma. The most recent recipient was Chiong-xian Pan, an assistant professor of hematology and oncology, whose work focuses on

the molecular foundations of cancer.

“The Landgraf grant has been very important to my research in developing small molecules that work like ‘smart missiles’ targeting cancer stem cells – the few cells where it is believed most cancers originate and possibly the reason why some of them can be so hard to cure,” Pan says. “I am deeply honored by their belief in and support for my efforts.”

Because it is part of a far larger pool of money invested by the university, the Landgraf fund has grown steadily over the years. As a result, Landgraf wants to double the annual research award to \$10,000.

“I'd like to do that immediately,” she says.

## “I can do this”

Raising funds for cancer research is always a challenge, says Ann Pridgen, development officer for the cancer center. The Amador group, however, has a lot of enthusiasm on its side, and Pridgen doesn't think the economic climate will stop people from giving.

“When people can't control the



“The Amador Foundation’s dedicated volunteer leaders are proof that there is **great power in bringing together** friends, neighbors and the community in **the shared cause** of advancing cancer research.”

~ Ralph deVere White

*D'Agostini Winery in Amador County, 1942, by Helen Landgraf*

big things, they want something good to happen for something that is really meaningful to them. They say to themselves, ‘I can’t do anything about the stock market, but I can do this,’” says Pridgen.

Landgraf has had to learn to live with something she wasn’t able to control – the death of her sister at age 27.

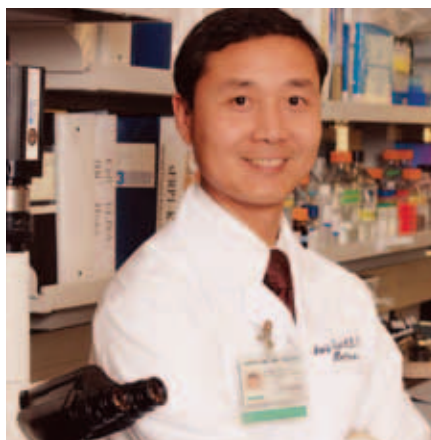
“It took a while for me to get my feet back on the ground,” Landgraf says. “Christine was such a unique, loving, gifted person,” she adds, her voice trailing off.

Talented like her mother, who was an accomplished painter, Christine was on track for a career in the arts. While studying art at Sacramento State, she learned she was seriously ill. Back then, in 1965, Hodgkin’s disease was much less treatable than it is today – or than it was just a few years later. Landgraf’s brother was diagnosed with the disease five years after Christine, but survived.

To hear her sister tell it, Christine didn’t let Hodgkin’s get her down. If anything, it intensified her unconventional personality.

“Christine was connected to a different source than the normal,

run-of-the-mill person,” recalls Landgraf, who adds that Christine had an irrepressible spirit. “In her short life, Christine deeply touched many people – you were fortunate to be a part of her world. That is why now, I know, it is not a



“The Landgraf grant has been **very important** to my research. ... I am **deeply honored** by their belief in and support for my efforts.”

~ Chiong-xian Pan

coincidence this fund has done so much and so many good people are involved in it.”

The sisters were also friends and, for a while, business partners. They opened one of Sacramento’s first hip clothing boutiques. The store lasted only a couple of years. Sadly, Christine lived just a few years after that. A heartbreaking situation was made worse by doctors who seemed to lack compassion.

“It was harsh,” Landgraf says. “The doctors told her she had only a year to live. They were really blunt. She actually lived another seven years.”

Landgraf says that the lack of sensitive care that her sister endured helps motivate her to carry on the Landgraf fund, which is one of the oldest endowments for UC Davis Health System.

“I know that at UC Davis the healing part of cancer care is important,” she says, referring to the work of Fred Meyers, a specialist in hospice and palliative care and close friend of Landgraf’s parents. “That’s one of the things that drives me. I want to support that so that no one will have to go through what my sister went through.”

## **Important work — and a lot of fun**

In addition to the family's continued dedication to the foundation — Landgraf's brother, John, his wife, Ann, and their daughter, Jago, are integral to the organization — it now represents something much broader: a community's effort to combat cancer. All board members have personal connections to the disease.

Board member Gary Little — a real estate broker and owner of the St. George Hotel in Volcano — became involved after making the move from Sacramento to Amador County a couple of years ago. He is helping the group seek corporate donations. He also held one of the foundation's most creative fundraising events — a "Count the Georges" contest to guess the number of dollar bills stuck to the ceiling of the St. George Hotel bar. Next, he'll hold a high-end collectables sale over Fourth-of-July weekend to coincide with Volcano's popular Cannonball Run, a vintage car show and parade.

"I am so grateful for the board members," says Landgraf, who runs a successful landscaping business in addition to leading the foundation. "They all have such busy lives but still give their time, talent and money toward this cause. We work hard together, have a great time and drink excellent Amador County wine."

Their next chance to have a great time will be in September, when they hold another Spaghetti Western and announce the new research award recipient. After that, Landgraf is considering a print sale and exhibit of her mother's original oil and watercolor paintings, which

date back to the 1940s and colorfully represent Amador's most historic and beautiful scenes, especially the Shenandoah Valley.

Ralph deVere White, who attends many of the group's events and is one of their biggest supporters, is confident of their continued success.

"The Amador Foundation's

dedicated volunteer leaders are proof that there is great power in bringing together friends, neighbors and the community in the shared cause of advancing cancer research," he says. "We are inspired by and grateful for their hard work, personal commitment and financial generosity, and we know they will reach their goal."

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Left to right: Tom Nesbitt, Scott Christensen, Laurence Heifetz and Ralph deVere White.

## Tahoe Forest Cancer Center affiliates with UC Davis

Tahoe Forest Cancer Center in Truckee celebrated joining the new UC Davis Cancer Care Network, which was established last October. The Cancer Care Network enables cancer patients throughout Northern and Central California to gain access to the latest diagnostic techniques and treatment approaches while remaining close to their community physicians, familiar surroundings, and friends and families. Tahoe Forest Cancer Center, a part of Tahoe Forest Hospital, is one of four hospital-based cancer centers that have united with the National Cancer Institute-designated UC Davis Cancer Center.

## “Tree of Hope” untrimming benefits cancer research

The family of Joan Giboney, a UC Davis breast-cancer patient who ultimately succumbed to the disease, has raised more than \$45,000 for breast-cancer research in her honor through year-round sales of decorative items and an annual Christmas tree “untrimming.” Joan’s daughters — Corrine and Thea — and her husband, Rich, fulfill a tradition that Joan started when she decorated the first Tree of Hope at the cancer center 10 years ago. After decorating the “Giboney Tree of Hope” at the cancer center, they sell the ornaments on it and donate the proceeds for cancer research.

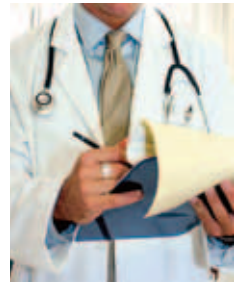


## Community groups provide party for kids with cancer

Pediatric cancer patients along with their families were treated to a holiday party sponsored by the “Active 20-30 Club #1 Sacramento” with help from the Keaton Raphael Memorial and Cure Kids Cancer — three organizations committed to helping children in our community. More than 100 children with cancer and their siblings received gifts from Santa in addition to enjoying food, crafts and games.

## Primary-care doctors miss colon cancer screening opportunities

Many physicians do not refer their patients for colon-cancer screening as consistently as they should, according to a study by researchers at UC Davis, the University of Washington and Group Health Cooperative in Seattle. “Colorectal cancer screening is not on the primary-care agenda as much as it should be,” said lead author Joshua Fenton, UC Davis assistant professor of family and community medicine. The team’s examination of the records of nearly 50,000 men and women aged 50 to 78 revealed that more than half with frequent primary-care visits did not receive screening. The study was published in the February edition of *Cancer Epidemiology Biomarkers and Prevention*.



## Researchers to study experimental breast-cancer vaccine

Cancer Center researchers led by Michael DeGregorio, professor of hematology and oncology, launched a study of a new, experimental vaccine to determine if it can arrest or prevent breast cancer when used in conjunction with standard hormonal therapies. The vaccine, Stimuvax<sup>®</sup>, aims to stimulate the immune system to target and destroy breast-cancer tumors. Results from the UC Davis study, which is funded with a \$3 million grant from Merck KGaA, will help direct the design of human clinical trials slated to begin worldwide this year.

## Prostate cancer expert to lead radiation oncology

Richard K. Valicenti has joined UC Davis Health System as professor and chair of the Department of Radiation Oncology, where he will lead the department's clinical, research, education and administrative operations. A renowned expert in radiation treatments for prostate cancer and other tumors, Valicenti has advanced the use of short-distance radioactive treatments (brachytherapy), image-guided radiation therapy and combined radiation treatments to improve the care of patients with cancer. He comes to UC Davis from Thomas Jefferson University Hospital in Philadelphia.



## Racial disparities exist in colorectal cancer screening

White patients with Medicare coverage receive colorectal cancer screening in higher proportions than do members of all other racial and ethnic groups, according to a new study by researchers at UC Davis and the University of Washington. The researchers found that colorectal cancer screenings were performed for 47 percent of whites, but for only 42 percent of Asians and Pacific Islanders, 38 percent of blacks and 33 percent of Hispanics. "We need more information about the barriers that different populations encounter when it comes to screening for colon cancer," said Joshua Fenton, lead author of the study, which was published in the March issue of the *Journal of the American Geriatrics Society*.



## Vegetables, fruit and fiber may reduce cancer recurrence

A secondary analysis of a large, multicenter clinical trial has shown that a low-fat diet rich in fruits, vegetables and fiber reduced the risk of cancer recurrence by 31 percent in a subgroup of early-stage breast cancer survivors who were not experiencing hot flashes. Absence of hot flashes is associated with higher levels of estrogen, the reduction of which is a major breast cancer treatment strategy. The study team included researchers from UC Davis and six other institutions. Ellen B. Gold, professor and chair of the UC Davis Department of Public Health Sciences and first author of the study, said the results suggest that a major change in diet may help improve cancer survival and recurrence rates among women who don't have hot flashes.

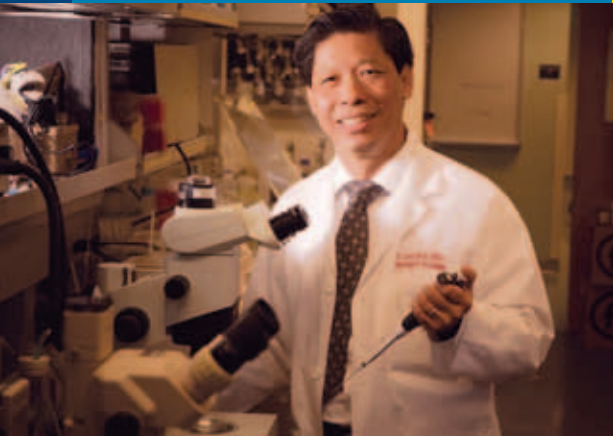
## Protein identified that may enable breast cancer

New research from UC Davis Cancer Center shows that a protein called Muc4 may enable breast cancer to spread to other organs and resist therapeutic treatment. Kermit Carraway, an associate professor of biochemistry and molecular medicine, is senior author of the study, which was published in the April 1 issue of *Cancer Research*. The results suggest that Muc4 somehow disrupts normal links between epithelial cells, from which breast-cancer cells are derived. "We now need to refine our understanding of this disruption process in order to find ways to interfere with it," said UC Davis graduate student Heather Workman, lead author of the study. "There currently are no drugs that target Muc4, and this research will help change that."

## Researchers refine cancer treatments to reduce nerve damage

A research team led by UC radiation oncologist Allen Chen has proposed new treatment guidelines that physicians nationwide can use to reduce the possibility of permanent nerve damage among patients undergoing radiation treatments for head and neck cancers. The researchers devised step-by-step techniques for identifying the brachial plexus nerve complex using anatomical "bench posts" delineated with computed tomography scans commonly used for treatment planning. Chen designed delivery contours to avoid those critically important nerves during intensity-modulated radiation therapy treatments. The team's recommendations were published in the December 2008 issue of the *International Journal of Radiation Oncology, Biology and Physiology*.





## Researchers find molecule that targets brain tumors

UC Davis Cancer Center researchers have discovered a molecule called LXY1 that targets glioblastoma, a highly deadly form of brain cancer. Kit Lam, senior author of the study and UC Davis chief of hematology and oncology, made the discovery with his colleagues while searching for a molecule that could be injected into a patient's bloodstream and deliver high concentrations of medication or radionuclides directly to brain tumor cells while sparing normal tissues. The team's finding, published in the January 2009 issue of the *European Journal of Nuclear Medicine and Molecular Imaging*, offers hope for an effective treatment for a presently incurable cancer.

## New funding for kidney cancer test

A \$1.25 million grant from the National Cancer Institute has funded a five-year UC Davis research project to identify the biomarkers of kidney cancer and develop a diagnostic test for the disease. Robert Weiss, professor of nephrology at UC Davis and principal investigator for the grant, is heading a research team that will focus on identifying metabolites — small molecules easily excreted by the kidneys — that are unique to kidney cancer. The ultimate goal is to develop a simple urine test that can be conducted in doctors' offices as part of routine examinations.

## Restaurant and pub host cancer center fundraiser

A restaurant and a bar in the newly renovated Firestone Building at 16th and L streets in Sacramento jointly staged a grand opening event to support UC Davis Cancer Center. Restaurateurs Mason, Curtis and Alan Wong of Mix Downtown and Simon and Henry deVere White of deVere's Irish Pub held "A Grand Opening for a Grand Cause" on Jan. 21. The two establishments donated proceeds to the cancer center's Outreach Research and Education Program, which provides art therapy and writing courses, a peer navigator program, lectures and a cancer resource center.

## Teenage brothers go bald for the seventh time

Tino Luigi, 13, and his brother, Jake, 15, have gone bald for the seventh year in a row, as participants in the fundraising St. Baldrick's Foundation head-shaving event that the Keaton Raphael Memorial hosted at UC Davis Cancer Center in March. The boys shaved their heads to celebrate Tino's seventh year of cancer remission since undergoing a new neuroblastoma protocol he received at age 5. Tino's mother, Jean, said, "He is proof of what can happen when new treatments become available. This is our boys' way of saying 'thank you' and getting the word out about just how important it is to give to research."



## Researcher awarded funding to develop ovarian cancer test

The Ovarian Cancer Research Fund has awarded a \$900,000 grant to UC Davis researcher Gary



Leiserowitz to develop an early diagnostic marker for ovarian cancer. Leiserowitz, professor and chief of gynecologic oncology, leads a team that is pioneering the use of glycomics analysis for cancer diagnosis. In 2006, the researchers identified specific changes in the sugars attached to cellular proteins in blood samples of ovarian cancer patients. "This generous funding will allow us to move forward more quickly with the next steps in identifying an early diagnostic marker and test for ovarian cancer," Leiserowitz said.

## Pregnancy does not affect colorectal cancer survival

UC Davis researchers have determined that women diagnosed with colorectal cancer during or shortly after their pregnancies have survival rates similar to those of nonpregnant women who have the disease. "There has been very little information so far on whether colorectal cancer discovered during or just after pregnancy leads to different outcomes. Our study clarifies these issues, so physicians can confidently provide guidance to patients," said Lloyd Smith, a gynecologic oncologist with UC Davis Cancer Center and senior author of the study, which appeared in the March issue of *The Journal of Maternal-Fetal Health and Neonatal Medicine*.

## Smoking linked with most male cancer deaths

A research team has completed a study indicating that increased tobacco-control activity could save more lives than previously estimated. Lead study author Bruce Leistikow, a UC Davis associate adjunct professor of public health sciences, said, "The full impacts of tobacco smoke, including secondhand smoke, have been overlooked in the rush to examine such potential cancer factors as diet and environmental contaminants. As it turns out, much of the answer was probably smoking all along."



The analysis, published online in *BMC Cancer*, linked smoking to more than 70 percent of cancer deaths among Massachusetts men in 2003.

## Discovery offers hope for treating kidney cancer

UC Davis researchers have made a pioneering discovery of a means to block a cancer gene's own repair mechanism and thereby make chemotherapy for kidney cancer more effective. After analyzing thousands of compounds, UC Davis nephrology professor Robert Weiss and his research team found three substances that decreased expression of the p21 gene that can restore cancer cell DNA and interfere with cancer treatments. "Our work offers hope that in the future these p21 inhibitors can be refined and used in concert with other conventional as well as novel cancer treatments to increase the comfort and life spans of patients with kidney cancer," Weiss said.



## AANCART recognized for health disparities leadership

The National Center on Minority Health and Health Disparities has presented its Health Disparities Leadership Award to the Asian American Network for Cancer Awareness Research and Training (AANCART). The largest nationwide project ever undertaken to curb cancer in Asian Americans, AANCART is based at UC Davis Cancer Center and funded by the National Cancer Institute. Moon Chen Jr., a UC Davis professor of hematology and oncology who specializes in developing linguistically specific, culturally tailored and population-based health interventions, oversees AANCART.

## Researcher urges change in sarcoma treatment strategies

New studies led by a UC Davis oncologic surgeon suggest that determination of appropriate treatment for soft-tissue sarcomas should be made with consideration of variant factors, including tumor size, location, grade and depth. Robert Canter, an assistant professor of surgery, said that even though the term "sarcoma" encompasses a broadly heterogeneous group of diseases, soft-tissue sarcomas are often lumped together because they are rare. "Our work shows that in order to improve outcomes, we need to think of and treat sarcomas as distinct rather than as just one disease," said Canter, who was the lead author of the studies evaluating data for more than 2,000 patients with low-grade, soft-tissue sarcomas.

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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 advancing cancer discoveries and delivering those outcomes 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 first-rate 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 NCI-designated cancer center.