Building a new generation of cancer scientists

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Dear Reader,

At UC Davis Cancer Center, we have dedicated ourselves to understanding cancer on multiple levels, from its most intricate molecular characteristics to the physical, emotional and social impact it has on people’s lives. This deep and far-reaching approach to the disease is especially important because we know that cancer affects different people in different ways.

In this issue of Synthesis, we will tell you about some of our efforts to uncover and address these differences. For example, in our review of UC Davis research into use of ionizing radiation for cancer diagnosis and treatment, we learn about one project to determine how various types of skin cells respond differently to radiation exposure. These findings could one day help personalize radiation therapy.

Another story examines research findings that suggest where a woman lives may determine whether she is offered breast reconstruction after mastectomy, an approach now considered standard of care, but not always followed.

Our story on “Be Smart With Body Art,” a public-health campaign to reduce the spread of hepatitis C, a virus that causes liver cancer, explores the risks young people face when they fail to ask key questions before getting tattoos or body piercings.

Because research into these and other cancer health disparities is critical to finding cures that benefit all cancer patients, we are supporting the development of a diverse cadre of cancer researchers. We explore those efforts in a story about ET-CURE, our National Cancer Institute-funded program to train college science students from underserved populations in emerging cancer therapies.

We hope you enjoy these and the other stories in our Spring/Summer 2010 issue of Synthesis.

Ralph deVere White
Director, UC Davis Cancer Center
Associate Dean for Cancer Programs
Professor, Department of Urology
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A National Cancer Institute-designated cancer center
Arginine deiminase, a novel drug for cancer, is like a saw to a carpenter who has had only a hammer, says Rick Bold, UC Davis chief of surgical oncology.

It is a tool that opens a new realm of possibilities for treating cancer and that is beginning to generate excitement nationwide.

Arginine deiminase triggers a function inside cells known as autophagy. A Greek term meaning “self eating” or “self digestion,” autophagy may be a way to kill cancer cells very specifically, or in oncology parlances, very elegantly — that is, to kill them without poisoning or harming normal cells as current approaches do.

With its research using arginine deiminase, the UC Davis Cancer Center is at the forefront of this burgeoning field.

Autophagy was first observed decades ago, but wasn’t paid much attention. More recently, however, the field has become so active it now has its own journal, called Autophagy.

Hsing-Jien Kung, a professor in the Department of Biochemistry and Molecular Medicine, is the lead researcher in the cancer center’s autophagy work. He and his team first became interested in arginine deiminase because some cancer cells lack the enzyme necessary to make their own arginine, a semi-essential amino acid. That meant by removing arginine from systemic circulation, cancer cells could theoretically be starved while normal cells would remain functioning.

Testing a theory
Studies sponsored by Phoenix Pharmacologics had shown that the drug was effective against liver cancer and melanoma when these two highly fatal cancers lacked the crucial enzyme.

So, Kung, Bold and the others in their group began investigating
whether other kinds of cancer also lacked the enzyme. They found two: prostate and pancreas, both types of cancer that also respond poorly to treatment other than surgery. Bold says that probably somewhere between 50 percent and 100 percent of these cancers lack the enzyme, and therefore might be susceptible to treatment with arginine deiminase.

At first, the group thought the cell killing occurred because starving the cells triggered apoptosis, a process by which cells self-destruct. But Kung had another hunch, recalling a research conference he had attended years earlier about autophagy. Autophagy, he had learned, is a method by which cells recycle proteins and cell organelles. When autophagy is triggered, the cell forms a membrane around an old, unnecessary organelle or protein, as if collecting it in a garbage bag. Then, another type of bag called a lysosome comes along and injects digestive enzymes into the membrane to break down the contents and make the materials available to the cell again. Kung learned that autophagy is often triggered when a cell is under stress and needs to hunker down and conserve its energy, as when
it is starving. He also heard that autophagy can be a method by which the cell can survive stress, and that sometimes the process switches and becomes a way for the cell to destruct.

Kung realized that this process seemed to mimic the process observed when his group used arginine deiminase, and he figured that autophagy must be involved. It was then that Kung and Bold’s work with arginine deiminase entered the exploding field of autophagy research.

“Autophagy is a cell-protection mechanism,” Kung says. “But we now realize it is also a mechanism of cell death.”

The group has since proven that autophagy is occurring in the cancer cells they treat. In fact, they have photographed the process happening—live—using technology developed by Frank Chuang and his colleagues at the National Science Foundation’s Center for Biophotonics Science and Technology, housed on the UC Davis Sacramento campus. The researchers now know that the process of collecting the organelles into a membrane, the injection of enzymes and, finally, the release of membrane contents back into the cell cytoplasm takes less than 30 minutes.

The group also has done experiments that suggest that autophagy may be one reason cancer cells can be resistant to traditional chemotherapy treatment.

Kung says there are many mysteries yet to be unraveled about autophagy. Why, for instance, does it sometimes result in cell survival and sometimes in cell death? And how does that switch happen? His group is exploring those questions.

A potential new treatment

They also are interested in moving forward into the clinic.

Ralph deVere White, director of the UC Davis Cancer Center and a prostate cancer expert, says a new approach is critical for prostate cancer. Currently the five-year survival rate for metastatic prostate cancer is less than 30 percent, a rate that has not improved in the last 30 years.

“Autophagy gives us another way to attack this cancer,” he says.

The arginine deiminase drug under study at UC Davis is owned by San Diego-based Polaris Pharmaceuticals. The company has been most interested in pursuing the potential of the drug in liver cancer, and has initiated trials in Asia, where liver cancer is much more common than in the United States. Those trials have demonstrated that the drug is safe and causes mild side effects, if it causes any at all, Kung says.

Bold notes that patients diagnosed with pancreatic cancer usually live less than a year, and gemcitabine, the only effective treatment, gives those patients, on average, only another six weeks. He has put together a group of researchers to conduct a preliminary clinical trial of arginine deiminase in pancreatic cancer.
cancer, a cancer rare enough that it usually requires a few centers to collect enough patients for an adequate trial. If fruitful, a trial in prostate cancer could follow.

Bold says the group has injected both pancreatic cancer and prostate cancer cells into animals and treated them with arginine deiminase, and it appeared to kill those cancer cells. But some tumors appeared to become resistant to the treatment. Because of that, Bold says that if arginine deiminase, or some other similar autophagy-related drug, is used routinely, it likely will be given with a traditional chemotherapeutic agent to provide a one-two punch.

“The benefits have really been outstanding in the liver,” Bold says. “Do we want to move it to clinical trials in pancreatic and prostate cancer? Absolutely. Now we have this whole new avenue open for cancer therapy.”

~ Richard Bold
Ionizing radiation: a double-edged sword in cancer

UC Davis researchers enhancing benefits and reducing harm of exposure

Imaging techniques that use ionizing radiation, such as computed tomography (CT) scanning and mammography, have had a tremendous impact on cancer care, allowing many tumors to be detected at a stage when they are easily treated. Radiation therapy, in which tumors are targeted with higher doses of radiation, has saved the lives of countless cancer patients.

“Radiation,” says Richard Valicenti, chair of the Department of Radiation Oncology at UC Davis, “is of great benefit in detecting cancer, eliminating cancer and improving survival.”

But as valuable as it is in cancer diagnosis and treatment, ionizing radiation must be used carefully, because it can cause side effects such as burns and hair loss that become apparent soon after the exposure, or arise many years later in the form of secondary cancers.

Recent news reports have highlighted a few cases of radiation overdoses in clinics and added urgency to efforts to ensure the safe use of radiation in diagnosis and treatment – efforts in which clinicians and researchers at UC Davis figure prominently.

“We were looking into this problem before it got all this publicity,” says Ralph deVere White, director of UC Davis’ Cancer Center. “We have a lot of experts, all basically asking the same question: How can we reduce exposure while maintaining the benefit?”
Surrounded by radiation sources

Ionizing radiation can damage DNA, but our bodies are adept at performing repairs, so we can handle low exposures.

“If you can repair the cell,” deVere White says, “it’s not going to be mutated and you’re not going to get cancer.”

Low levels of radiation are naturally present in the environment: cosmic radiation from outside our solar system constantly bombards Earth; rocks and soil can contain radioactive atoms; and radiation from radon gas is a significant problem in some parts of the country.

“We get the equivalent in background radiation of a head CT every year,” says John Boone, professor and vice chair of the Department of Radiology at UC Davis Medical Center, who is an expert on the physics of CT scanning and serves as chief science officer for the American Association of Physicists in Medicine.

David Rocke, a biostatistician at UC Davis, researches the effects of low-dose radiation in the environment and in medical imaging. He explains that humans have evolved mechanisms to deal with the damage that comes from exposure. He’s also looking at the effects of radiation at a molecular level, using skin discarded from surgery and other procedures and an artificial skin model.

“There are a lot of differences between individual people in their

“It would be a tragedy if patients who truly needed CT scans didn’t get them because they perceived that the risk was too great.”

~ Jerrold Bushberg
problems in soft tissue, such as pneumonia.

Computed axial tomography, a diagnostic imaging tool that uses X-rays, was introduced in the 1970s. CT has enabled clinicians to detect and monitor many types of cancer, as well as other diseases, and to assess the extent of injuries.

“The CT scan is one of the most important inventions of the 20th century,” says Ramit Lamba, director of CT at UC Davis Medical Center and assistant professor in the Department of Radiology.

Ensuring patient safety

UC Davis researchers also are involved in reassessing and standardizing procedures for CT scanning and other radiation-based techniques for the hospital and clinics, as well as the industry.

At UC Davis, diagnostic and therapeutic procedures involving radiation have been reviewed to ensure patient safety, and new quality control procedures have been implemented to ensure proper functioning of machines, training of staff and thorough review of protocols for delivering radiation during diagnosis or therapy.

Ionizing radiation was first used in medicine in 1895 when Wilhelm Conrad Roentgen produced an image of the bones of his wife’s hand, calling it an “X-ray.” Later, X-rays became an invaluable tool to examine the skeletal system and to investigate

response to radiation,” says Rocke. “If you know who is radiosensitive and who is not, it may influence the choice of therapies.”

Imaging errors rare

Among imaging techniques that use ionizing radiation, CT scanning delivers the highest dose, and some researchers have suggested a link between CT scans and cancer. DeVere White, however, says many other risk factors may be involved, and notes that cancer patients, often diagnosed and monitored using CT scans, are more likely to get secondary cancers in any case.

“These studies really do raise questions, but they don’t answer them,” deVere White says.

As a result, Lamba says, “we have to treat CT scanning as potentially carcinogenic – without causing alarm.”

Several cases of radiation overdoses from CT scans – in which human error led to incorrect doses – have made headlines recently. And while tragic, such occurrences are extremely uncommon among the 62 million CT scans performed every year, according to a 2007 study in the New England Journal of Medicine.

“CT scans are extraordinarily safe,” deVere White says. “And there’s absolutely no doubt that CT scans have saved a lot of lives.”

Jerrold Bushberg, clinical professor of radiology and director of health physics programs at UC Davis, adds that CT scanning “has quite literally revolutionized the practice of medicine.” In some cases, without it, the patient would be having exploratory surgery.

“It would be a tragedy,” Bushberg added, “if patients who truly

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~ Richard Valicenti
At UC Davis, **diagnostic and therapeutic** procedures involving radiation have been reviewed to ensure patient safety, and **new quality control procedures** have been implemented to ensure **proper functioning of machines**, training of staff and thorough **review of protocols** for delivering radiation during diagnosis or therapy.

needed CT scans didn’t get them because they perceived that the risk was too great.”

Before ordering a CT scan, clinicians should consider if it’s really necessary, says Nathan Kuppermann, chair of emergency medicine at UC Davis and co-author of an article on overuse of CT scanning in injured children, which appeared in the journal The Lancet. Although CT scans have greatly improved our ability to care for the trauma patient, CT scans should be used selectively to avoid unnecessary exposure to ionizing radiation.

If a CT scan is justified, the radiation dose should be optimized to be as low as possible while still sufficient for diagnostic purposes.

**High doses required for treatment**

Radiation doses delivered during diagnostic tests are small compared to those used to treat cancer, which can be thousands of times higher. Prostate cancer treatments, for example, typically involve daily doses to the prostate that total, over the course of treatment, “more than 10 times what would kill a person if their whole body was exposed to it,” Rocke says.

Radiation is a valuable anti-cancer weapon because cancer cells can’t repair radiation damage as readily as normal cells, and so are more susceptible.

“You can eliminate pretty much any cancer growth with minimal effects to the patient,” Valicenti says, “but all that is very much dependent on one’s ability to apply technology to ensure the greatest degree of safety and accuracy.”

Radiation treatment used to involve a more scattershot approach, he says, but now, the radiation beam can be more accurately targeted at a tumor, so “treatments have become very precise and much more intensified,” Valicenti says.

Although much of the process of radiation therapy is automated, humans still play an important role, Valicenti says. New procedures have been put in place to ensure treatment plans are peer-reviewed, and that each treatment is evaluated as if it’s the first – to avoid the possibility of an error being perpetuated.

“We’ve reengineered and re-designed our quality assurance systems,” Valicenti says, “with a focus on continuous quality control.”
Imagine conducting leading-edge cancer research as an undergraduate student.

Angela Echeverri-Lompre and eight other UC Davis students are at the forefront of medicine through the cancer center’s Emerging Technologies Continuing Umbrella Research Experiences program (ET-CURE).

For about 10 hours each week, the nine undergraduates don lab coats and work in one of four cancer center research laboratories. The students conduct research into developing new cancer diagnostic tools and therapies, and work with mentors who help guide their careers.
“Diversity is sorely lacking in cancer research. We wanted to create a program that would bolster the number of students who traditionally are not represented in this field, especially in upper research echelons.”

~ Marco Molinaro

“I’ve never really had a chance to work in a lab hands-on before,” says Echeverri-Lompre, 25, who immigrated to California from Colombia at 17. “It’s been so extraordinary to learn what cancer can do – how it can affect the body. I want to be able to learn how we can stop this.”

The goal of the ET-CURE program is twofold: Professors hope to give undergraduate students a taste of hands-on lab research, and cancer center leaders hope the experience will entice underrepresented minority students to pursue careers in cancer research and treatment.

The approach appears to be working. Echeverri-Lompre and several other students in the program say they now intend to pursue dual careers as cancer physicians and researchers.

“It’s allowed me to see that I have the potential not just to treat patients, but to go into a lab to research the diseases,” says Echeverri-Lompre, who transferred to UC Davis after two years at Solano Community College.

That’s what Marco Molinaro, director of ET-CURE and chief education officer for the Center for Biophotonics Science and Technology (CBST), is hoping to hear from participating students.

“Diversity is sorely lacking in cancer research,” says Molinaro. “We wanted to create a program that would bolster the number of students who traditionally are not represented in this field, especially in upper research echelons.”

The program, which started in the summer of 2009, is funded through the National Cancer Institute’s Center to Reduce Cancer Health Disparities, and the National Science Foundation, which funds CBST. Another CBST program, CURE High School Research, which began four years ago, links high school students from St. HOPE Academy at Sacramento High School with UC Davis cancer scientists and clinicians. Both programs aim to increase the number of members of underrepresented groups in the sciences and, specifically, cancer research.

“We want them to see that careers in science and medicine are doable,” says Molinaro.

The push for greater representation of minority students in cancer research is grounded in the idea that physicians and researchers from underrepresented groups are more likely to treat and research cancer disparities in those groups.

For ET-CURE student Leah Meza, 22, that approach makes sense.

“It’s allowed me to see that I have the potential not just to treat patients, but to go into a lab to research the diseases.”

~ Angela Echeverri-Lompre
“Who better to serve these same individuals and groups and cultures than those who come from those groups?” says Meza, who is of Mexican and Puerto Rican descent. Meza is pursuing an undergraduate degree in cell biology and has applied for a two-year post-bachelor’s degree program at the National Cancer Institute in Maryland. Ultimately, she will apply to medical school and pursue a dual M.D. and Ph.D., possibly in oncology.

Meza says her eyes were opened to such career possibilities by her mentor, Kit Lam, who runs the cancer research lab where she works through the ET-CURE program.

“I try to encourage them and inspire them,” says Lam, professor of medicine and chair of the Department of Biochemistry and Molecular Medicine.

Lam hosts four ET-CURE researchers in his lab. He stresses that the students are not just repeating what other researchers do in the lab, but are conducting “state-of-the-art” research themselves. Meza had a paper published recently in the journal Medicinal Chemistry, Lam says.

Meza is researching peptide ligands, small proteins that bind to receptors on the surface of cancer cells. Researchers are hoping to find peptide ligands that will bind to cancer cells but not to normal cells, and use them to deliver drugs to the cancer cells for treatment.

Echeverri-Lompre is focused on pancreatic cancer, working to identify a ligand that binds to the cell surface so that physicians may one day be able to attach an imaging agent to it. The imaging agent would allow earlier detection of cancer, hopefully before it has spread to other parts of the body.

“This way, we’ll be able to see where the cancer is and treat it,” says Echeverri-Lompre.

Tem Woldeyesus, 20, a junior at UC Davis in neurobiology and another ET-CURE student, says he “fell in love with clinical research” in Lam’s lab. Woldeyesus, whose parents immigrated to the United States from the east African country Eritrea shortly before he was born, is interested in researching brain tumors.

“A lot of things that I learn in class, I apply in the lab,” says Woldeyesus.
Woldeyesus says that Lam gives the students room to really analyze their lab results. “He doesn’t spoon-feed us everything,” he says. “He makes us think.”

Woldeyesus says that he, too, would like to pursue a combined M.D.-Ph.D. program in medicine. “In a perfect world, I hope I could be a professor at a medical school, having my own lab and practicing medicine,” says Woldeyesus. “I’d like to prescribe a drug I discovered.”

Molinaro says helping ET-CURE students envision various career trajectories is a critical goal of the program. He says the mentors’ approach is akin to “life coaching.” Mentors help guide the students by advising them of the various programs available and then helping with the application process.

“But we take a very holistic view,” says Molinaro, adding that one student is planning a stint in the Peace Corps before he pursues his medical degree.

Through the CURE program, high school students are exposed to the world of research and medicine. The students study cancer in their science classes the first semester of the program, then conduct independent research projects, typically investigating toxicology, throughout the second semester. During the summer, they conduct research in cancer laboratories with the help of cancer center researchers.

“The idea is that if you get kids interested in science at a younger age, you might open up the door for a college experience or potential career they hadn’t considered,” says Michelle McCombs, CURE program manager for CBST.

ET-CURE student Meza, the only member of her family to attend college, says that she now has a strong sense of certainty what she wants to do with her life – treat cancer and research cures for the killer disease.

“In the perfect world, I hope I could be a professor at a medical school, having my own lab and practicing medicine. I’d like to prescribe a drug I discovered.”

~ Tem Woldeyesus

“I’ve never been more sure,” Meza says of her career path. “I never would have had that opportunity if not for a program like ET-CURE.”
Patient focus>>

Healing that’s more than skin deep

Cancer surgeon tracks disparities in post-mastectomy breast reconstruction

As soon as she was diagnosed in January 2009, Shadowens, 42, was determined to get the treatment she both needed and wanted. She found herself in the care of Dr. Steve Martinez, a surgical oncologist at UC Davis Cancer Center. After her second lumpectomy and on Martinez’ recommendation, Shadowens opted for a double mastectomy, followed by plastic surgery to reconstruct her breasts.

“For me, it was never an option to do nothing. I felt I would feel more normal,” Shadowens says. “I didn’t even give him a chance to offer reconstruction. I said, ‘fix me, and make me look like a woman, not a maimed woman.’”

Recently, she participated in the annual Susan B. Komen Race for the Cure. At least seven women on her race team have battled the disease and have had breast reconstruction after undergoing mastectomy.

This may be because Shadowens and her teammates live relatively close to urban Sacramento. According to a new study by Martinez, breast cancer survivors in more rural counties are less likely than their more urban counterparts to receive breast reconstruction after their mastectomies.

Martinez studied a database with information about the treatment of more than 7,000 Northern California breast cancer patients. Of these, 3,552 had complete information regarding the use of breast reconstruction. All resided in Sacramento and 13 neighboring counties. When Martinez examined where these patients lived, he found stark differences in the extent of treatment they received. Patients from primarily rural counties or counties with only smaller cities, such as Amador, Butte, Stanislaus and San Joaquin counties, were 27 percent to 49 percent less likely to receive breast reconstruction.
than their urban neighbors.

“Maybe the people who wish not
to receive breast reconstruction
happen to be the same ones who live
in rural areas,” says Martinez. “But
I have no reason to believe most of
those women would live in Alpine
or Amador counties; they don’t
sequester themselves there.”

Nor can the difference be
ascribed to patient affluence.
Insurance companies are legally
mandated to cover breast recon-
struction after mastectomy, whether
or not the care is delivered by a
network provider.

Martinez suspects that the
disparity boils down to access to care.
In outlying areas, medical facilities
are probably less likely to offer
reconstruction to patients. This
might be due to a paucity of plastic
surgeons or even a failure to educate
patients that the procedure is an
option. If the procedure isn’t available
in local hospitals, women are forced
to travel long distances to receive
treatment, at a cost of additional time
and expense that many cannot afford.

“People say that all politics is local.
The same is true for medical care.
How you get treated depends on
where you are,” Martinez says.

Martinez began the study last
year after being awarded funds for his
breast cancer research by the Amador
County Cancer Research Foundation.
With a desire to give something back
to the community that sponsored
him, he decided to examine how
Amador County and surrounding
areas performed in terms of breast
reconstruction. “I wanted to look at
the disparities in outlying areas
relative to Sacramento,” Martinez says.

Warren Tseng, a UC Davis general
surgery resident, assisted him in the
research project.

Martinez called the project the
“Sacramento Area Breast Epidemiology
Study,” or SABES, which is also
Spanish for “you know.” He considers
the study a pilot for a larger investiga-
tion of whether disparities exist
across a wider spectrum of breast
cancer care, including radiation

According to a new study
by Martinez, breast cancer
survivors in more rural
counties are less likely
than their more urban
counterparts to receive
breast reconstruction
after their mastectomies.
therapy, hormonal therapy and chemotherapy. Together, these measures should provide a strong indicator of cancer care availability in Northern California.

Although breast reconstruction is not medically necessary, other studies suggest it is a good indicator of patient outcomes. Women who receive reconstruction have improved rates of survival. While this may be due to factors such as insurance coverage or cancer stage, Martinez says it also is associated with a woman’s investment in her own treatment. Patients who receive reconstruction are more likely to be involved in their care, more willing to commit to multiple surgeries, and must receive a greater degree of medical care and surveillance afterward.

“Perhaps we shouldn’t consider it reconstruction but rehabilitation,” Martinez says. “It’s all part of the process of feeling better and moving on from the cancer.” Martinez himself does not perform reconstruction surgeries, which are done by plastic surgeons.

Wendy Shadowens would certainly agree, despite the fact that breast reconstruction is a long and often painful process. While still on the operating table after her mastectomy in March 2009, Shadowens had temporary expanders – bags filled with saline solution – inserted in her chest. Their job is to gradually stretch the muscle and skin to accommodate permanent silicone implants. After about a month of healing, Shadowens began visiting her plastic surgeon every week to have more fluid added to the expanders.

“The expansion process is a pain,” she says. “It hurts. You spend six months taking Vicodin.” Eventually, she had an operation in which the expanders were replaced with silicone implants. A mismatch between the size of her rib cage and her implants meant that Shadowens had to undergo an additional surgery. She still has weakness in her pectoral muscles, and faces one final surgery later this summer to reconstruct her nipples. “But the end results are worth the pain you go through.”

Even after the discomfort and inconvenience, Shadowens is extremely happy that she decided to have her breasts reconstructed. “If I didn’t tell anyone I was a breast cancer survivor, they would never know,” she says. “It’s almost as if you went through a terrible car accident that hasn’t left a major mark – there are no scars to show the world.”
African-American women have poorer survival rates than their white and Hispanic counterparts regardless of whether they receive radiation therapy following lumpectomy or mastectomy, Steve Martinez, assistant professor of surgery at UC Davis Cancer Center, has found.

Martinez determined that while Hispanic and African-American women with advanced breast cancer are less likely to receive radiation therapy than their white counterparts, only African Americans have poorer outcomes than white patients with the same stage disease.

The findings, presented recently in Washington, D.C., at the Association for Clinical Research Training and the Society for Clinical and Translational Science meeting, suggest that the lack of radiation therapy treatment is not responsible for the poorer survival noted among African-American patients.

“Is this a biological difference?” Martinez asks. “Do black patients benefit from post-surgery radiation therapy to the degree that Hispanics and whites benefit?”

These questions are part of Martinez’ ongoing exploration of cancer health disparities as they affect patients’ response to therapy and overall survival. A surgical oncologist, Martinez is one of many clinicians at UC Davis Cancer Center who also are finding ways to address the disproportionate cancer burden for certain patient populations.

The current study is one of two Martinez undertook to examine factors influencing survival for breast cancer patients. In the first, he looked at data from more than 12,000 women from throughout the country who had breast cancer that had spread to 10 or more lymph nodes and that had resulted in either lumpectomy or mastectomy.

“By definition, all of these patients should get radiation therapy,” he says. What he found was that Hispanic patients were 20 percent less likely to get radiation therapy than their white counterparts, and black patients were about 24 percent less likely to receive radiation therapy.

For the second study, he wanted to learn whether the disparities in receipt of radiation therapy resulted in poorer outcomes for Hispanic and African-American women.

“That is not what we found,” he says. “Hispanic patients were not significantly different from white patients in overall survival rates, but black patients did worse. This survival disparity seen in black patients was unrelated to whether or not they received radiation therapy as part of their treatment.”

Martinez examined 10-year survival rates in patients from each group who received radiation therapy and those who did not. While he found dramatic differences in survival for white women who had radiation therapy (an 11 percent survival boost), black patients had just a 3 percent improvement in survival.

Martinez plans to continue his research into factors that may influence whether patients receive radiation therapy and that may also affect outcomes, including possible biological differences.

“We are trying to see which treatments work best for which people,” he says. “Ultimately, we can figure out treatments that may work well for you, but not for someone else. This is a step on that path.”

What he found was that Hispanic patients were 20 percent less likely to get radiation therapy than their white counterparts, and black patients were about 24 percent less likely to receive radiation therapy.
The idea seemed irresistible to Holly Degner at the time, a surefire ticket to teen coolness – a tattoo.

Degner was 17 then, a high school senior whose friend knew a guy performing body art in his Sacramento garage.

“It was fast, it was cheap and he didn’t check my ID,” recalled Degner, now 29. “Just like that, I had a butterfly on my back and my five minutes of fame on campus.”

Fortunately, the young student did not contract a blood-borne virus from the experience. Older and wiser now, Degner still loves her tattoo but wants other teens to take precautions before making a similar leap. As part of an educational campaign jointly sponsored by the UC Davis Cancer Center and Sacramento State University, she is warning college students about the risks of contracting hepatitis C virus (HCV) and other dangerous viruses from tattoos and body-piercing.

A startling 40 percent of students believed tattooing and body piercing were unlikely to pose health risks.
students knew little about hepatitis C — a chronic disease with no cure that is a leading cause of liver cancer — or how it is spread, according to Marlene M. von Friederichs-Fitzwater, a faculty member with the cancer center and UC Davis School of Medicine, and director of the UC Davis Cancer Center Outreach Research and Education Program. “There were a lot of misconceptions about it,” she says. “Many students thought they had already been vaccinated against it, most likely confusing it with hepatitis B. In fact, there is no cure for hepatitis C, and treatments are only about 40 percent effective in controlling it.”

Von Friederichs-Fitzwater and her principal partner in the project, Sacramento State health sciences professor Heather Diaz, says their aim is not to ban, or even discourage tattooing and piercing. Body art has been around for thousands of years, they note, and young people today are embracing it in unprecedented numbers.

Instead, their goal is to ensure that those seeking tattoos or piercings simply ask some important questions about sterilization and other practices before going under the needle. Many customers may believe body art parlors are required to observe minimum safety standards, but they are in fact largely unregulated businesses in California and many other states. “The goal is to help students make sound decisions and think twice

“The place looked clean, and they shaved my arm and cleaned it with alcohol. They opened the needles so the package was new. But to tell you the truth, I wasn’t too worried. I’d heard the place was pretty legit.”

~ Jeremy Scott
before acting on the spur of the moment,” Diaz says. “One of our targets is the girl who goes to a party and, on impulse, decides to get a little half-inch heart on her body and winds up years later suffering from hepatitis C.”

For von Friederichs-Fitzwater, the issue is as personal as it is professional, because one of her grown sons is battling chronic HCV and resulting liver cirrhosis.

Two years ago, at the age of 50, Richard was diagnosed with the disease and given six months to live. He is still undergoing alternative treatments and believes he picked up the virus from a tattoo in the 1970s or 1980s.

“Like many patients, my son had this disease for years and never knew it because he had no symptoms,” von Friederichs-Fitzwater says. “That’s one reason hepatitis C is often called ‘the silent epidemic.’”

Epidemic is not an understatement, she added, because experts predict hepatitis C eventually will kill more people worldwide than AIDS. Nearly eight in 10 people infected with the virus go on to develop chronic hepatitis C, putting them at risk of liver disease, cirrhosis and liver cancer.

Despite its severity, hepatitis C is not well-understood by the public—students included. Many believe it is a disease that affects only prisoners and intravenous drug users, but that perception is outdated.

“I think when students think about hepatitis at all, they think about the kind you get from a bad salad bar,” Diaz says, referring to hepatitis A, which is spread differently and is typically not deadly. “There really is very little awareness of how serious this disease is and how easy it is to get it.”

Jeremy Scott, a senior majoring in engineering at UC Davis, is among those acknowledging that they have “no idea” how big a health threat hepatitis C can be. Scott got his two tattoos—one on each shoulder—at a shop in Davis from an apprentice who was giving them out for free.

“The place looked clean, and they shaved my arm and cleaned it with alcohol,” says Scott, 23. “They opened the needles so the package was new. But to tell you the truth, I wasn’t too worried. I’d heard the place was pretty legit.”

When UC Davis senior Curt di Cristina went into a local shop called Urban Body for his ankle tattoo, he was somewhat more informed about the disease, in part because he had worked at his father’s dental office, where sterilization is a workplace priority. Di Cristina and a handful of brothers in his Sigma Chi fraternity have tattoos depicting the fraternity’s letters and three dots symbolizing its organizational aims—friendship, justice and learning.

“The health risk was definitely

Their aim is **not to ban, or even discourage tattooing and piercing.** Instead, their goal is to ensure that those seeking tattoos or piercings simply **ask some important questions** about **sterilization** and other practices before going under the needle.
something I worried about going in, because when you’re using needles, there is potential for HIV or a lot of other scary, bad diseases,” di Cristina says. “But when I saw that the artist was using a type of sterilization instrument my father uses, that allayed a lot of my fears.”

To reach students, Be Smart with Body Art campaign organizers are working on multiple fronts, and have enlisted support from leaders of the professional tattooists and body piercers associations as well as representatives from the piercing and tattooing industries. They have aired radio ads; run TV spots in English, Cantonese and Vietnamese; distributed materials to student health centers at colleges and universities in California; and planned campus events to highlight the hazards and provide students with five simple safety questions to ask before obtaining body art.

Working with the student public health club at Sacramento State, leaders of the effort also plan to hold workshops for incoming residents of campus dormitories.

“We’re trying to hit freshmen coming in because that’s when they feel the need to let loose,” says Jasmine Pettis, 22, who is president of the public health club and, with three tattoos, has some personal experience to lend the campaign.

“We want to make sure students don’t just get drunk one weekend and get a tattoo in someone’s garage.”

Degner, for one, hopes the message gets through.

“I’m living proof of what not to do,” says Degner, a Sacramento State senior heading to nursing school in the fall. “I can’t change the past, but I can help others avoid the mistake I made.”

5 QUESTIONS TO ASK WHEN GETTING A TATTOO OR PIERCING

1. Do you use only new needles?  
   [watch the artist open the package]

2. Do you use new ink caps for each client?

3. Do you sterilize all equipment that may come into contact with blood?  
   [ask to see sterilization process and log]

4. Do you wear single-use latex gloves?

5. Do you cover fresh tattoos to prevent infection or hepatitis C virus transmission?  
   [Make sure your tattoo is covered with a sterile, absorbent dressing]

Learn more about safe tattooing and piercing at www.besmartwithbodyart.org.
Extending the reach of research

Auburn community’s endowment fund fuels discovery engine

Basic cancer research rarely delivers slam-dunk results right after the game clock starts. Scientists often spend years on a painstaking quest to unravel elusive mysteries defying our full understanding of the disease.
Finding funds to support pioneering laboratory work is almost as arduous as the science itself. That’s what makes the support of the Auburn Community Cancer Endowment Fund so vital to the UC Davis Cancer Center.

The endowment fund got its start in 2001 after three friends in the Sierra foothills city got together over a cup of coffee and decided to raise money for the war on cancer. By 2006, they had enlisted dozens of friends and businesses in the campaign and had amassed a whopping $1.5 million, enough to fund an endowed chair in basic science research.

Their accomplishment was a first. While other endowed chairs at UC Davis have been named after individuals and corporations, never had one been created in honor of an entire community.

Since its establishment, the fund has produced annual dividends of about $70,000 to support work coordinated by Hsing-Jien Kung, director of basic research at the cancer center who also holds the endowed chair in basic research.

Kung says the financial help from Auburn is “absolutely critical” to the cancer center’s research mission, particularly at a time when the scramble for federal dollars is more competitive than ever.

“Even in a good funding climate, this endowment allows recipients to do highly innovative, ‘out-of-the-box’ research beyond what federal funding normally supports,” Kung says.

Typically, he noted, government funds are reserved for established research supported by promising data. Newer ideas that may be “a bit premature for prime time” are more difficult to fund, so the endowment “gives us much needed flexibility in our work,” Kung says.

Kung joined UC Davis in 1998 as the center’s deputy director and chief of basic science, and since then, he has built the research program into a powerful engine delivering advances in cancer treatment. Today, his campus lab is abuzz with the work of 10 talented students and postdoctoral researchers tackling prostate cancer and other projects.

Among them is Ling-Yu Wang, 34, who earned a Ph.D. in
Finding funds to support pioneering laboratory work is almost as arduous as the science itself. That’s what makes the support of the Auburn Community Cancer Endowment Fund so vital to the UC Davis Cancer Center.

“A research in our lab, in close collaboration with another lab at UC Davis, indicates that this protein has an important role not only in prostate cancer but in several other cancers,” she says. “Initially, this idea looked interesting but was risky because we did not have any data. The endowment money allowed us to pursue something that wouldn’t have been possible otherwise, which is a huge benefit.”

Kung says that researchers in a third project aided by the Auburn endowment are examining how withholding certain nutrients from prostate cancer cells can effectively kill those cells. Specifically, Kung says his colleagues and researchers from Richard Bold’s lab have identified a particular amino acid that, when withheld, causes “nutritional starvation” in the tumor cells without harming healthy cells.

“Most cancer therapies try to poison the cancer cells, but of course this approach can have toxic side effects for patients that are sometimes devastating,” Kung says. “The new trend is to starve the cells to death with a treatment that would remove certain critical nutrients from the blood, causing autophagy, or ‘self-eating.’” (See “Building on basics” in this issue.)

For Virgil Traynor, this news from the lab is immensely rewarding. Traynor, a retired veterinarian, was one of three buddies who launched the Auburn fund, and he has been a spark plug for continual fundraising ever since.

A prostate cancer survivor, Traynor says the endowment is an achievement of the many, not the few. Countless barbecues, golf tournaments, motorcycle rallies, Christmas parties, fun runs and other events – along with individual donations – have combined to make the endowment flourish.
Thunder Valley Casino, operated by the United Auburn Indian Community. “We’re very proud and inspired by what this has become,” Traynor says. “And while I think any money that goes anywhere for cancer research is good, the advantage that we have is we personally hand them the money and get to see what happens from there.”

For Kung, the personal connection also matters. Prior to joining UC Davis, he held an endowed chair at Case Western Reserve University. “That was a single donor, a grateful patient,” Kung says. “But with the Auburn fund it’s like a grassroots campaign, with contributions from multiple people who share our goal of curing cancer. “In that way, this endowment is something that I especially cherish.”
Young patient visits the president

Jabril Malik Debrow could have had a PlayStation 3, or taken a ride on a private airplane or shaken hands with a movie star. When given a chance for a wish come true, however, the 10-year-old Fairfield boy had a better idea.

“I thought about it for a few days, and I decided I wanted to meet Obama,” he says. “I thought about how nice he seems, all the stuff he does, and how he is trying to help people and make the world a better place.”

Thanks to the Make a Wish Foundation, Jabril got his wish. The trip, at first fraught with complications, was everything he had hoped for, including a chat with the president in the oval office, a few frames of bowling in the White House bowling alley, a gift of a presidential yo-yo and an introduction to a bomb-sniffing dog and secret serviceman.

Jabril returned home and wrote a story about his experiences to share with other people who might be facing their own cancer diagnosis and treatment. He gave the story to the doctors and nurses caring for him in the UC Davis Pediatric Cancer program.

“I wrote the story so that it could help other people who have cancer, so they can have a positive attitude so they won’t get sad and cry – or only cry for one day and then let it go – and start being happy like it never happened,” he says.

Since his trip, Jabril was an invited guest at a Kings game, helped raise money for pediatric cancer research at the St. Baldrick’s fundraiser at deVere’s Irish Pub and went on air to benefit Children’s Miracle Network during the radiothon.

Jabril Debrow was diagnosed in October of last year with a very rare, aggressive and difficult-to-treat kidney cancer called renal medullary carcinoma, which has spread to his liver and lungs. His is one of only about 140 cases in the world, and he is among just a handful of children with the disease.

Promising findings on walnuts

Walnut consumption slows the growth of prostate cancer in mice and has beneficial effects on multiple genes related to the control of tumor growth and metabolism, research from UC Davis and the U.S. Department of Agriculture Western Regional Research Center in Albany, Calif. has shown.

Paul Davis, nutritionist in the Department of Nutrition and a researcher with the UC Davis Cancer Center, said the findings provide additional evidence that walnuts, although high in fat, are healthful.

“This study shows that when mice with prostate tumors consume an amount of walnuts that could easily be eaten by a man, tumor growth is controlled,” he says. “This leaves me very hopeful that it could be beneficial in patients.”

Prostate cancer affects one in six American men. It is one in which environmental factors, especially diet, play an important role. Numerous clinical studies have demonstrated that eating walnuts – rich in omega-3 polyunsaturated fats, antioxidants and other plant chemicals – decreases the risk of cardiovascular disease. These findings prompted the U.S. Food & Drug Administration in 2004 to approve, for the first time, a qualified health claim for reducing heart disease risk for a whole food.

Davis fed a diet with whole walnuts to mice that had been genetically programmed to get prostate cancer. After 18 weeks, they found that consuming the human equivalent of 2.4 ounces of walnuts per day resulted in significantly smaller, slower-growing prostate tumors compared to mice consuming the same diet with an equal amount of fat, but not from walnuts.

Davis, whose research was funded by a grant to UC Davis from the California Walnut Board, said additional research is needed to further explore how walnuts reduce tumor cell growth.

“The bottom line is that what is good for the heart – walnuts – may be good for the prostate as well,” he says.

Grant helps boost minority clinical trials accrual

In its ongoing commitment to reduce the cancer burden on underserved groups, UC Davis Cancer Center will help lead a national effort to increase minority recruitment in cancer clinical trials.

Entitled EMPaCT (Enabling Minority Participation in Clinical Trials), the 18-month grant comes from the National Center on Minority Health and Health Disparities.

UC Davis will lead the western region in the five-center effort to assess...
existing approaches to minority clinical-trials accrual and then develop models for use by cancer centers nationwide.

Moon Chen, professor in the UC Davis Division of Hematology and Oncology, and EMPaCT regional principal investigator, explains that only when minorities take part in clinical trials can researchers find the best therapies for those patients.

“If we want to achieve the goal of customized therapy, we need to know a lot about how people are different, so we can tailor therapy to the individual’s specific genetic metabolic makeup,” he says.

Chen, who also is associate director of Population Research & Cancer Disparities at UC Davis, says some of the challenges for cancer physicians are language and cultural barriers, which, studies have shown, can perpetuate the misperception that participation in a clinical trial is coercive, punitive or dangerously uncertain for the patient.

UC Davis research has found that mass media campaigns and use of the internet do little to influence a patient’s decision about whether to join a clinical trial. Chen said assessment work for EMPaCT at UC Davis will focus more on the role of the physicians, research nurses and others in the accrual process.

**Meyers earns special honor**

Frederick J. Meyers, executive associate dean of the UC Davis School of Medicine, has been awarded the prestigious Lane Adams Quality of Life Award from the American Cancer Society, which recognizes excellence in the provision “of compassionate care and support to individuals with cancer.”

Meyers accepted the honor at a special American Cancer Society event in Atlanta on May 6.

The award is named for Lane W. Adams, a former executive vice president of the society, who established the award in 1985. According to the American Cancer Society, the award recognizes those “unsung heroes of cancer care who provide what Lane W. Adams himself affectionately referred to as the warm hand of service.”

Meyers is a nationally respected expert in hematology and oncology and played a pioneering role in the hospice movement. He established programs that now serve as national models for compassionate, end-of-life care.

**Brain tumor group celebrates anniversary**

When Juan Chapa was first diagnosed with a brain tumor in 2004, he looked to several sources for guidance, all of which offered this advice: choose a medical center with a support group.

Chapa found that at UC Davis Health System, where he was successfully treated and has been an avid member of the brain tumor support group ever since.

The group celebrated its 20th anniversary earlier this year at the Lawrence Ellison ambulatory care building. Although the group’s membership has changed over the years, it has consistently provided the kind of support and education patients need when navigating a brain tumor diagnosis, treatment and any ongoing complications.

Karen Smith, the neurosurgical nurse and volunteer, has led the meeting since its inception. Carolyn Guadagnolo, a licensed clinical social worker, is the co-facilitator.

“It’s like therapy, because it’s a group of people that can understand where you are at,” says Chapa. “At the same time you have Karen and Carolyn who can guide you through the whole thing.”

Smith, who has been a neurosurgical nurse at UC Davis since 1975 and now works at the hospital only two days a week, said the brain tumor group welcomes people from throughout the region, regardless of where they receive treatment. Most participants bring a family member to meetings, as well.

“They like to share anything new that has happened in their life,” she says. “Maybe they had an MRI, but don’t have the results yet, and they are frightened. It seems to help them to talk about it.”

Pam Guillin started attending the support group because she was looking for more information after being diagnosed in 1996 with a type of brain tumor called a glioblastoma multiforme. She has since had five surgeries and can no longer work, but lives life to its fullest. Now she attends support group meetings to help others.

“People walk in there and they are just shell-shocked with their diagnosis,” she says. “It’s so scary. If I go and say, ‘I’m doing OK,’ I feel like it’s a way of giving back.”

For more news stories, visit www.ucdmc.ucdavis.edu/cancer, click on “newsroom.”
Long-time patient Francesca Arnaudo facing new challenges with grace

By the age of 10, Francesca Arnaudo already had survived two cancer diagnoses – osteosarcoma, a bone cancer, and acute myeloid leukemia, a white blood cell malignancy – along with surgeries and months of chemotherapy and radiation. She pulled through with cheer and tenacity, earning the nickname “miracle girl” from UC Davis Cancer Center nurses.

Francesca went on to become the California representative in the 2007 Champions Across America tour, an awareness campaign for Children’s Miracle Network. The national philanthropy operates in 170 hospitals, including UC Davis Children’s Hospital. The tour took Francesca to the White House for a press conference and then to Disney World for the taping of a television show. She was also a Hyundai Hope on Wheels “Spokes-Kid” for 2006 and 2007.

One would think the child, now 13, had worn enough hospital gowns to last anyone’s lifetime. But in March 2009, Francesca’s doctors found a black dot on her lung.

Fortunately, it was discovered early, says her mother, Mary Arnaudo.

When surgeons removed the upper right lobe, “they found it was another type of cancer not related to any of the other ones I’ve had,” adds Francesca.

Not only was it a new cancer, but one that rarely appears in younger patients.

“Her particular lung lesion – bronchioalveolar carcinoma-like lesion – is better known to adult oncologists,” says Douglas Taylor, associate professor of pediatrics and Francesca’s oncologist. “In this case, the treatment was simplified by early detection and an excellent resection.”

Early detection helped spare Francesca chemotherapy and radiation therapy. After surgery, with strengthening exercises, Francesca said she got the hang of “breathing a little bit more in my left lung.”

But her ordeal didn’t end there. In December, she needed surgery to repair the prosthesis in her right humerus.

For the procedure, surgeons Robert Szabo and Robert Tamurian employed a cutting-edge technology used in orthopaedic oncology and limb-salvage reconstruction.

“The relatively new prosthesis utilizes static compression to induce her remaining bone to get stronger and ‘grow’ into the prosthesis, which we hope will provide life-long fixation,” Tamurian explains.

Thankfully, the bone is healing well, and Francesca’s attitude is – as always – even better. She’s student-body president and earns straight A’s, is active in hip-hop and tap (her teacher modifies the more strenuous moves, so that she can protect her arm), and she still loves to draw. In August, she is excited to become a freshman at Ripon High School.

“Shes doesn’t let anything stop her,” Mary says with admiration. “The other day there was a function at school – you can imagine how ugly the scar is, what with so many surgeries in the same place – and one lady said, ‘Well, bless her heart, she’s my hero; I would never wear a sleeveless dress!’ ”

The scars don’t bother the teen. “It’s God’s molding of me,” Francesca says. “Even though I lost out on a lot of my childhood, it made me more aware of who I am, and realize that I want to help others because of what I went through.”

Dear Synthesis editor,

I would like to thank you for running the wonderful article, “Man’s Best Friend, and then some.” My dog, (Clyde), too was a patient at the Center for Companion Animal Health, he was involved in the melanoma trial. Losing him to cancer was the single hardest thing in my life, a loss made easier by the knowledge that his participation in the trial would help further the research into finding a cure.

I also want to thank the wonderfully caring doctors and staff, especially Dr. Carlos Rodriguez and Teri Guerrero (the trial coordinator and Clyde’s buddy), at the hospital. I look forward to reading about the research into finding a cure through the participation of our canine companions in hopes of one day finding a cure. ~ Matt Havens, Clyde’s Dad
Spaghetti Western at Cooper Vineyards
Hosted by Amador Cancer Research Foundation to benefit UC Davis Cancer Center

Authentic Chuck-Wagon, Tri-tip Barbecue and Spaghetti Dinner

Also featuring:
• Tram rides, country-western band and dancing, silent and live auctions
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For more information, contact Cathy Landgraf, 209-245-6777 or Jago Landgraf, jcaliope@hotmail.com

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Ralph deVere White
Director, UC Davis Cancer Center

EXECUTIVE EDITOR
Carole Gan

EDITOR
Dorsey Griffith

ART DIRECTOR
Jodi Adkins

GRAPHIC DESIGN
Page Design Group

PHOTOGRAPHERS
Robert Durell
Keith Sutter

ILLUSTRATION
Circle Design

WRITERS
Ana Cotham
Anna Davison
Dorsey Griffith
Tim Kirn
Pamela Martineau
Jenifer Warren
Kathleen Wong

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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.

The 2010 St. Baldrick’s fundraising events at Westfield Galleria in Roseville and deVere’s Irish Pub in Sacramento raised nearly $200,000 for pediatric cancer research. Some 600 men, women and children shaved their heads for the cause, sponsored by the Keaton Raphael Memorial for the St. Baldrick’s Foundation. The UC Davis Cancer Center thanks everyone for their tremendous contributions.