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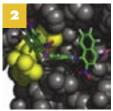
Using nanotechnology, bits of sugars, amino acids and polymers can be combined into new molecules known as synthetic high-affinity ligands (SHALs). Researchers at Lawrence Livermore National Laboratory and UC Davis Cancer Center are collaborating to create SHALs that will target cancer cells (see story on page 2).

UCDAVIS Cancer Center

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Designing nanosize molecules that seek out

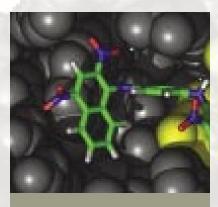
and infiltrate cancer cells

NANO oncology

Rod Balhorn, a biochemist at Lawrence Livermore National Laboratory, has always been fascinated with biological molecules and their surfaces. Their complex, convoluted structures determine which other molecules they will interact with among the thousands they encounter as they carry out their various functions.

"What if I could design molecules to interact in ways that I decide are important?" Balhorn often wondered. "What if I could create something that seeks out, recognizes, and sticks to the surface of a toxin. for instance, then destroys it?"

With the help of computer technology, biochemical manipulations and plain old trial and error, this sci-fi scenario is becoming a reality. With his collaborators at Lawrence Livermore and UC Davis Cancer Center, Balhorn has constructed unimaginably tiny molecules. He calls them SHALs (for synthetic high-affinity ligands). And his novel creations are beginning to show promise.



"What if I could design molecules to interact in ways that I decide are important?"

SHALs have a diameter of three to four nanometers (a nanometer is one-billionth of a meter). A virus, in comparison, is an ungainly 30 to 50 nanometers wide. To put this infinitesimally small scale in context, the distance between two lines of a fingerprint is about 80,000 nanometers.

SHALs are an example of nanotechnology, a young field that may have far-reaching implications for cancer. SHALs are among the most exciting results to emerge so far from the pioneering partnership between the UC Davis Cancer Center and Lawrence Livermore National Laboratory, in which scientists are turning biodefense technology into a new cancer offense.

Balhorn originally conceived of SHALs as a way to thwart bioterrorism. He wanted to design molecules to bind to potential bioterror agents like botulism or anthrax, in order to quickly and efficiently detect and neutralize them.

But it wasn't long before the biochemist envisioned

"Nanotechnology
is poised to
enable radical
new approaches
in cancer research
and care."

medical applications for his technology. "When I attended meetings with UC Davis Cancer Center researchers," he says, "I saw the potential of SHALs to fit their needs."

Prostate cancer weapon?

One cancer researcher excited about this potential is Hsing-Jien Kung, deputy director of the UC Davis Cancer Center and director of its basic science program.

Kung's research focuses on the androgen receptors on the surface of prostate cancer cells. When these receptors are "activated," they go into high gear, resulting in rapid cancer growth and a poor prognosis for the patient. But distinguishing this activated form of the disease from less aggressive prostate cancer has always been problematic. Enter Balhorn and his SHAL toolkit. Based on knowledge of the conformational structure of the activated receptor, Balhorn can design a SHAL that will bind to it. Attached to a fluorescent tag, the SHAL can lock onto activated androgen receptors and alert Kung that they are present in the prostate cancer cell.

Tiny Trojan horses

The work is still in its initial phases, but Kung is optimistic about its potential. "SHALs may be able to help a clinician predict whether a cancer needs aggressive therapy before it grows out of control," Kung says. "This is a remarkable technology with far-reaching applications that no other current method offers."

Kung also hopes SHALs may be used to fight prostate cancer directly. By competing with the androgens (male hormones) that would otherwise bind to activated receptors, Balhorn's SHALs may block the signal for more rapid cell growth and thereby inhibit the cancer.

Most cancer treatments today damage normal as well as malignant tissue, making such side effects as hair loss and nausea all too familiar to cancer patients undergoing conventional therapy.

But SHALs, like a Trojan horse, can be designed to carry their means of destruction with them, in the form of a radioactive isotope or potent anti-cancer drug. After seeking out and binding to cancer cells, SHALs can unleash their weaponry locally, minimizing the risk to normal cells. This would be a particular boon to patients with metastatic disease,

in which a cancer has spread throughout the body.

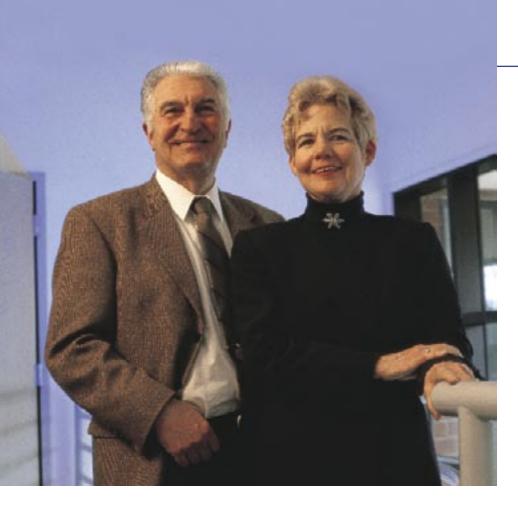
Gerald and Sally DeNardo, co-directors of the Radiodiagnosis and Therapy Program at UC Davis, are testing radionuclide-toting SHALs to attack non-Hodgkin's lymphoma cells in mice, an application that may be used in human clinical trials within the next few years. If this is successful, doctors one day may be able to deliver lethal radiation specifically to cancer cells, sparing normal tissue.

Nano-bandwagon

Nanotechnology, which encompasses minute biologics and machines on the scale of nanometers, has the potential to transform every medical discipline as well as a host of industries. Governments and private companies worldwide are jumping on the nano-bandwagon, investing around \$8.6 billion in 2004.

"Nanotechnology is poised to enable radical new approaches in basic cancer research and clinical cancer care," says Anna D. Barker, deputy director for strategic scientific initiatives with the National Cancer Institute, which last summer earmarked \$144.3 million for nanotechnology research over the next five years.

Nanotechnology's diminutive size gives it such enormous potential in medicine: nanosize molecules can cross membranes, enter cells and interact with other molecules within and among cells. "You need to get to a certain scale to gain access," Balhorn says. "Nanotechnology gives scientists the ability to actually mimic biologic processes."



Gerald and Sally DeNardo are testing radionuclide-toting SHALs against lymphoma cells in mice.

How to make a SHAL

To design a SHAL, Balhorn and his team perform computer searches of databases that list all commercially available organic molecules, including sugars, amino acids, dyes and detergents – some 300,000 in all – to find the best match for a target site. He then combines the chosen fragments into a single molecule and mixes this newly created particle with his target to see if they bind.

High affinity for the target is important, not just so the SHAL can do its job, but also so that it can outperform other molecules in the body that may fit the same target. If necessary, Balhorn can tinker with a SHAL to enhance its affinity for a particular target. For example, he has found that connecting two of his "best-fit" molecules with a "linker"

molecule improves its affinity up to a million-fold.

The synthetic molecules he creates act just like antibodies in the immune system, Balhorn explains. But unlike natural antibodies, SHALs are often too small to elicit an immune response – and therefore aren't destroyed by our body's natural defenses.

Along with his colleagues in the new field of nanotechnology, Balhorn has big dreams for these tiny tools: He hopes SHALs will revolutionize how researchers and clinicians learn about, diagnose and treat cancer and many other diseases of our time.

"This is a remarkable technology with far-reaching applications that no other current method offers."

A day in the adult infusion center at UC Davis Cancer Center

Lessons in living

The young Eastern European woman, her frail frame wrapped in a bulky blue sweater, shuffles into the infusion center, gripping her husband's bent arm for support. She speaks no English. Her fear is palpable.

Nurse Ester Molina greets her and steers her to one of the 19 adult infusion chairs at UC Davis Cancer Center. Molina gives the patient a pillow for her head and blanket for her legs. Her husband takes a seat at her side.

Forty-nine people will receive treatment in the infusion center today, several for the first time. But this young woman's arrival is cause for quiet excitement among the infusion staff. Diagnosed with lymphoma, the frightened patient has cancelled every appointment and refused all treatment, until now.

"If this goes well," charge nurse Gale Gibson says at the morning meeting, "she may decide to consent to treatment."

Of the nearly 3,000 new patients who are seen at UC Davis Cancer Center each year, many will pass through the



"Cancer
patients
don't sweat
the small
stuff."

infusion center. Chemotherapy drugs are administered here, and blood transfusions are given. Here patients receive care for their pumps, ports and PIC lines – technologies that improve delivery of anti-cancer drugs and enable patients to spend less time at the cancer center. Patients also learn how to take medications at home, how to cope with side effects and when to call the doctor.

Infusion center nurses are a special breed, versed in the latest chemotherapy drugs, equipped to recognize and handle allergic reactions and other medical emergencies, and skilled at managing such side effects as nausea and fatigue. They are also gifted vein-finders, humorists and listeners.

Over the course of the day the nurses will carefully review patients' lab test results to make sure each patient is strong is enough for treatment. If a patient's liver function is too compromised or a blood count is too low, treatment may be postponed. The nurses will check and double-check the name of each drug against the name of each patient, ensuring no one gets the wrong medication. They will give patients anti-nausea medications, timed for optimal effectiveness, and observe patients for adverse reactions. They'll offer crackers and bring juice. Between patients, they'll disinfect infusion stations, change pillowcases, fold laundry and stock supplies.

Sense of humor

Fear may be common here, but so are laughter, grace and courage. "When they walk through the door here for the first time, a lot of people are just terrified," Gibson says. "So we try to keep it light, keep a sense of humor. The people who work here are really good at that."

At one infusion station, nurse Marlene Perkins is swapping wisecracks with John Hauck, a retired trucker. The West Sacramento man is here for an infusion of mitoxantrone, a treatment for prostate cancer. The chemotherapy solution, flowing slowly from a bag over his head to a vein in his arm, is Popsicle blue. "When you leave here," quips Perkins, who has worked at the cancer center for

Nurse Anne Beatie checks in on retired engineer Frank Tate, a lung cancer patient, and his wife Pamela. more than 30 years, "you're going to feel like a giant Smurf." A conversation ensues about the Smurf cartoon show.

Later in the day, Jennifer Ducray-Morrill, former deputy treasurer of California, comes to her appointment bearing gag gifts for the nurses – yellow and pink bunny rabbit watches, finds from a trip to the Dollar Store. Gibson and Perkins gather to admire the gifts, but talk quickly turns to the upcoming wedding of Ducray-Morrill's brother. Despite her illness, she intends to host the reception in her Land Park home. She thinks she can make room in the fover for dancing.

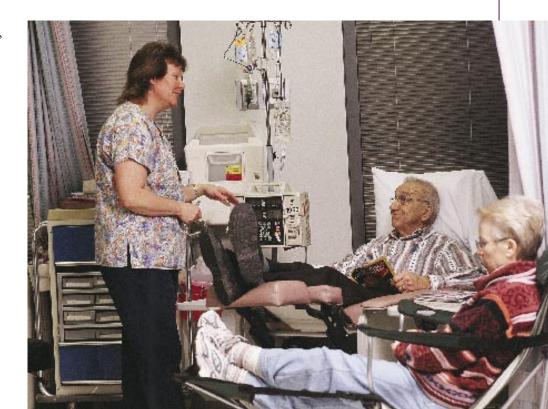
To keep her colon cancer at bay, Ducray-Morrill spends four consecutive days here every other week. It's a regimen she may need to remain on indefinitely.

"I certainly wouldn't choose this," she says. "But the staff couldn't be better. They keep everyone – and themselves – cheerful. Nobody is ever down. I don't know how they do it. They help you make the best of a bad situation. And I appreciate it so much."

Safe haven

Other patients express similar sentiments. "I know this sounds funny," says Nancy Spain, an administrative assistant in the ophthalmology department at UC Davis Medical Center, "but I never want to leave here. I don't know how to explain it. This is a safe haven."

Spain arrived at 8 a.m. and won't be released until 1:30 p.m. For five and a half hours, she will be tethered to a humming, beeping pump that will deliver a fixed rate and volume of taxol, a breast cancer treatment, into her bloodstream via the port implanted in her chest. Yet Spain feels so at home here, where everyone has cancer, that she spends the day with her hat off, bald head bare.







Joanie McCreary says her cancer makes her appreciate life more – even the traffic jams.



Freshly laundered blankets are warmed in an oven before patients get them.

"They are so great here," Spain says. "They hold your hand, all along this path."

The admiration is mutual. "You spend the best time you can with the patients while they're here," says Robert Araiza, a nine-year veteran. "And they show you how to live. A lot of cancer patients don't sweat the small stuff. They focus on what's important to them, their friends and family – and they remind me that I don't really have that many problems."

Joanie McCreary, a 46-yearold mother of two, arrives for her infusion armed with knitting, a portable CD player, earphones and a book. Her colon cancer diagnosis last year was a tough shock, but she says it now seems like a blessing. Her faith is stronger than ever, she says, and she feels grateful for every day. "I used to complain about all the traffic in Folsom when I'd drive my kids around to all their lessons and activities," she says. "Now I like sitting in traffic because I *can* sit in traffic."

Along with gratitude, generosity infuses this center. At the reception counter is a large basket with a hand-lettered sign: "Caps for chemo

patients. Please take one." Volunteers sew and donate the hats. Next to the hat basket is a candy jar filled with peppermints. Nurses keep the jar stocked using proceeds from the juice cans they save and recycle.

The gifts from patients to their nurses are ubiquitous: A bag of sugar-coated chick peas in the pantry, a giant tin of Almond Roca in the lunchroom, plants and thank you cards everywhere.

Patients also give to each other: They bring in their magazines, from *Harpers* and *The New Yorker* to *Teen People* and *Star*, hundreds in all. Last year a



"I just take one step at a time," says Nancy Spain, with nurse Chris Sharkey.





The day starts with a 7:30 a.m. staff meeting.



patient and her husband donated an ultrasound machine that makes it easier for nurses to find veins. One personal DVD player has been donated to the infusion center, with eight DVD movies. The nurses are seeking donations of 18 more mini DVD players, so that even when the center is full, every patient can watch a movie.

By mid-afternoon, five patients have pushed back their recliners, footrests up, and are asleep under their blue blankets. The lights in two of the infusion stations have been dimmed. The patient in station 9 is snoring softly behind a drawn curtain.

If not for the IV poles and needles, it might pass for an airplane cabin on an overnight flight.

The Eastern European woman has been asleep for most of her transfusion. Her husband hasn't left her side. Molina arrives to unhook her from the infusion pump, smile and say goodbye. The patient walks out, on her husband's arm. They both look relieved. She keeps an appointment with her doctor the following week, and begins chemotherapy the week after that.

"It's a rewarding job," says
Chris Sharkey, a nurse who has
also worked in hospice, home
health and management settings.
At 3:30 p.m., she finally has time
to fit in a half-hour lunch break.
Infusions are scheduled from
8 a.m. to 4 p.m. Monday through
Friday. Infusion center nurses
work four 10-hour days a week,
from 7:30 a.m. to 6 p.m. each
day, except when a treatment
runs late.

"Sometimes it can be sad," Sharkey says, "but we have the opportunity to help people, wherever they are in their journey. And that's always rewarding."

Reading helps pass the time for the Tates.



A ar ta

At right, nurse Robert Araiza tends Cynthia Leffler's PIC line. Leffler is being treated for breast cancer. At left, John Hauck and Marlene Perkins talk Smurfs.

Ambitious new information grid will translate

into better patient outcomes

WORLD WIDE Cancer Web

Cancer research has created an arsenal of diagnostic, prognostic and treatment strategies, putting powerful tools in the hands of clinicians.

But another mighty weapon – information – resides in the laptops, notebooks and minds of cancer investigators everywhere. For all of this data to be of real benefit, it has to be shared.

An ambitious new project aims to speed both information-sharing and scientific progress. Known as caBIG – for cancer Biomedical Informatics Grid – the project is lauded as the future of collaborative research.

"Sharing data, methods, computer programs and reagents is important in avoiding inefficient use of resources and in enabling broad-front research progress," says David Rocke, professor of biostatistics at UC Davis and one of the architects of caBIG.

A brainchild of the National Cancer Institute and the cancer research community, the \$20 million caBIG network



everything on the grid will be freely available to researchers and the public.

will enable cancer and biomedical researchers to develop and share tools and data in an open environment. Everything on the grid will be freely available to researchers and the public world-wide. The goal is to accelerate progress in all aspects of cancer research.

The grid will leverage the combined strengths of the NCI, its 60 national cancer centers, including UC Davis Cancer Center, and others in the cancer research field. In California, UC Davis is among five institutions tapped by the NCI to get the grid off the ground. Overall nearly 50 organizations are collaborating on the three-year project.

"UC Davis Cancer Center will help develop the cutting-edge communications capabilities that will be at the forefront of cancer research nationally," says Cecil Lynch, chair of the UC Davis Medical Informatics graduate group and an assistant professor in the UC Davis Department of Anesthesiology and Pain Man"Sharing data is important in avoiding inefficient use of resources and enabling broadfront research progress," David Rocke says.

agement. Together, Lynch and Rocke are responsible for the UC Davis contribution to the caBIG grid.

Sharing the harvest

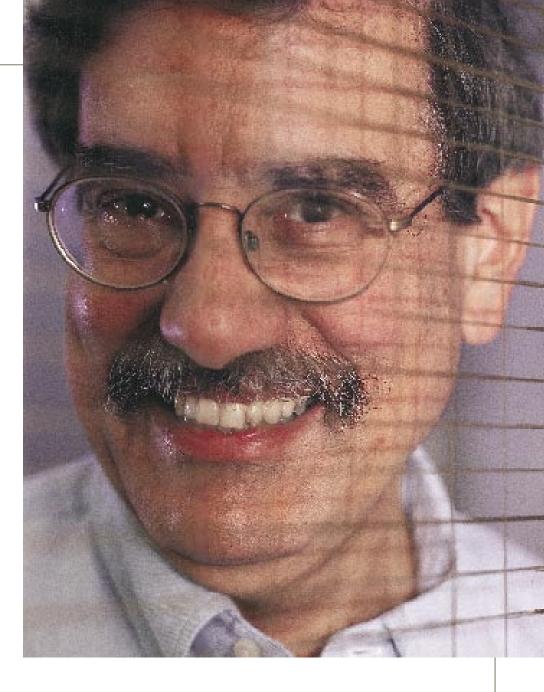
In the field of cancer research, information about cancer – from genetic and protein studies to clinical trials – is an abundant crop.

But cancer researchers may not always do a good enough job of sharing this harvest.

"It is currently difficult to combine and share data, information tools and knowledge in the cancer-centric and greater bioinformatics community," says Timothy Patrick, associate director of the National Library of Medicine's Biomedical and Health Informatics Research Training Program.

Indeed, NCI literature frequently laments that cancer researchers work in isolated "silos." But if silos are for farms, not laboratories, why are they so widespread in science?

"Silos – or islands of data, information, tools and knowledge – are difficult to integrate for both technical and possibly



social reasons," says Patrick, who is also a professor of health management and informatics at the University of Missouri-Columbia School of Medicine.

One technical reason: lack of common standards. "There is no systematic method for general, broad data sharing," notes Rocke, who also co-directs the UC Davis Institute for Data Analysis and Visualization.

Launched in July 2003, caBIG aims to change all that by promoting common standards, data sharing and team-tested technologies brought together in an informatics infrastructure that NCI director Dr. Andrew von Eschenbach calls "the World Wide Web of cancer research."

"Any time interoperability, sharing and combining of otherwise disparate resources is made possible, it can certainly have an effect on the practice of research," Patrick says. "The caBIG project appears to be addressing these needs."

(continued on page 21)



Researchers are determined to find a screening test for ovarian cancer, and new treatments for the disease

For Jennifer's sake

They call it the disease that whispers. Ovarian cancer doesn't announce itself with obvious signs. Its early symptoms are so subtle and nonspecific that two-thirds of women with the illness aren't diagnosed until they have advanced disease.

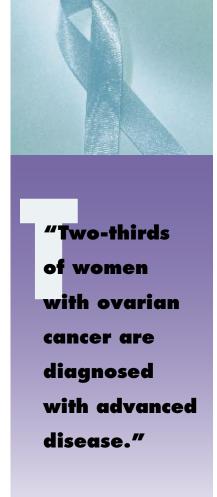
Jennifer Whitney's experience was all too typical.

When the Folsom mother of two began having vague gastrointestinal complaints early last year, she consulted her primary care doctor. As her discomfort worsened, he ordered first a colonoscopy, then a pelvic ultrasound.

The colonoscopy was normal. The ultrasound wasn't: Both ovaries appeared grossly enlarged.

Whitney was referred to Gary Leiserowitz, chief of gynecologic oncology at UC Davis Cancer Center. Surgery was scheduled. The 39-year-old woman wouldn't know until afterward whether she had cancer or a benign problem, such as ovarian cysts.

Whitney's husband, Brian, gave her the news in the recovery room. It was cancer.



When ovarian cancer is diagnosed at the earliest stage, stage 1-A, the five-year disease-free survival rate is about 90 percent – meaning about nine in 10 patients will be alive in five years with no evidence of disease. Whitney's cancer, which had spread to her abdomen, was stage III-C. For women with this stage of the illness, the five-year disease-free survival rate is 25 to 30 percent.

"It's unacceptable," Leiserowitz says, "that a woman could have such a devastating disease, and we have no way to find it earlier. It's imperative that we find a screening test for ovarian cancer."

Says Sidney Scudder, Whitney's hematologist-oncologist: "If we had the same kind of early detection tools available for ovarian cancer that we have for cancers like breast cancer, we could expect the same survival – 85 to 95 percent at stage I."

With patients like Whitney never far from their thoughts, UC Davis Cancer Center investigators are working hard to develop such tools – as well as



Suzanne Miyamoto, in her lab at UC Davis Medical Center, works on a potential screening test for ovarian cancer. new, more effective treatments for advanced disease.

One potential screening tool has shown particular promise in early testing. Cancer center researchers including Kit Lam, professor and chief of hematology and oncology, Suzanne Miyamoto, a research biochemist, and Leiserowitz are collaborating on the project with Carlito Lebrilla, a professor of chemistry on the Davis campus.

The investigators have developed a technique to identify

changes in bloodstream sugars that appear to be characteristic of ovarian cancer. The team has used the technique to test blood samples from 24 women with confirmed ovarian cancer and 24 healthy women. "So far it's been highly accurate," Lebrilla says.

The blood test is in preliminary investigation, but the researchers are hopeful the approach could lead to a test that would allow doctors to detect ovarian cancer early, when it is most curable.

Women like Whitney – who

faithfully gets her mammogram and Pap smear every year – potentially would add one more test, a blood test for ovarian cancer, to the annual exam.

There is one commercial blood test available for ovarian cancer, but it is too unreliable for screening. That test, which measures levels of a tumor marker known as CA-125, is no more accurate than a coin toss when it comes to detecting early ovarian cancer. CA-125 testing is currently used for monitoring treatment response and disease recurrence in ovarian cancer patients.

Better treatments

Lam is also working on better treatments for ovarian cancer. He has discovered one compound that may double as both a detection method and a treatment for ovarian cancer. He developed the compound using combinatorial chemistry, a high-tech science that allows researchers to rapidly create and test potentially therapeutic new molecules en masse.

In early testing, Lam's new compound binds to ovarian cancer cells but not to any other cells. He hopes the compound will be useful for tagging ovarian cancer cells for diagnosis, or for delivering drugs directly to cancer cells.

Several antibody-based anti-cancer agents, which work in much the same way, are already on the market. Examples include Herceptin, which binds to breast cancer cells, and Zevalin, which attaches to lymphoma cells.

Lam's compound is much smaller than an antibody, however – and therefore may be more successful than current molecularly targeted agents at penetrating deep inside tumors. No currently available agent specifically targets ovarian cancer cells

Clinical trials

Meanwhile, five other new treatment approaches for ovarian cancer are available through clinical trials at UC Davis Cancer Center. Leiserowitz is the principal investigator of two of the trials. David Gandara, professor of hematology and oncology and the cancer center's associate director of clinical research, heads the others.

These investigational therapies mean more options for patients with advanced ovarian cancer than ever before. Increasingly, ovarian cancer is becoming a chronic disease – one that can be controlled for many years through a succession of treatments.

Mid-way through her chemotherapy, wearing a soft periwinkle cap, Whitney is ready to get back to her normal activities – cheering for the boys at Folsom Junior Bulldogs games, enjoying the family's new backyard pool and taking occasional weekend camping trips.

"I want to be done and move on with my life," she says.

Whitney's doctors want the same for her – and better chances for every woman with ovarian cancer.



"It's imperative that we find a screening test for ovarian cancer."

— Gary Leiserowitz



Dileep Bal, who helped make California the nation's no-smoking section, is teaming up with UC Davis

Cancer Center to snuff out ethnic disparities in cancer

Formidable partnership

Dileep G. Bal's three-letter last name may have become a fourletter word to tobacco and fast food companies. So be it.

It's fine by Bal, chief of the Cancer Control Branch of the California Department of Health Services, that he's been politically unpopular from time to time.

What does put him on edge, however, is getting any undue credit for the state's leaps forward in cancer control.

And they have been significant leaps: California adults now purchase about 45 packs of cigarettes per person per year.

That compares to about 120 packs per person in 1998, when the state passed Proposition 99, which added a 25-cent tax to each pack of cigarettes sold in California, and remains less than half the average pack-per-person rate for the other 49 states combined.

"The community norm 15 years ago in California was ubiquitous tobacco use," Bal says. "Now, we've cut them off at the pass. Since 1995 you can't smoke in restaurants; since 1998 you can't even smoke in bars.



"Collectively we have had an impact."

We have all kinds of occupational health controls; we have youth-access regulations. We have all kinds of educational programs and media programs. And all that in a political environment."

The Cancer Control Branch is taking the same approach to combat dietary risk factors for cancer. "McDonald's and various fast-food outlets and producers — the junk-food producers — they all peddle their stuff using Madison Avenue glitz," Bal says. "And we do counter-advertising."

Bal has been given armfuls of awards for his branch's cutting-edge work, a fact he finds a bit embarrassing. Credit instead should go to a team effort that encompasses mainly his state colleagues, cancer centers, private organizations and local public health officials, he argues. "Collectively," he says, "we have had an impact."

In his own office, Bal preaches using the "we" word not the "I" word, and tries to live up to that principle. "I have no intention of taking credit for what this has become, but I had

"We went to the heart of the beast. We demonized the industry."

the wisdom to hire some very good people and to provide them the resources that were needed," he says. "I've had the privilege to work with a group of very clever people who have built empires with my assistance, providing funds on occasion and on occasion providing them political cover. Equally important, I've stayed the hell out of their way."

Public servant

For all his modesty, Bal has plenty of admirers. Marc Schenker, professor and chair of public health sciences at UC Davis, says Bal "has been instrumental in advancing public health in California."

"His contribution to the health of Californians is immense," Schenker says. "He is a dedicated, selfless public servant who has truly made a difference."

Says Moon S. Chen, Jr., professor of public health sciences and co-leader of the UC Davis Cancer Center's Cancer Prevention and Control Program: "If I had to name a single individual who was responsible for making California America's no-smoking section, it would be Dileep Bal."

But Bal says that what he's done, as much as anything, is give permission for people to "try crazy things."

Nowhere has the branch's creative approach to motivating healthier lifestyles shown more results than in tobacco use in California. Bal characterizes the effort as a David vs. Goliath battle — a state agency going toe-to-toe with big tobacco, often on the industry's own turf: advertising.

Hitting hard

"We went to the heart of the beast. We demonized the industry," Bal says. "We said, 'They're peddling a product that's as addictive as cocaine and heroin and causes nearly half a million deaths in the United States every year.'"

"They get people hooked with their predatory marketing practices ... and once they draw them in with advertising, they maintain them as customers because of the addictive nature of the product. It was a connection everyone knew but nobody had

countered, so we went to the 'community norm change model.' The community norm was tobacco use, so we hit very hard."

The Cancer Control Branch hasn't stopped there.

"We're doing some of the same things with diet. Some of the people responsible say comparing fast food to cigarettes is an overdrawn analogy. I don't think so," Bal says. "They say we're acting like the 'food police' it's not the food police. We're simply trying to move consumers more towards fruits, vegetables, trying to keep them away from alcohol, trying to get them to exercise more – again, to change community norms. We're countering the predatory marketing practices that take primarily low-income people and get them habituated to fast food, the wrong food."

Modern plagues

Changing community norms is the only way to tackle the country's leading killers, like cancer, coronary heart disease and obstructive lung disease, Bal argues. Gone are the days when health authorities believed top killers might be foiled solely in the lab.

"The plagues of today are all related to today's lifestyles: using tobacco, using drugs, using alcohol, being too fat, being indolent, not eating the proper things, not walking up stairs but taking elevators," Bal says. "So the question is: How do we

change the current behavior of Americans, without doing it in a way that intrudes into their personal rights and privileges?"

Trained as a doctor

Bal's own interest in public health dates to his early days as a doctor in his native India. Bal trained as a physician at the All India Institute of Medical Sciences in New Delhi, India, where he specialized in public health and preventive medicine. Practicing afterward in rural areas, he witnessed the chasm between health care for the rich and poor.

When he came to the United States as a scholarship student at Columbia in the late 1960s, Bal again found a two-tiered health system in which the poor and uneducated – more often than not people of color – didn't fare as well as the better-off and educated.

After graduating from Columbia and later Harvard, Bal began a career in academia at the University of Arizona before opting for a life in public health. Before taking the helm of California's then relatively small Cancer Control Branch in 1981, he headed the Pima County, Ariz., Public Health Department.

Over the years Bal has also served as the president of the American Cancer Society at both the state and national level, while continuing to publish extensively and to serve as the principal investigator of several major cancer prevention and control projects funded by the National Cancer Institute and the U.S. Centers for Disease Control and Prevention.

In addition, he has worked with UC Davis Cancer Center leaders to unite and coordinate the talents of the two institutions in a partnership aimed at improving the health of all Californians.

Special relationship

Indeed, the deeply rooted relationship between UC Davis Cancer Center and the Cancer Control Branch of the California Department of Health Services has never been closer. The relationship unites a preeminent state health department with a major cancer center, in a concerted effort to prevent and control cancer statewide.

For example, Dileep Bal holds an academic appointment at UC Davis, as a professor of public health sciences. He also serves as the principal investigator for the Sacramento regional office of AANCART (Asian American Network for Cancer Awareness, Research and Training). This National Cancer Institute-funded project, the largest ever undertaken to reduce cancer in Asian Americans, is headquartered at UC Davis. It encompasses investigators at seven other universities, from the University of Hawaii to Harvard. Bal provides regional leadership

as well as support staff and office space for Sacramento AANCART.

The Cancer Control Branch and UC Davis recently co-sponsored the 5th Asian American Cancer Control Academy, which drew 450 public health experts and community leaders from around the country to Sacramento. Kurt Snipes, chief of Cancer Control Planning, Research and Disparities for DHS, served as academy superintendent. In addition, DHS staff provided extensive administrative support. And DHS research was prominent at the academy. Included were reports on tobacco use, diet and exercise patterns, and cancer incidence and mortality among Asian Americans in California.

"Do people get upset?
Sure. Does it faze us?
No."

"Cancer rates in California, which were lower than the rest of the United States to start with, are in an accelerated decline."

"But," Bal says, "if people are injuring themselves, it's incumbent on us to point out alternate ways of operating. That's what we do.

"Do people get upset? Sure. Does it faze us? No."

Success breeds success

Bal says success is the key to getting things done in a shifting political landscape. "When you've done things as controversial as we have, you have to have successes in order for people to back off. In television and radio, you're only as good as your last Nielsen (ratings). Happily, the ratings for our anti-tobacco ads have been phenomenal.

"Tobacco use in California has plummeted. But the proof is in the pudding – cancer rates in California, which were lower than the rest of the United States to start with, are in an accelerated decline.

"We calculate that the net savings from our plummeting tobacco use rates is something like \$8 to \$10 billion for California. So we have some capital built up."

For his part, Bal, 59, says he plans to retire in four or five years. He's not sure just what he'll do yet, besides spending time with his wife, Muktha, and their children, Sarah and Vijay.

Rest assured, however, that – ever the team player – Bal will only be a phone call away. "If anyone needs me in the cancer control fight," he says, "I'll be there."

Through AANCART, UC Davis Cancer Center and DHS have worked together to host quarterly cancer education sessions for Sacramento's Asian American population, attracting about 125 people to each session.

With AANCART as a model, UC Davis Cancer Center and DHS are now developing new cancer-control initiatives targeted at Sacramento's African American, Hispanic and Native American communities.

"It is personally very rewarding for me to do on-the-ground work with UC Davis folks," Bal says.

Making the effort to change community norms, however well meaning, can bring plenty of heat – especially when it comes to messing with the like of big tobacco companies.



A WAY OUT OF THE SMOKING JUNGLE

California Smokers' Helpline ee information and counseling on how to quit amoking

English 1-800-7-NOBUTTS

Español 1-000-45-NOTUME ENGRY 1-000

Not be up the Cultural Department of Track Service

Ads like these, produced by the California Department of Health Services, helped change attitudes statewide about smoking, across ethnic groups. The ad is available in English and several Asian languages.

World Wide Cancer Web

(from page 11)

Cancer research is a big field comprised of contributions from molecular biologists, geneticists, pathologists, zoologists, biologists and a host of clinical subspecialists.

To be effective, these multidisciplinary researchers must integrate information from tumor pathology, genome studies, proteomics, clinical trials and digital reams of computerized analyses.

Then the researchers must take the most promising ideas from bench to bedside, and back to the bench again, for further refinement.

Streamlined collaboration

The collaborative thinkers behind caBIG say this painstaking work is no job for a closed system of disparate databases and creaky communications.

"CaBIG will make cancer research and cancer care more efficient and effective," Rocke says. "It will help avoid needless duplication of efforts, and will assist in keeping cancer research and treatment more uniformly state-of-the-art."

Lynch goes so far as to predict that caBIG will gradually replace the traditional system of scientific sharing through presentation at scientific meetings and publication in peer-reviewed scientific journals. That time-honored system, he says, makes it difficult for independent researchers to discover related projects until late in the process. In contrast, caBIG will allow data sharing in near real time.

Grids within grids

The caBIG grid is divided into smaller grids or "work spaces" made up of experts in such areas as clinical trial management, pathology tools and the language of cancer researchers.

At UC Davis, the NCI saw research teams capable of helping to rewrite the protocols of cancer communications by redefining and standardizing both language and practice – a task central to the grid's eventual success as an open and accessible information "collaboratory."

"My proposal involved use of an open-source (freely available) tool to bridge the gap between clinical trials adverse events and hospital lab information systems," Lynch says. "This was precisely the kind of project the NCI was looking for."

For UC Davis, involvement in caBIG is a boon to the university and a benefit to cancer researchers and the cancer patients their work aims to heal.

"It is important for UC Davis Cancer Center to be included in caBIG – both for our sake in participating in this national effort, and for the sake of caBIG itself," Rocke says.

This unprecedented endeavor provides UC Davis with an opportunity to have input into the development of caBIG from the very beginning, Lynch notes.

In addition, a highly visible project such as caBIG has one other powerful benefit: as a beacon that attracts the best and the brightest.

"It should help translate into recruitment efforts for fellows and faculty in both cancer and informatics research," Lynch predicts. "It will also improve the relationship between the cancer center and informatics faculty by laying a foundation for further work together."

As its name implies, caBIG is an ambitious undertaking, without precedent in medical research.

Unprecedented scale

"It is perhaps the largest, bestfunded project of its kind," Rocke says. "Other such projects I am aware of have been grassroots efforts, accomplished without specific funding. Having the NCI behind caBIG makes it unique."

Lynch predicts the grid will have a big impact on the rate of discovery of new therapies, and will provide improved safety for clinical trial patients by more rapid reporting and aggregation of adverse events related to these therapies.

Size matters in research. Larger endeavors with the greatest funding often yield the most promising results. If caBIG lives up to its potential, the giant grid will have a huge national impact.

A small gold-rush town, with help from neighboring communities, raises \$1 million for cancer research at UC Davis

ONE in a million

Like most communities, Auburn, Calif., has seen its share of cancer.

But this Gold Rush-era town has done something perhaps no other similar-sized city has accomplished. In a little less than four years, the small city has raised a million dollars for cancer research.

"What made it work was a just cause and a committed community," says Virgil Traynor, an Auburn veterinarian who spearheaded the fund-raising effort with his good friend Dick Azevedo, an Auburn-based businessman.

"This is a first," says Ralph deVere White, director of the UC Davis Cancer Center. "The generous people of Auburn are a model for how fundraising can become a community effort. And they have become great friends."

Auburn is nestled in the Sierra foothills about 35 miles northeast of Sacramento. Once a mining camp known for bear fights and public hangings, the



town's Old West origins are still evident. Every April the community welcomes the Wild West Stampede, one of California's oldest rodeos, and crowns a new Miss Auburn Stampede. The town recently dubbed itself "the endurance capital of the world," for its role as host to some of the world's toughest endurance events - the Tevis Cup Western States Trail Ride, for example, a 100-mile horse race from Auburn to Lake Tahoe. through rugged Sierra high country, and the Western States Endurance Run/UltraMarathon, a 100-mile run from Squaw Valley over Emigrant Pass to Auburn. About 12,500 people now live within the city limits, and about 44,000 in Auburn and the surrounding area.

The Auburn Community Cancer Endowment Fund got its start in April 2001. By August of that year, \$100,000 had been raised from ten donors.

The other \$900,000 came in more slowly, generated during three years of barbecues, golf

tournaments, motorcycle rallies and fun runs, as well as from continued personal donations.

It took a community with grit and stamina to raise the million dollars, but a few individuals worked especially hard. Football Hall of Famer Jim Otto, who moved to Auburn after retiring from a storied career with the Oakland Raiders, joined the effort after he completed treatment for prostate cancer at UC Davis Cancer Center.

"The type of cancer I have ... ten years ago, you died," Otto says. "I'm very fortunate, and I wanted to help."

Jim and Sally Otto hosted the first Jim Otto Celebrity Golf Classic in June 2003 at the Auburn Valley Golf Club. Football legends like Fred Biletnikoff, Willie Brown, Daryle Lamonica, Otis Sistrunk and more than two dozen others participated. The event raised \$150,000. The second tournament last May, featuring another all-star guest list and also held at the Auburn Valley Country Club, raised \$200,000.

Besides Otto, other big names volunteered their help: the Ladies Professional Golf Association, Auburn Harley Davidson, Magnuson Toyota in Auburn, and the Thunder Valley Casino, operated by the United Auburn Indian Community.

It takes a village: Members of the Auburn Community Cancer Endowment Fund gather at the Placer County Department of Museums. Virgil Traynor is standing in the foreground, third man from the right. More and more individuals in Auburn and nearby towns signed on as well. Recruits included Bart O'Brien, superintendent of the Placer Union High School District, and Bruce Dear, Placer County Assessor.

Cancer touches everyone

As a school administrator, O'Brien works long hours. But he made time when Traynor recruited him. "My mother is a cancer survivor," O'Brien says. "She had surgery 20 years ago, and she's 95 now. All our families have been touched by cancer, and we can all relate to it."

Dear's mother died of cancer at an early age. He was further swayed by the range of participants he encountered at a motorcycle club benefit for the fund.

"Seeing this long line of Harley riders, and the tremendous diversity of the people, and the idea that they're all there raising funds to cure cancer ... That was a striking moment," Dear says. Dear credits Traynor for keeping the ball rolling. "It's Virgil's energy, rounding the troops up, providing leadership. That's what's made this a success."

New goal

Now that the town has reached the million-dollar mark, organ-izers have set a new goal: to raise the total to \$1.5 million. That will fund, in perpetuity, a faculty chair in basic cancer research at UC Davis Cancer Center. Endowed chairs, one of the highest honors in academia, allow universities to retain or recruit the best minds in each generation.

The endowed chair will be named in honor of the Auburn Community Cancer Endowment Fund. That, too, will be a first. Other endowed chairs at UC Davis have been named after individuals and corporations — but never a whole community.

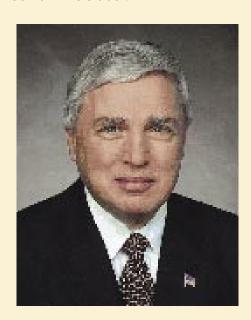


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NATION'S TOP CANCER DOCTOR RENEWS PLEDGE

Andrew C. von Eschenbach, director of the National Cancer Institute, renewed his pledge to eliminate the suffering and death due to cancer by 2015 during a two-day visit to UC Davis Cancer Center in October.

Andrew C. von Eschenbach, director of the National Cancer Institute.



The nation's top cancer doctor delivered back-to-back keynotes, speaking first at the cancer center's annual research symposium on Oct. 21 and the following morning at the cancer center-hosted AANCART Academy. AANCART – for Asian American Network for Cancer Awareness, Research and Training – is an NCI-funded project that unites investigators from nine cancer centers in five states in a common effort to reduce cancer in Asian Americans. UC Davis is national headquarters for AANCART.

Von Eschenbach first issued his 2015 challenge in the spring of 2003. "We are not saying that we will 'cure' or eliminate all cancer," he said. "Rather, we aim to pre-empt the worst outcomes of the disease: We will prevent more cancer; we will detect many more cancers earlier and eliminate them with fewer side

effects; and we will modulate the aggressiveness of cancer so that people live with, but do not die from, the disease."

Von Eschenbach is the 12th director of the NCI since its creation in 1937.

ROBOTIC-ASSISTED PROSTATECTOMY

Now there's "band-aid" surgery for prostate cancer. The UC Davis Department of Urology performed eight robotic-assisted laparoscopic prostatectomies in the first six months after introducing the procedure last August, giving the medical center more experience with this new, minimally invasive prostate cancer surgery than any other center in the region.

Laparoscopic prostatectomy is performed via several small incisions, each about the size of a dime. In a robotic-assisted procedure, miniature robotic arms and a robotic laparoscope – essentially a tiny telescope – are introduced through dime-sized incisions in the abdomen. The surgeon operates the tools from a nearby console.

Because the procedure involves smaller incisions, patients may be able to return to their normal activities more quickly than with standard prostatectomy. However, urologic oncologists warn that, as with any surgical procedure, this one has risks as well as benefits. The procedure is not appropriate for all prostate cancer patients, and men who are interested in robotic surgery should discuss the pros and cons with their urologists. Men should also choose a surgeon with extensive training in the new technology.

Of the first eight men to undergo robotic prostatectomy at UC Davis, all have seen their prostate-specific antigen (PSA) levels drop to zero, as would be expected with traditional prostate removal surgery. PSA levels are a marker for cancer.

HEALTHY YUBA COUNTY

A coalition led by UC Davis Health System is launching a campaign to reduce Yuba County's cancer rate, the highest in the state.

Yuba County's all-cancer mortality rate is the highest among California's 58 counties. The county also ranks 56th in deaths from coronary heart disease, and 55th in deaths from diabetes.

The Healthy Yuba County project will study contributing factors to the high rates – tobacco is a top suspect – and propose programs to reduce that incidence, according to Bruce Leistikow, associate professor of public health sciences at UC Davis School of Medicine and Medical Center and lead epidemiologist for the project.

Besides UC Davis Health System, the other founding partners in the Healthy Yuba County Initiative are the Yuba County Health and Human Services Department and the Fremont-Rideout Health Group, based in Yuba City. The three groups provided start-up funds to collect baseline data, examine local health-care patterns and analyze preliminary results. The partners will seek public and private grants for ongoing funding.

More than a dozen other community organizations will join the effort, including the American Cancer Society, the American Heart Association, Harmony Health, the American Lung Association, Del Norte Clinic, Peach Tree Clinic, the Marysville Unified School District, the Beale Air Force Base public health department, the Yuba County Tobacco Coalition, the Migrant Workers Association, the Hmong Association, the Cancer Surveillance Program, Region 3, Yuba County for Healthy Children and the Yuba County Office of Education.

UC Davis Cancer Center and the Fremont-Rideout Health Group are partners in Fremont-Rideout Cancer Center, a comprehensive cancer treatment center in Marysville. The partnership enables cancer patients in Yuba and Sutter counties to receive treatment from UC Davis Cancer Center specialists without having to drive to Sacramento.

RIPON GIRL LAUNCHES 2005 ST. BALDRICK'S CAMPAIGN

Francesca Arnaudo was 6 when she lost a bone in her right arm to osteosarcoma. Now 8, the Ripon third-grader was diagnosed in December with a second form of cancer, leukemia. One of the gymnastics enthusiast's first concerns: that chemotherapy for her leukemia would cheat her of the chance to participate in St. Baldrick's day, held each March to raise money for childhood cancer research.

The little girl's solution: to shave her head right away, before her sandy blond hair could fall out due to chemotherapy. Moved by Francesca's decision, the New York-based St. Baldrick's organization chose the two-time cancer patient to kick off the organization's 2005 head-shaving



Francesca Arnaudo gives her doctor, Ted Zwerdling, a makeover.

campaign in California. The shave took place at UC Davis Medical Center on Jan. 14. At Francesca's request, Ted Zwerdling, her pediatric oncologist, acted as barber. Afterward, he let Francesca shave him bald. Dino, Francesca's

News in Brief

CALENDAR OF EVENTS

March 8

"Supportive Cancer Care—Maximizing Your Quality of Life"
Learn at Lunch Series for cancer patients and survivors
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5786

March 17

St. Baldrick's Celebration & Public Head Shaving A fund-raiser for pediatric cancer research Woodcreek Golf Club, 5 p.m. to 9 p.m. 5880 Woodcreek Oaks Boulevard, Roseville (916) 784-6786

March 19

St. Baldrick's Celebration & Public Head Shaving
A fund-raiser for pediatric cancer research
Empire Club, noon to 6 p.m.
1417 R Street, Sacramento (916) 784-6786

March 29

"The Benefits of Modern Radiation"
Learn at Lunch Series for cancer patients and survivors
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5786

April 5

"Popular Diets and Cancer"

Learn at Lunch Series for cancer patients and survivors

UC Davis Cancer Center auditorium, noon to 1 p.m.

4501 X Street, Sacramento (916) 734-5786

April 20

"Managing Cancer Pain and Fatigue"
A community forum sponsored by UC Davis Cancer Center
and the American Cancer Society
UC Davis Cancer Center auditorium, 6 p.m. to 8 p.m.
4501 X Street, Sacramento (916) 734-5786

May 3

"Advance Directives and HIPAA"
Learn at Lunch Series for cancer patients and survivors
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5786

10-year-old brother, let her shave his head as well.

The St. Baldrick's head-shaving campaign has raised nearly \$7 million dollars for child-hood cancer research since 2000, when three Irish insurance executives from New York City conceived the idea to have volunteers in cities across the country shave their heads in public on or near St. Patrick's Day in return for financial pledges from friends and family.

To make a pledge in Francesca's name, contact the Keaton Raphael Memorial at (916) 784-6786 or info@childcancer.org. The Keaton Raphael Memorial is a Roseville-based organization that coordinates St. Baldrick's activities in the Sacramento region. The 2005 shave dates are March 17, at the Woodcreek Golf Course in Roseville, and March 19, at the Empire Club in Sacramento. For more information, visit www.childcancer.org or www.stbaldricks.org

NEW LAND, NEW THREAT



Hmong dancers performed in traditional dress at the Asian American Cancer Control Academy.

The Hmong in California face rates of nasopharyngeal, cervical, stomach and liver cancer up to 16 times higher than those of non-Hispanic whites and three times higher than those of Asian Americans overall, according to research presented at the 5th Asian American Cancer Control Academy in October. The academy is the annual meeting of

the Asian American Network for Cancer Awareness, Research and Training (AANCART), headquartered at UC Davis.

More than a third of the nation's 169,000 Hmong live in California. In 2003 the U.S. State Department granted permission for another 15,000 Hmong to enter the country from Thailand. About half of these newest immigrants are also expected to settle in California.

"This research points to the need for increased cancer education, awareness and screening among the Hmong both in California and nationally to help them confront cancer, one of their biggest health threats," said Moon S. Chen, Jr., professor of public health sciences at UC Davis School of Medicine and Medical Center and principal investigator of AANCART.

With the Hmong Women's Heritage Association in Sacramento, UC Davis investigators have translated cancer information pamphlets into Hmong, compiled a Hmong-English cancer glossary and taught cancer awareness courses to Hmong community leaders and medical interpreters. They've also launched a patient "navigator" program, in which a Hmong medical interpreter accompanies Hmong cancer patients to medical appointments. And they are distributing free health kits containing cancer screening and early detection information to new Hmong immigrants.

The NCI, U.S. Office of Minority Health, California Department of Health Services and the American Cancer Society co-sponsored the AANCART Academy.

ONE THOUSAND PAPER CRANES

"Sadako and the Thousand Cranes" is one of 10-year-old Abby Scurfield's favorite books. It tells the story of Sadako, a Japanese girl with leukemia, who focuses her energy on folding 1,000 paper cranes. Sadako's determination made her a national symbol of courage and hope.

Abby, a fifth grader at Leonard DaVinci Elementary School in Sacramento, decided to

June 4

National Cancer Survivor's Day Richard and Annette Bloch Cancer Survivors Park, 9 a.m. 2601 Stockton Blvd., Sacramento (916) 734-9023

June 7

"Chemo-brain: Chemotherapy-Related Memory and Thinking Changes" Learn at Lunch Series for cancer patients and survivors UC Davis Cancer Center auditorium, noon to 1 p.m. 4501 X Street, Sacramento (916) 734-5786

June 28

3rd Annual Jim Otto Swing at Cancer Celebrity Golf Classic Auburn Valley Country Club 8800 Auburn Valley Road, Auburn (916) 734-9675

August 26

"Chipping Away at Childhood Cancer" Golf Tournament A Keaton Raphael Memorial fund-raiser for pediatric cancer research The Ridge Golf Course, Auburn (916) 784-6786

August 27

Celebration Gala
Benefiting research at UC Davis Cancer Center
Hyatt Regency Hotel
Sacramento (916) 418-1667

September 10

Second Saturday — With a Cause A fund-raiser for leukemia and lymphoma research The Hen House, 5 p.m. to 9 p.m. 10119 Fair Oaks Blvd., Fair Oaks (916) 984-8000

September 26

"Chipping Away at Childhood Cancer" Golf Tournament
A Keaton Raphael Memorial fund-raiser for pediatric cancer research
Montreux Golf & Country Club
Reno (916) 784-6786

Please check our Web site for calendar updates:

www.ucdmc.ucdavis.edu/cancer

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Olivia Bowman, member of Junior Girl Scouts Troop #1725, displays one crane.



reenact Sadako's achievement for the benefit of children with leukemia and other cancers at UC Davis Cancer Center. With her friends in Junior Girl Scouts Troop #1725, Abby folded a thousand paper cranes that adorned a tree for pediatric cancer patients at UC Davis Cancer Center. The girls also asked their friends and relatives to pledge \$1 per crane. The result: a check for \$1,000 to help establish a children's cancer resource center at the medical center.

Breast reconstruction

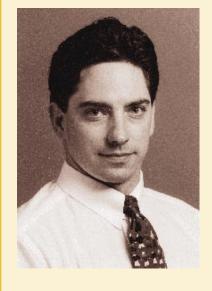
Performing breast reconstruction surgery at the time of mastectomy does not delay post-operative chemotherapy for women with breast cancer, according to the first study designed to answer the question. The study appeared in the September issue of Archives of Surgery.

"At most academic centers that routinely care for women with breast cancer, immediate breast reconstruction is the norm for women who opt for mastectomy," said Richard Bold, associate professor of surgical oncology at UC Davis Cancer Center and senior author of the study. "However, a number of our patients come to us after having been told elsewhere that they should not have immediate reconstruction because it delays chemotherapy. We felt it was an important question to settle."

Although breast reconstruction can lessen the impact of mastectomy on a woman's self-image and psychosocial wellbeing, some surgeons – concerned about skin infections and other wound complications that might delay chemotherapy – advise women to post-pone reconstruction.

In the study, Bold and his colleagues reviewed the charts of 128 women who underwent mastectomy at UC Davis Cancer Center between 1995 and 2002. They found that while wound complications were more common with immediate reconstruction, the complications were too mild – minor skin infections and small scabs, primarily – to warrant any delay in starting chemotherapy.

In addition to the potential psychological benefits of immediate breast reconstruction, Bold said cosmetic outcomes also tend to be better with immediate surgery.



Surgical oncologist Rick Bold showed that immediate breast reconstruction does not delay post-operative chemotherapy for women who undergo a mastectomy.