

SYNTHESIS

A PUBLICATION OF
UC DAVIS CANCER CENTER

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FALL/WINTER 2004



***Fighting cancer
in the Hmong***

***Metabolomic
fingerprints***

Soy power

To our readers

Dear Reader:

The battle to defeat cancer progresses on multiple fronts. This issue of *Synthesis* takes you to two of the most important: patient education and biomedical research.

Dr. Moon Chen will describe our education-based efforts to reduce cancer in Asian Americans, the only ethnic group in the United States for whom cancer is the leading cause of death. As principal investigator of a National Cancer Institute-funded project, Dr. Chen coordinates Asian American cancer-control efforts at UC Davis and seven other academic institutions nationwide, from the University of Hawaii to Harvard. Each institution focuses on reducing cancer in a different Asian American population. Their common goal is to build partnerships with community-based organizations that can effectively deliver cancer-prevention messages.

In Sacramento, our focus is on the Hmong. This past summer, after two decades in Thai refugee camps, 15,000 Hmong began arriving in the United States. About 4,000 are expected to settle in our region. Dr. Chen has partnered with the Hmong Women's Heritage Association in Sacramento to assess cancer incidence and risk factors among the Hmong, translate cancer education materials, and develop courses that teach the basics of cancer prevention and early detection.

On the biomedical research front, you'll read in this issue about an emerging science known as metabolomics. This new discipline holds tremendous potential for oncology. Ultimately, metabolomics may give us a single blood test that can diagnose cancer and monitor treatment response, much like the glucose test used in diabetes management. You'll meet metabolomics pioneers from diverse disciplines — entomology, genetics, agricultural sciences, biology and biochemistry — from UC Davis and Lawrence Livermore National Laboratory. Their combined talents create a formidable collaboration. You'll also read about our new Genome and Biomedical Sciences Facility, and how it has been designed to cultivate collaboration within and beyond the cancer research program to advance science and improve human health.

Indeed, collaboration is a theme throughout this issue. You'll see it in our story about a clinical trial of a promising new chemopreventive agent that may slow early prostate cancer. Investigators in the Department of Nutrition on the Davis campus and the Prostate Cancer Research Group at the medical center collaborated to make this trial a reality. You'll also see collaboration at work in the story about the Institutional Research Grant program, in which the American Cancer Society helps us foster a new generation of cancer researchers. Collaboration is also manifest in our groundbreaking canine-human clinical trials consortium. Funded by a generous grant from the Sacramento Region Community Foundation, this novel consortium will enable medical and veterinary oncologists, working together, to test new cancer treatments more quickly than they could working separately. It's a collaboration that will benefit both species.

We end this issue, appropriately enough, with photos and a brief report from our last National Cancer Survivors Day celebration. Survivorship is the fundamental objective of all of our collaborations, whether with the Hmong Women's Heritage Association or Lawrence Livermore. We look forward to the day when, together, we eliminate the suffering and death caused by cancer.

Sincerely,



Ralph deVere White, M.D.
Director, UC Davis Cancer Center



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Ralph deVere White
 Director
 UC Davis Cancer Center

Claudia Morain
 Editor

Pat Grind
 Art Director

Wolfe Design Marketing
 Graphic Design

José Luis Villegas
 Photographer

Nora Steiner Mealy
Gail McBride
 Writers

About the cover:
 Against the backdrop of a traditional Hmong embroidery, a shaman holds a txab neeb, used to protect patients from bad spirits during healing ceremonies, center, and picks medicinal herbs, above left. In the upper right corner, Vang Chou holds a photo of his late wife, Chong Yia Xiong, who died of cancer. Cancer is a chief cause of death among the Hmong.

UC DAVIS CANCER CENTER

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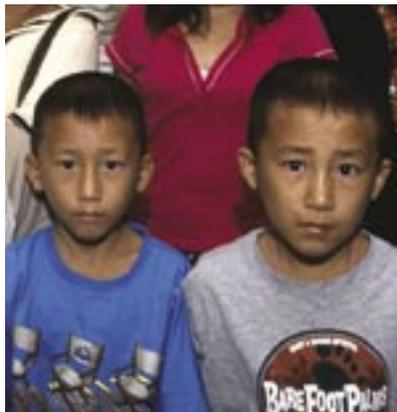
***Bringing cancer-prevention information to the Hmong,
a people whose native language has no word for cancer***

Cancer Awareness 101

At the Wat Tham Krabok refugee camp, a settlement of makeshift corrugated steel and bamboo huts about 60 miles north of Bangkok, Aeng Chang fought his bladder cancer. He hired a shaman to perform a soul-calling ceremony. A cow, buffalo and pig were sacrificed. Herbs, roots and tree leaves were tried. The only treatment Chang rejected was radical cystectomy, the surgical removal of the bladder, recommended by a medical doctor in a nearby town.

On June 16, after three years battling his illness and 25 in refugee camps, the former soldier arrived in California. He, his wife, See Thao, and his eight children, ages 2 to 17, were the first of 15,000 Hmong refugees from Wat Tham Krabok granted permission to settle in the United States this year. Chang's advanced cancer propelled his family to the front of the immigration line. The hope was that American doctors might save his life.

Nine days after arriving in Sacramento, however, Chang died at UC Davis Medical Center of inoperable, metastatic cancer



**UC Davis
launches
a major
campaign
to prevent
cancer in
the Hmong.**

of the bladder and rectum. He was 41.

It's a tragedy Moon Chen doesn't want to see repeated. "The new Hmong immigrants have waited so long and come so far, we want to arm them with the information they need to live long, healthy lives," says Chen, co-leader of the Cancer Control and Prevention Program at UC Davis Cancer Center.

Unprecedented effort

Through a National Cancer Institute-funded project known as AANCART — for Asian American Network for Cancer Awareness, Research and Training — Chen is leading an unprecedented effort to address the fears and traditional beliefs that prevent many Hmong from getting regular cancer screenings, recognizing early cancer symptoms, and, when cancer occurs, undergoing effective treatment.

Over the past two years, Chen and his colleagues have gathered a wealth of information about the cancer incidence, risk factors and



At his funeral, portraits of Aeng Chang look out over the shoulders of his widow, See Thao, and six of their children.

information needs of the Hmong, and mobilized one of the area's largest Hmong organizations, the Hmong Women's Heritage Association, to spread the word.

An unnecessary burden

"The cancer burden facing the Hmong and other Asian American communities is unique, unusual and unnecessary," Chen says. "Unique, because Asian Americans are the only racial group who experience cancer as the leading cause of death. Unusual, because the leading cancer killers of Asian Americans are infectious in nature. Unnecessary, because the risk factors for many of the cancers, such as those due to viruses or tobacco, are preventable."

Bladder cancer, for example, can be caused by a chronic

parasitic disease, schistosomiasis, endemic in Southeast Asia. The Hmong also have high rates of liver cancer due to chronic hepatitis B infection.

Cervical cancer is prevalent as well. Pap smear rates are low, and the disease is often diagnosed at an advanced stage.

Hawaii to Harvard

UC Davis is headquarters for the \$8.5 million AANCART program, which is made up of seven other institutions across the country: Harvard, Columbia, M.D. Anderson Cancer Center at the University of Texas, UCLA, UCSF, University of Washington and University of Hawaii.

With AANCART funding, each institution focuses on a particular cancer in a particular Asian community. In Seattle,

for example, it's cervical cancer in Cambodian women. In Los Angeles, it's breast cancer in Japanese American women.

In Sacramento, the focus is on basic cancer awareness in the Hmong, with an emphasis on cancers caused by preventable infections, particularly liver cancer caused by chronic hepatitis B infection.

California's Hmong

California is home to at least 65,000 Hmong, most of whom arrived as refugees in the late 1970s and 1980s, driven from their homeland by the Pathet Lao after the United States withdrew from the Vietnam War. Of the new wave of Hmong immigrants, an estimated 4,000 are expected to settle in Sacramento, which has the nation's third-largest con-

1961



CIA recruits Hmong military leader Vang Pao to form a guerilla army, *Armee Clandestine*, to fight the communist North Vietnamese and Pathet Lao in Laos.

Hmong and Lu Mien mountain guerrillas fight the communists to a standstill in northern Laos, block the Ho Chi Minh Trail, and rescue more than 100 downed U.S. pilots.

1973



U.S. agrees to a cease-fire in Vietnam, establishment of a coalition government for Laos, the withdrawal of all troops and an end to supplying any resisting army, including *Armee Clandestine*.

1975



Pathet Lao officially take over Laos and vow to wipe out the Hmong resistance.

In traditional Hmong culture, it is believed that illness occurs when the soul wanders from the body. Shamen, like Kang Thao, help call the soul home.

centration of Hmong after Fresno and St. Paul, Minn.

For the newest Hmong immigrants, AANCART's focus is on eliminating infectious causes of cancer, primarily through hepatitis B immunization. For the Hmong who have been in the United States for a decade or more, the focus is on preserving the community's low rates of lung, colon and breast cancer through education about the risks of such Western behaviors as smoking, a high-fat diet and a sedentary lifestyle.

Cancer basics

A course called "Cancer Awareness 101" is the centerpiece of AANCART's Hmong outreach. It is designed to give members of the Hmong community, particularly the elders and shamen who



often serve as medical decision-makers for their families, the same baseline cancer knowledge that more mainstream Americans grow up knowing: Excess sun exposure can cause skin cancer. Regular Pap tests prevent deaths from cervical cancer. Smoking causes lung cancer. Breast self-exams can detect tumors while they are small and easier to treat.

It's a straightforward idea, but the first all-day Cancer Awareness 101 course, offered at a hotel conference room on the Medical Center campus in the spring of 2003, encountered unanticipated complexities.

Reginald Ho, a past president of the American Cancer Society, served as instructor for the pilot course. He quickly realized how

1985



Between 1975 and 1985, more than 100,000 Hmong flee to Thai refugee camps.

The Hmong population in the U.S. grows to 250,000, with more than 65,000 in California.

December 2003 June 16 2004



U.S. Department of State grants permission for 15,000 Hmong residents of Wat Tham Krabok to resettle in the U.S.

The first of the Wat Tham Krabok immigrants arrive in California.



Chong Yia Xiong of Stockton displays a photo of his late wife, Chou Vang, who died of cancer. UC Davis offers Hmong-speaking “navigators” to help families through cancer treatment.

few Western medical terms have counterparts in the Hmong tongue.

What’s a cell?

The word “cell” alone took 20 minutes to communicate. Ho’s Hmong translator chose the Hmong word *nqaj*, meaning “the smallest thing,” a controversial choice. Some in the audience, fluent in both Hmong and English, preferred *noob*, meaning “seed.” Others made a case for adopting the English word, cell. Similar debate ensued over translation of the many internal organs that have no name in Hmong.

At the end of the day, UC Davis medical students of Hmong ancestry agreed to prepare Hmong-language versions of the course.

With AANCART support, the Hmong Women’s Heritage

Association went on to translate three National Cancer Institute guides dealing with liver, skin and cervical cancer into the two predominant Hmong dialects, White Hmong and Green Hmong. Dao Moua, cancer program coordinator at the Hmong Women’s Heritage Association, now teaches the course in both English and Hmong.

A second course, Cancer Awareness 201, was designed to teach Hmong-English medical interpreters the vocabulary and concepts they need to effectively translate conversations about cancer prevention, screening, diagnosis and treatment.

Building trust

The two courses have been offered to more than 200 members of the Hmong community over the past year, with plans

for further classes. “Participants have told us they want more cancer courses offered to the Hmong community,” Moua says. “There is a need to address such concerns as treatment side effects, lack of knowledge about cancer, language barriers, lack of trust between patients and providers and misuse of medication.”

Through AANCART, Moua has developed an orientation program for new Hmong arrivals to Sacramento. Families receive free health kits, hepatitis B information and “What is Cancer?” brochures in Hmong. She has established a Cancer Support Network that provides Hmong patients at UC Davis Cancer Center with a Hmong-speaking “navigator” who can accompany them to medical appointments, provide interpreting and translation services, and act as advocates when needed. Working with AANCART investigators at UCLA, Moua has also conducted focus group research to assess the diet and exercise habits of California’s Hmong.

Empowering community organizations like the Hmong Women’s Heritage Association is central to the AANCART approach.

UC Davis hosts national Asian American Cancer Control Academy

“When we engage community-based organizations to aid their own, train their own and perform research to help their own, we see the power of their commitment to their own,” says Kenneth Chu, chief of the NCI’s Disparities Research Branch. “This is the secret to their success.”

Three-day funeral

Aeng Chang’s three-day funeral was held over the July 4 weekend at a Veterans of Foreign Wars hall in South Sacramento. Local Hmong radio stations reported on the death of the first immigrant from Wat Tham Krabok and announced his long wake. Outside the hall, stacks of 50-pound rice bags, brought by mourners as gifts to the family, flanked the entrance doors. Inside, Chang’s clansmen beat drums and played the *qeej*, a traditional bamboo flute. From a kitchen inside the hall, women prepared rice, vegetables and meat for family and guests.

“It’s very tragic,” a cousin said, standing next to a photo of Aeng Chang. “He never even got to see the apartment where his wife and children will live. But we are a large clan, and we will make sure his family is taken care of.”

AANCART will be there, too, to help ensure Chang’s children, and others in the new generation, grow up with the information they need to protect themselves from the leading killer of Asian Americans. [UCD](http://www.ucdavis.edu)



Andrew von Eschenbach

At the fifth Asian American Cancer Control Academy in Sacramento, more than 100 leading authorities from throughout the United States will gather to share best practices and research findings.

Academy highlights:

- keynote addresses by Andrew von Eschenbach, director of the National Cancer Institute, and Ralph Vance, national president of the American Cancer Society
- groundbreaking research into dietary risk factors for cancer among Asian American Pacific Islander groups in California
- new Asian American Pacific Islander cancer incidence and mortality statistics for California, including new data about the Hmong
- new data on tobacco use and tobacco-control programs in Asian American Pacific Islander communities nationwide
- updates on Asian American Pacific Islander participation in cancer clinical trials

“We have high hopes that this meeting will advance the cause of reducing cancer health disparities for Asian Americans and ethnic minorities in general,” said academy superintendent Kurt Snipes, chief of the California

Department of Health Services’ Cancer Control, Planning, Research and Disparities Section.

The Asian American Cancer Control Academy is the annual conference of the Asian American Network for Cancer Awareness, Research and



Ralph Vance

Training, made up of investigators from UC Davis, UCSF, UCLA, the University of Hawaii, the University of Washington, M.D. Anderson Cancer

Center at the University of Texas, Harvard University and Columbia University. Known as AANCART, the network is funded by an \$8.5 million grant from the National Cancer Institute. Its goal is to reduce cancer in Asian Americans nationwide. UC Davis is the network’s national headquarters.

The academy is co-sponsored by AANCART, UC Davis Cancer Center, the California Department of Health Services, the National Cancer Institute, the American Cancer Society and the U.S. Office of Minority Health, Region IX.

Hosts of the academy include the Hmong Women’s Heritage Association and the Council of Asian Pacific Islanders Together for Advocacy and Leadership. Both organizations are based in Sacramento.

For more information about the academy, visit www.aancart.org.



Richard Michelmore

**Richard Michelmore has a plan
for harvesting new cancer knowledge**

Genome FARMER

Richard Michelmore, professor of genetics in the UC Davis College of Agricultural and Environmental Sciences, is passionate about diseases of plants. Why does a pathogen attack one plant and not another? How does genetic resistance against a pathogen change over time? And how can answers to such questions be used to improve crop resistance to disease?

As director of the Genome Center on the main UC Davis campus, Michelmore will bring that passion to bear on a spectrum of scientific investigations — cancer prominently among them.

“Understanding the consequences of genetic variation is a central challenge throughout biology,” he says. “It cuts across all disciplines.”

Internationally renowned in plant genomics, Michelmore’s own research focuses on genetic mapping and gene function in lettuce, tomatoes and aridopsis, a model plant related to mustard. Educated at the University of Cambridge in England, he has been with UC Davis since 1982.

Michelmore has a strong interest in translational research, in which basic scientific information is translated into new approaches to society’s needs. He’ll foster the same translational focus within the Genome Center, whether it’s creating a more virus-resistant plant or strengthening the body’s ability to repair mutations leading to cancer.

To Michelmore’s mind, basic and translational research go hand in hand. That approach has helped to make the UC Davis College of Agriculture one of the best agriculture schools in the world: Scientists and farmers work closely together, new ideas germinate, and research stays relevant.

He anticipates similar collaboration among basic researchers at the Genome Center and scientists and physicians at the Cancer Center, resulting in unique opportunities to address important questions and needs in clinical oncology.

The Genome Center will be part of the six-floor, 225,000-square-foot Genome Biomedical Sciences Facility on the main campus. The new building will house an unparalleled array of genomics, proteomics, transcriptomics and metabolomics research facilities (see “Intro to ’omics” on page 11).



Ken Burtis, pictured in the new Genome Biomedical Sciences Facility, says the building will be a resource for 'omics researchers throughout the university and medical center.

“The whole facility is designed in the hopes that sparks will fly as researchers bounce ideas off each other,” says Ken Burtis, professor of genetics and an associate director of the Genome Center. An expert on DNA repair mechanisms in fruit flies, he was a participant in the sequencing and annotation of the fruit fly genome.

Shared resources

Scientists throughout the university and medical center will be able to use the resources of the Genome Center through a system of “technological cores.”

Michelmores and Burtis both understand the potential for expensive, wasted efforts when scientists work independently to develop and apply new technologies, without knowledge of one another’s efforts.

“There’s a lot of reinventing the wheel,” Michelmores notes.

“Our aim is to have an institutional, rather than a lab-by-lab, learning curve,” he says.

Over the next three years, the Genome Center, in consultation with faculty from the Cancer Center, will recruit 15 scientists from around the world to set up laboratories in the new building. The Genome Center’s multidisciplinary, collaborative approach will be manifest in the new recruits.

“Our goal has been to seek out faculty who are technology-driven,” Michelmores says. “We want scientists who are constantly exploring what is new, and who have a proven track record of adopting new approaches.”

Two of the first scientists hired for the Genome Center have a strong interest in cancer-related research.

Michael Wright, from the Institute of Systems Biology in Seattle, uses a mass spectrometry-based proteomics approach to

understand androgen-receptor function in prostate cancer cells.

Significant advances

Androgen-receptor function is one of the most important puzzles in prostate cancer research today, and a major focus of inquiry at UC Davis Cancer Center. If scientists can determine how some prostate cancer cells develop androgen independence, the knowledge may help to prevent or reverse the process, an advance that would extend the lives of thousands of men.

Peggy Farnham, who recently arrived from the University of Wisconsin, has developed a powerful method that allows her to identify where transcription factors bind to the genome, a crucial step in cell division.

The new Genome Center recruits will join the 240-member UC Davis Integrated Cancer Research Program, a multidisciplinary team of scientists from the medical center, Davis campus and Lawrence Livermore National Laboratory in Livermore.

Michelmores predicts genomics research will generate technological change on a scale comparable to the Industrial Revolution or computer age, and that UC Davis will play an instrumental role in ushering in the 'omics era. 

Intro to 'omics

For generations, scientists have worked to understand the cell down to its smallest components. Today researchers in the fields of genomics, proteomics, transcriptomics and metabolomics seek to understand the cell as a whole, in all its complexity.

Elbert Branscomb, associate director of the Biology and Biotechnology Research Program at Lawrence Livermore National Laboratory, likens cells to small cities.

“Think of a cell as the whole city of Chicago, at rush hour, busily making another Chicago,” says Branscomb, who is also a member of the UC Davis Integrated Cancer Research Program.

Macro biology

The mind spins at the immensity of the challenge: Each human cell has at its disposal about 30,000 genes, the sum of the human genome. Together these genes are capable of producing, via a manufacturing process known as transcription, perhaps 100,000 different proteins. It's the proteins that carry out the cell's work, or metabolism. How many byproducts of metabolism there are — the metabolites — is unknown; a common estimate is 3,000.

For cancer research, the implications are tremendous. “We are moving towards an understanding of cancer that will

enable us to tailor-make the optimal treatment for each person,” says Hsing-Jien Kung, deputy director of the UC Davis Cancer Center and director of its basic science program. “This university has made a tremendous, multidisciplinary commitment to this revolution, and we are leading the way into the future.”

A dramatic convergence of new developments fueled the 'omics revolution. Foremost was the mapping of the human genome, followed closely by gene-array analysis. This powerful new technology allows scientists to sequence thousands of genes at a time in a matter of days. Once-formidable tasks, like pinpointing the genetic differences between two populations — with and without a certain cancer, for example — today are commonplace.

At the same time, old tools have become super-efficient. Less than a generation ago, mass spectrometry could screen for 20 metabolites in a milliliter of urine or blood. The newest machines can screen for thousands in a sample as small as 1/1,000th of a milliliter.

A new mindset

But Branscomb says the biggest factor driving the 'omics revolution is a new mindset. “The most important lesson we've learned from the genomics revo-

An 'omics GLOSSARY

Genome:

The total set of genes carried by an individual or cell.

Genomics:

The analysis of the complete genome in order to understand the function of single genes.

Proteomics:

The genome-wide study of proteins manufactured or “expressed” by genes. Proteins do most of the work of the cell.

Transcriptomics:

The genome-wide study of messenger RNA, used by genes as templates to manufacture or “express” proteins.

Metabolomics:

The genome-wide study of byproducts of a cell's work, or metabolism.

lution is that it is often as easy to measure many things as to measure one thing,” he says. “Now that we have the capacity to do mass analysis, we are approaching, systematically, problems that were unthinkable just three to four years ago.”

Like using genomics, proteomics, transcriptomics and metabolomics to develop a unique fingerprint for each individual. With this information, scientists look forward to the day they will be able to predict an individual's propensity to develop cancer or a cancer patient's response to a certain therapy. Doing so will make cancer a controllable, if not a preventable, disease. 



Bruce Hammock

**Why a distinguished bug man
wants your metabolite profile**

METABOLOMIC *fingerprint*

As a scientist, Bruce Hammock is a rare hybrid: A cancer researcher whose training is in entomology, the study of insects.

A member of the UC Davis entomology faculty since 1980, the distinguished professor has made insect science the jumping-off point for a career devoted to basic questions in biology and biochemistry, from mammalian xenobiotic metabolism to the development of recombinant viral pesticides. In 1999, his body of work earned him a seat on the National Academy of Sciences, one of the highest honors that can be accorded a scientist in the United States.

Today Hammock's considerable talents focus on metabolomics, the 'omics discipline he predicts will be the first to yield advances in the clinic (see "Intro



Metabolites offer clues that may help scientists de-bug cancer mysteries.

to 'omics" on page 11). One of his first targets: prostate cancer.

Defining metabolites

A metabolite is any product of metabolism. Doctors have been able to measure a couple dozen metabolites in blood and urine specimens for years. Uric acid, left over when certain proteins in foods are metabolized, is just one example. Too much of this metabolite in the blood can signal gout, too much in the urine can signal kidney stones. Beyond uric acid, scientists believe there are perhaps 3,000 other metabolites present in our bodies, the vast majority still to be identified.

Hammock and other scientists hope to identify the most important of these, and determine

(continued on page 19)

**The American Cancer Society and
UC Davis Cancer Center cultivate a new
generation of cancer researchers**

Rewarding PROMISE

For a young scientist, the road to a successful research career is paved with catch-22s: No research without funding, no funding without research

To help address the dilemma, David Gandara, director of clinical research at the Cancer Center, in 1995 applied to the American Cancer Society's Institutional Research Grant program. This venerable awards program is designed to cultivate future cancer researchers. Some 30 institutions apply for the three-year grants each funding cycle. About half are accepted.

"Cancer is a challenging disease, and curing it will depend on a continual infusion of new talent," says Gandara, a professor of hematology and oncology and one of the nation's foremost lung cancer specialists. "The Institutional Research Grant program offers our institution an important means of supporting our most promising young investigators."

**"Cancer is a
challenging
disease. Curing
it will depend
on a continual
infusion of
new talent."**

To date the Cancer Center has received nearly \$600,000 in Institutional Research Grant funds and distributed the money among 20 junior faculty members. The dean of the School of Medicine has provided additional support to the program since its inception.

A local peer-review committee selects Institutional Research Grant recipients at UC Davis, scoring their research proposals in much the same way as the National Institutes of Health.

Seed money

Each awardee receives about \$20,000, typically enough to fund a research project that yields preliminary results in a pilot study.

The investigator then uses these initial studies to apply larger grants from the American Cancer Society, the National Cancer Institute, or other national sources.

The American Cancer Society renews an institution's

David Gandara and
Zelanna Goldberg



three-year grant based on the quality of its Institutional Research Grant-funded work and the productivity of its awardees. UC Davis has won three renewals; it will apply for a fourth this year.

The American Cancer Society launched its Institutional Research Grant program in 1947. "Support for beginning investigators is a priority for the ACS," says Ginger Krawiec, national administrator of the Institutional Research Grant program.

"The Institutional Research Grant program allows us to partner with research institutions to support the early careers of cancer researchers. Moreover, individual awardees go on to publish and obtain national peer-reviewed grants. The program also promotes strong relationships between the local ACS and the institution and its awardees."

The Davis advantage

Many of the UC Davis Institutional Research Grant awardees do not work at the Cancer Center. Institutional Research Grant funds are available to promising young cancer researchers no matter which department, school or college they are associated with.

At UC Davis, cancer-related work takes place not only in the School of Medicine, but also in the School of Veterinary Medicine, Division of Biological Sciences, College of Engineering, and College of Agriculture and Environmental Sciences, among others.

"We call this the 'Davis advantage,'" says Joel Kugelmass,

an administrative analyst at the Cancer Center who helps oversee the Institutional Research Grant program. "Our cancer program benefits from the varied disciplines of these other schools, colleges and divisions."

Neil Hunter, an assistant professor in the Center for Genetics and Development, is a good example. His Institutional Research Grant grant allowed him to investigate the functions of a gene called BLM. Individuals who inherit a defective BLM gene are at increased risk for many forms of cancer. Understanding how the gene defect operates could point the way to future therapies aimed at correcting cancer-related chromosomal instability.

"Receiving the grant was a great confidence boost at an early and unsure stage of my academic career," Hunter says.

Julie Sutcliffe-Goulden, an assistant professor of biomedical engineering, is another case in point. Her Institutional Research Grant allowed her to pursue her work in molecular imaging. She radioactively labels small molecules that bind to certain cancers in laboratory animals, then images the tumors using a miniaturized positron emission tomography (PET) scanner. Her

aim: to find a radioactive compound that, in combination with the miniaturized PET scanner, can reveal how mouse models of human cancers progress and respond to therapy.

Getting started

Zelanna Goldberg arrived at UC Davis Cancer Center as an assistant professor of radiation oncology in 1999, eager to build on the promising work she'd done in mentor J. Martin Brown's lab at Stanford.

"Receiving an Institutional Research Grant award allowed me to get on my feet," Goldberg says. With it, she showed that an investigational anti-cancer drug, UCN-01, makes cancer cells more vulnerable to radiation. The finding was a springboard to bigger grants, publication in *Radiation Research* — and her own laboratory. Today Goldberg's work is supported by grants from the UC Office of the President, the Radiation Society of North America and the U.S. Department of Energy.

When promising young cancer investigators get the seed funding they need, everyone benefits: the scientists, the institutions, and, most importantly, the patients. [UCD](#)



Clair Bishop with Louie

***The soybean, cultured with shiitake mushrooms,
may slow prostate cancer***

SOY POWER



Faced with a choice of surgery, radiation, doing nothing or taking a daily handful of soy-mushroom capsules to treat his early prostate cancer, Clair Bishop went with the nutritional supplement. The retired insurance company executive is part of a study to determine if the capsules can indeed control early, localized prostate cancer.

“It’d be great if it works,” says Bishop, 75, an avid golfer and tennis player living in Placerville. “I’ve never been in the hospital a day in my life, and never taken any medicine. I’d rather keep it that way, if I can. And I’m definitely more comfortable doing something than doing nothing.”

Bishop is a volunteer in a UC Davis Cancer Center study of the efficacy of an extract cultured from soybeans and shiitake mushrooms. Known as genis-

“It would be an important development in our treatment of prostate cancer.”

tein combined polysaccharide, or GCP, the extract has shown promise as a way to slow or halt prostate cancer progression in men with early, untreated disease.

It’s not a cure, and it’s unknown how long its therapeutic effects might last. But GCP could enable men like Bishop to postpone the day they’ll need aggressive medical treatment.

Watchful waiting

Many men with low-grade prostate cancer decide against surgery or radiation, treatments that can result in impotence or incontinence. But the conservative alternative, often called “active surveillance” or “watchful waiting,” can be tough psychologically.

Ralph deVere White, professor and chair of urology and principal investigator of the study,



Ralph deVere White is launching the first phase II trial of genistein combined polysaccharide for early prostate cancer.

says a new option like GCP could help ease that anxiety, enabling more men to stay a conservative course and avoid the significant risks of surgery or radiation.

“It’s a promising approach,” deVere White says. “If we can find a chemopreventive agent capable of slowing or stopping the progression of early, localized prostate cancer, it would be an important development in our treatment of the disease.”

Long used in Asia

GCP is used as a complementary therapy for prostate cancer in Japan, Korea and other parts of Asia. UC Davis has been studying the extract in the laboratory for many years, with unrestricted support from a Japanese company that makes the supplement.

The first clinical study, a small phase I trial involving 13 prostate cancer patients, took place at the Cancer Center two years ago. Results of the study

appeared in the *Journal of Urology* last year.

In the study, deVere White found that the supplement reduced PSAs by as much as 61 percent in the prostate cancer patients who had received no previous treatment for their disease. For unknown reasons, GCP didn’t benefit men who had received radiation, surgery or hormone therapy. The only side effect was diarrhea.

Phase II trial begins

The new trial, a phase II study, ultimately will enroll 64 men. The volunteers will receive either GCP or a placebo for six months. Neither the patients nor the study investigators will know who is taking the placebo until the six months are over.

At that point, patients who received the placebo, along with patients who received GCP but had minimal change in their PSAs, will be offered a six-month supply of the supplement

at no cost. When that second six-month period is up, all patients who continue to show a decreased or stable PSA may continue receiving GCP for free, as long as they have their PSAs checked every six months.

If the results are promising, deVere White will seek National Cancer Institute funding for a much larger phase III study.

Nature’s pharmacy

GCP wouldn’t be the first cancer therapy to come from natural sources. According to the American Cancer Society, a third of new cancer therapies reaching the market today are derived from natural substances. To earn FDA approval, all of the agents first demonstrated safety and effectiveness through rigorous laboratory and clinical testing.

Taxol is probably the best-known example. Derived from the bark of the Pacific yew tree, taxol was subjected to four decades of scientific investigation and clinical trials before earning FDA approval and becoming widely available in 1994.

Because of the double-blind nature of the GCP study, Bishop won’t know for several months whether the capsules he’s been taking contain GCP or a placebo. Nevertheless, he seized the chance to participate.

“I did a lot of research, and got several medical opinions,” he says. “I thought this was definitely worth a try.” 

Metabolomic fingerprint

(from page 13)

what they signify. Ultimately the knowledge could enable doctors to take our metabolomic “fingerprints,” complex profiles of metabolite levels and patterns that may open up a new era in clinical diagnosis.

For example, Hammock is betting that prostate cancer cells leave their own trail of tell-tale metabolites.

With Katja Dettmer, a post-graduate fellow in his lab, he plans to systematically map the metabolic profiles of a diverse selection of prostate cell lines: some derived from highly aggressive prostate cancers, some taken from very slow-growing prostate tumors, and others harvested from healthy prostates. The task is made possible by advances in technology, pioneered in Hammock’s lab, which allow analysis of thousands of metabolites at a time.

Prostate cancer test?

Hammock’s hope: to develop a simple metabolite test that would allow urologists to accurately distinguish life-threatening prostate tumors from those unlikely to grow beyond the prostate itself.

Such a test would spare thousands of men with indolent prostate cancers the risks and side-effects of aggressive treatment, while ensuring that men with life-threatening tumors get the most aggressive therapy possible.

And if metabolomics yields new tools to fight prostate cancer,

tools for other cancers no doubt will follow.

“The beauty of this field is that once you have a good system in place, you can apply it to any problem,” Dettmer says.

Metabolomics is a hot topic throughout the UC Davis Integrated Cancer Research Program, a network of more than 240 scientists on the Davis campus, at the medical center in Sacramento and at Lawrence Livermore National Laboratory in Livermore.

Secret factories

Like Hammock, Rod Balhorn, a biochemist at Lawrence Livermore, believes the end-products of cell activity — the metabolites — may provide the quickest and most useful ways to monitor cellular function.

Balhorn likens metabolomics researchers, trying to discover how a cell works, to intelligence agents, trying to figure out what a secret factory does.

“Let’s say the factory makes buckets,” he suggests. “You could look in the factory’s office at the enormous catalogue of machines available for use; that’s equivalent to the factory’s ‘genome.’”

“But if you took this approach, it would take a very long time to learn anything about what was going on in the factory.

“Or, you could examine all the machines that are actually present in the facility. They would correspond to the pro-

“Metabolomics is the best thing we’ve received from the rush to sequence the human genome.”

teins in the cell. Upon looking carefully at each one, you might discover that one machine cuts sheets of metal, another rolls the pieces into a cylinder, and another fuses the edges together.

“This would make it possible to more easily guess what the factory might be doing, but there would still be a lot of different possible answers.

“Or, you could simply look at the factory’s end product: the bucket. The bucket would be analogous to the metabolite of the cell — the product of all the activity,” he says.

Finding the bucket

If finding the bucket is the easiest way to figure out what the factory is doing, finding metabolites may be the easiest way to figure out what individual proteins do, Balhorn says. The approach has tremendous potential for advances in understanding, preventing and treating cancer and other diseases.

Says Hammock: “Metabolomics is the best thing we’ve received from the rush to the human genome. “Of all the various ‘omics, it has the greatest potential for the fastest clinical applications.” 

A gift to bark about

**The Sacramento Region Community Foundation funds
a unique canine-human clinical trials program**

Dogs have long been treasured as companions and protectors. Now, thanks to a \$75,000 gift from the RCA Community Fund of the Sacramento Region Community Foundation, dogs are helping their human friends find a cure for cancer. The knowledge will benefit canines and humans alike.

The \$75,000 gift will fund the first year of a three-year clinical trials consortium will combine the resources of the Cancer Center with those of the School of Veterinary Medicine, perhaps the

first canine-human clinical trials collaboration ever undertaken. The School of Veterinary Medicine and the Cancer Center will jointly fund the last two years.

The consortium will concentrate on investigational treatments for cancers that occur more frequently in dogs than in people, including sarcomas and lymphomas. This approach will give canine cancer patients at the vet school access to more anti-cancer drugs than ordinarily would be available to them. At the same time, physicians at

the Cancer Center will get valuable information about the efficacy of new treatments sooner than they otherwise would.

“It’s truly a win-win proposition for both species,” says Joseph Tuscano, an associate professor of hematology and oncology at the Cancer Center. He and Cheryl London, an assistant professor of surgery and radiological sciences in the veterinary school, will serve as principle investigators for the groundbreaking collaboration.

William Hegg, treated at the Cancer Center a decade ago for prostate cancer, was instrumental in securing the new gift. A member of the board of directors for the RCA Community Fund, Hegg convinced his fellow directors that an investment in the Cancer Center would have far-reaching benefits for Sacramento and the region.

“In my opinion, the Sacramento community is fortunate to have a leader in the

Dogs are helping their human friends find a cure for cancer, knowledge that will benefit both species.



The annual tree “untrimming” sale at the Cancer Center supports breast cancer research.



cancer field like UC Davis Cancer Center,” says Hegg, who is chairman of the board of Alleghany Properties, Inc.

The RCA Community Fund is a permanent endowment created when RCA Information Services, Inc., a national credit company, donated its office and other assets to the Sacramento Region Community Foundation.

The Sacramento Region Community Foundation is a nonprofit community foundation dedicated to helping people connect to causes they care about. It has distributed more than \$38 million since its inception in 1983.

In addition to Hegg, the foundation’s board is made up of some of Sacramento’s most distinguished business and community leaders, including Elizabeth Rindskopf Parker, dean of the University of the Pacific McGeorge School of Law; Jeanne Reaves, president and CEO of River City Bank; and Frank Whittaker, vice president of the McClatchy Company.

“The results of this novel consortium may motivate drug companies to investigate cancer drugs they might not otherwise invest in, medications that could benefit both human and canine patients,” says Ralph deVere White, director of the Cancer

Center. “We are grateful to the Sacramento Region Community Foundation for helping to make this research possible.” 

Tree “untrimming” party benefits research

Help raise money for breast cancer research and add new ornaments to your tree at the annual Joan Giboney Tree of Hope untrimming party and ornament sale in the UC Davis Cancer Center lobby on Thursday, Dec. 16, from 11 a.m. to 3:30 p.m. Holiday cookies and punch will be served. Local choral groups will perform holiday songs.

The professionally decorated, 15-foot tree, trimmed with more than 700 ornaments and 2,000 lights, is the legacy of the late Joan Giboney, a Lodi interior designer who wanted to raise the spirits of her fellow cancer patients during the holidays. Her family and friends have carried on the tradition in her memory. This year’s tree will be decorated in a winter-wonderland theme. Tree and ornaments can be viewed in the Cancer Center lobby from Friday, Nov. 19, through the sale. All proceeds go to breast cancer research at UC Davis Cancer Center. For more information call (916) 734-5800. 

Swing at cancer

Nearly 170 golf enthusiasts raised \$200,000 for the Auburn Community Cancer Endowment Fund at the second annual Jim Otto Swing at Cancer Celebrity Golf Classic. The tournament was held at the Auburn Valley Country Club on June 28. A celebrity cocktail reception and silent auction took place the evening before.

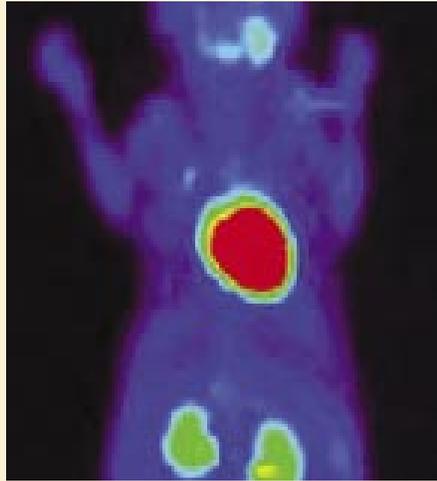
The Auburn Community Cancer Endowment Fund has raised \$650,000 for cancer research at UC Davis Cancer Center since 2001. The group’s board of directors recently increased its fund-raising goal from \$1 million to \$1.5 million to establish an endowed chair in basic cancer research. Proceeds from the golf tournament bring the fund’s balance to \$850,000, well on the way toward the new goal.

Otto, an NFL Hall of Famer and former all-pro center for the Oakland Raiders, was treated for prostate cancer at UC Davis. He has since declared a personal vendetta against the disease.

Among the celebrities enjoying a day on the links were former Oakland Raiders stars Fred Biletnikoff, Daryle Lamonica, Ben Davidson, Otis Sistrunk, Cliff Branch and Clem Daniels. 

SMALL-ANIMAL IMAGING YIELDS CANCER CLUES

Positron emission tomography or PET imaging is widely used to detect and follow cancer in human patients. Now UC Davis researchers have come



up with a micro-PET machine that can do the same in animals as small as a mouse.

Simon Cherry, a professor of biomedical engineering at UC Davis, led the micro-PET effort. Craig Abbey, also in the Department of Biomedical Engineering, designed image analysis methods to go along with it.

A first research target for the new machine: mouse model of ductal carcinoma in situ, or DCIS, a precursor to breast cancer in humans. Using the micro-PET, cancer researchers Alexander Borowsky, Robert Cardiff and Jeffrey Gregg, all at the UC Davis Center for Comparative Medicine, are able to non-invasively follow the natural growth of the DCIS-like lesions in mice over a long period of time.

Such investigation is impossible in human patients, because the standard of care is to remove DCIS tissue. Most invasive breast cancers are thought to develop from DCIS.

"Not only can we see the DCIS-like lesion in the mouse, but we can detect its earliest transition to an invasive tumor," Borowsky says.

The next step: using Cherry's micro-PET to assess treatments aimed at slowing or stopping that transition. The UC Davis research was published July 26 in the *Proceedings of the National Academy of Sciences*. [UCD](#)

TOO MANY COLONOSCOPIES

Doctors may be recommending too many follow-up colonoscopies for patients who have had colon polyps removed, according to recent research led by UC Davis gastroenterologist Pauline Mysliwicz.

The researchers found that 24 percent of gastroenterologists and 54 percent of general surgeons recommend surveillance colonoscopy for small, hyperplastic polyps. For patients with single small, low-risk adenomas, many of the physicians recommend surveillance every three years, or even more often.

Evidence-based guidelines, in contrast, call for no extra surveillance after removal of a hyperplastic polyp, a benign growth not believed to become cancerous. And while the guidelines do recommend surveillance colonoscopy following removal of adenomas, which can develop into cancer, at most the exams are recommended only every three to five years.

"We believe colonoscopy can be a life-saving procedure, but it shouldn't be done more often than necessary," Mysliwicz says. "When it's used inappropriately, it strains health care resources and puts patients at unnecessary risk."

The findings affect the estimated 20 to 30 percent of Americans age 50 and older who will have a polyp removed as a result of colon cancer screening, a population of some 12 to 18 million people. The National Cancer Institute-funded study appears in the Aug. 17 issue of *Annals of Internal Medicine*. [UCD](#)



"BIG C" AD CAMPAIGN

"You've got the big C. Cancer. A word that changes your life the moment you hear it."

So opened a novel TV, radio and newspaper ad campaign conducted in the greater Sacramento area this spring. Primo "Lucky" Lara, associate

professor of medicine, won a grant from the National Cancer Institute and five major pharmaceutical companies last year to design and test the campaign as a way to increase awareness of and participation in cancer clinical trials. The UC Davis Health System helped underwrite the cost.

Only 3 percent of adult cancer patients nationally participate in clinical trials, the rigorous scientific studies that determine whether a new treatment is safe and effective. Such low participation rates prolong drug development and delay patient access to potentially effective new agents.

Preliminary "Big C" results are encouraging: 760 people called the toll-free campaign hotline or visited www.ucdavisclinicaltrials.org. E-visitors used the site's patient-friendly search tool more than 1,000 times to look up clinical trials by cancer type. And 125 cancer patients who responded to the ad were referred to the Cancer Center for possible participation in a clinical trial.

Lara is now at work comparing public awareness surveys he conducted before and after the campaign in Sacramento and San Diego (which served as a control). If the campaign meets expectations, the NCI will be able to use it throughout the nation. [UCD](http://ucdavis.edu)



ULTRASOUND FOR CANCER TREATMENT?

Ultrasound scans might be most familiar for getting a peek at a developing fetus, but the technology could also be used to

treat cancer. A partnership between UC Davis, Siemens Medical Systems and ImaRx Inc., funded by a National Cancer Institute grant, will study ways to deliver drugs to tumors using focused ultrasound. The five-year, \$7 million Biomedical Research Partnership grant is

October 17- November 19

"The Art of Healing Breast Cancer: A Union of Science and Design"
UC Davis Design Museum, 145 Walker Hall Davis
(530) 752-6150 or <http://designmuseum@ucdavis.edu>

November 2

"Cancer and the Caregiver"
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5786

November 17

"Ancient Roots to Modern Health: Complementary Cancer Therapies"
UC Davis Cancer Center auditorium, 5- 7:30 p.m.
4501 X Street, Sacramento (916) 734-5786

December 6

"Understanding Chemotherapy and Managing Side Effects"
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5800

December 7

"Eating Hints for the Holidays"
UC Davis Cancer Center auditorium, noon to 1 p.m.
4501 X Street, Sacramento (916) 734-5786

December 16

Joan Giboney Tree of Hope UnTrimming Sale,
UC Davis Cancer Center lobby, 11 a.m. to 3:30 p.m.
4501 X Street, Sacramento (916) 734-5800

January 11

"Cancer and Intimacy for Women"
UC Davis Cancer Center auditorium, noon 1 p.m.
4501 X Street, Sacramento (916) 734-5786

February 8

"Spirituality and Cancer"
UC Davis Cancer Center auditorium, noon 1 p.m.
4501 X Street, Sacramento (916) 734-5786

March 8

"Supportive Care in Cancer"
UC Davis Cancer Center auditorium, noon 1 p.m.
4501 X Street, Sacramento (916) 734-5786

designed to bring together academics and industry to develop new medical technology.

The idea is to encapsulate cancer-fighting drugs into tiny bubbles that can be injected into the bloodstream and steered to a tumor using ultrasound. Once there, the bubbles bind to the tumor by means of antibodies or other molecules coating the bubble surface. A focused pulse of ultrasound can then be used to burst the bubbles, delivering a drug directly to tumor cells.

UC Davis researchers led by Katherine Ferrara, professor and chair of biomedical engineering, will carry out preclinical studies on the system. Siemens Medical Systems will design and build the imaging equipment, and develop ways to direct pulses of ultrasound to a three-dimensional volume. ImaRx, Inc. of Tucson, Ariz., makes the bubbles for drug delivery. [UCD](#)

ON THE SAME TREATMENT, JAPANESE PATIENTS LIVE LONGER

A chemotherapy regimen commonly used to treat non-small cell lung cancer is both more effective and more toxic in Japanese patients than in American patients, researchers reported at the annual meeting of the American Society of Clinical Oncologists in New Orleans this spring.

The first of its kind, the analysis underscores the importance of genetic variations in medicine and points to a need for increased international collaboration in trials of new cancer treatments.

Median survival time was 12 months for the Japanese patients who received paclitaxel and carboplatin, versus 9 months for American patients receiving the same regimen. "The reasons for the increased survival among the Japanese patients remain to be determined, but the implications of this observation are of considerable interest," says lead investigator David Gandara, director of clinical research at UC Davis Cancer Center and professor of medicine at the UC Davis School of Medicine.

The U.S. trial was conducted through the Southwest Oncology Group, one of the country's largest National Cancer Institute-sponsored cancer clinical trials cooperative groups. The Japanese study was conducted through the Four-Arm Comparative Study Group. Gandara is a member of the ASCO board of directors, and serves as its secretary/treasurer. He also chairs the SWOG Lung Committee. [UCD](#)

BREAST CANCER PREVENTION STUDY SEEKS VOLUNTEERS

Healthy, post-menopausal women at high risk for breast cancer may be eligible to participate in a major new international study to determine whether the drug exemestane can prevent the disease. UC Davis

Medical Center is the first center in the United States chosen to participate in the study, funded by the Canadian National Cancer Institute. Ultimately more than 5,000 women throughout North America will be enrolled in the trial, which will last eight years.

"Exemestane may present a new breakthrough in the prevention of breast cancer, and has the potential to greatly decrease the risk of this deadly disease, with fewer side effects than currently available preventive medications," says John Robbins, professor of general medicine at UC Davis School of Medicine and Medical Center and principal investigator of the study.

Exemestane is one of a new class of anti-cancer medications known as aromatase inhibitors. Aromatase inhibitors have shown promise in preventing breast cancer recurrences in women previously treated for the disease, but have not yet been clinically studied as a way to prevent the disease in the first place. The new study will be the first designed to answer this question.



For more information about the exemestane study at UC Davis Medical Center, please contact Elizabeth Winward at (916) 734-5562, or e-mail Robbins direct at jarobbins@ucdavis.edu. [UCD](#)

CARE CLOSER TO HOME

Cancer patients in Roseville, the Central Valley, and Yuba-Sutter counties may be able to get some or all of their care closer to home.

Comprehensive treatment, overseen by specialists from UC Davis Cancer Center, is now available at Mercy Cancer Center in Merced. Since opening its doors in 2000, Mercy Cancer Center has offered state-of-the-art radiation oncology services provided by UC Davis Cancer Center physicians. In August the center also began offering chemotherapy and other hematology and oncology services. The hematology and oncology service is staffed by UC Davis faculty physicians.

With the recruitment of a new, full-time cancer specialist, the UC Davis Cancer Center Roseville Clinic has started offering patients access to a wide range of cancer clinical trials. That's in addition to the comprehensive hematology and oncology services already offered at the Roseville site.

With Fremont-Rideout Hospital, UC Davis Cancer Center also operates the Fremont-Rideout Cancer Center in Marysville, which offers comprehensive cancer care and access to clinical trials for the Yuba-Sutter area. [UCD](#)

NATIONAL CANCER SURVIVORS DAY WALK

From a climbing wall to a one-mile survivors' walk, UC Davis Cancer Center celebrated National Cancer Survivors Day on June 6 with activities that drew hundreds of cancer survivors and their supporters to the Richard and Annette Bloch Cancer Survivors Park on the Medical Center campus. A dozen local cancer organiza-

tions and support groups, from the UC Davis Cancer Center Prostate Cancer Support Group to the Leukemia & Lymphoma Society, planned the morning. In keeping with the climbing theme, Dasha Drab, a breast cancer survivor who leads fellow survivors on hikes in the Sierra, delivered the keynote. Other highlights: Face-painting by local Brownie troops, laughter therapy and free massages. [UCD](#)



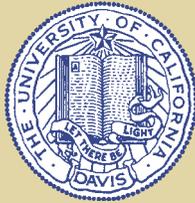
Hundreds of cancer survivors and their supporters turned out for National Cancer Survivors Day at UC Davis Cancer Center.



UC DAVIS CANCER CENTER

SYNTHESIS

syn·the·sis (sin'thə sis) **n.**,
pl. - **ses** (-sez') [[Gr. < *syn-*,
together + *tithenai*, to place,
DO¹]] **1** the putting together
of parts or elements so as
to form a whole **2** a whole
made up of parts or elements
put together **3** *Chem.* the
formation of a complex
compound by the combining
of two or more simple
compounds, elements, or
radicals **4** *Philos.* in Hegelian
philosophy, the unified whole
in which opposites (thesis and
antithesis) are reconciled.



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