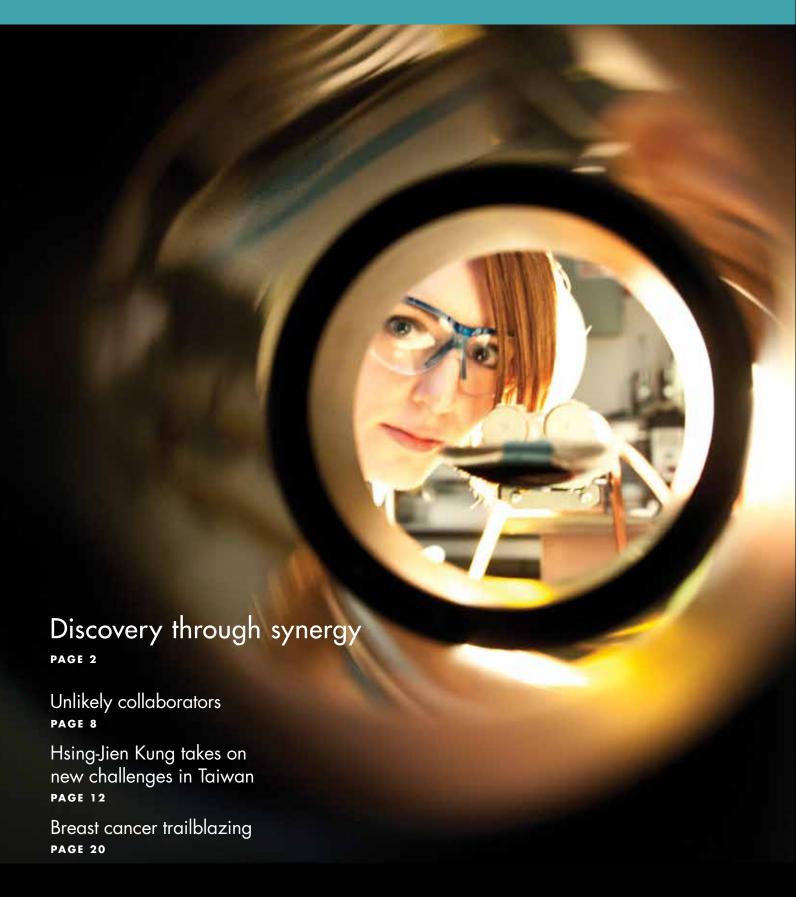
SYNTHESIS

THE MAGAZINE OF UC DAVIS COMPREHENSIVE CANCER CENTER VOL 16 • NO 1 • SPRING/SUMMER 2013



Dear Reader,

UC Davis Comprehensive Cancer Center had a lot to celebrate in 2012: first, our designation by the National Cancer Institute as the nation's 41st comprehensive cancer center, and then our new building expansion opening. These are important milestones in our 21-year history.

Today is a new day, and with it comes renewed determination to tackle cancer on every front. That means pouring energy into basic and translational research that result in better treatment options. It means collaborating on technologies to improve ways to find and target treatments. And it means making sure that our patients have the resources they need to navigate through the challenges presented by a cancer diagnosis.

This issue of *Synthesis* sheds light on some of these innovations. Our robust biomedical engineering work takes center stage in a story describing the synergistic work of Julie Sutcliffe and Ramsey Badawi, who are working to improve cancer detection technologies. Another story highlights Jian-Jian Li's breast cancer stem cell research on a subset of breast cancer tumors – HER2-negative – paradoxically found to respond to drugs that target HER2-positive tumors.

The cancer center's basic science work is essential in the global fight against cancer, and Hsing-Jien Kung has led those efforts since 1996. Our story about Kung's new role running Taiwan's National Health Research Institutes highlights his achievements as a scientist and mentor.

Taking discoveries from the laboratory to the clinic is the cancer center's mission, and Lucky Lara's collaboration with Marta Van Loan at the

U.S. Department of Agriculture's Western Human Nutrition Research Center to find prostate cancer biomarkers will help personalize treatment for advanced disease.

Personalized treatment already has benefited lung cancer patient Elizabeth Lacasia, whose story describes how genetic analysis and clinical trials of new, targeted lung cancer treatments have given her hope and inspiration.

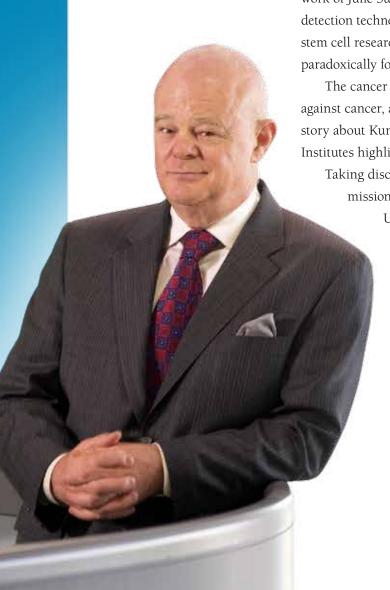
We hope you enjoy this issue of Synthesis.

RALPH DE VERE WHITE

Director, UC Davis Comprehensive Cancer Center

Associate Dean for Cancer Programs

Distinguished Professor, Department of Urology



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Breaking Barriers to Beat Cancer^{ss}

INSIDE THIS ISSUE

First steps

Biotechnologies combine to improve cancer detection

Patient focus

Bay Area patient embraces personalized approach

In translation

Research partnership yields prostate cancer biomarker

Connections

Hsing-Jien Kung takes on new challenges in Taiwan

Outreach

Supportive Services introduces a new team, more resources

Building on basics

Stem cell discovery broadens treatment options

Benefactors

Fund benefits women's cancer advocacy and research

News briefs

26 Researchers discover promise in soybean extract for prostate cancer, Chong Pan wins national investigator leadership award, New device reduces radiation treatment times, and more.





A National Cancer Institute-designated comprehensive cancer center

cancer.ucdavis.edu



Discovery through synergy

Biotechnologies combine to improve cancer detection

We are slowly gaining ground on cancer.

Targeted treatments, like Herceptin against breast cancer, have been remarkably successful. New approaches to immunotherapy also are showing great promise. However, the best treatments in the world may not be good enough if the disease is not detected early. Cancer is a disease of mutations, and the longer it goes undiscovered, the more mutations it can develop – variations that can make tumors resistant to treatment.

Both researchers and clinicians recognize this problem and are working hard to solve it. At the National Cancer Institute-designated UC Davis Comprehensive Cancer Center, scientists are building a new class of scanners, as well as developing new imaging agents that will shine a light on hidden cancers. These technologies could help detect cancers when they're smaller and easier to treat.

Before cancer can be treated, it must be detected. The earlier cancers can be detected, the better the patient's prognosis. That's where imaging comes in.









The promise of PET

For more than 30 years, positron emission tomography (PET) has been a powerful tool to detect cancer. The technology is relatively simple; a radioactive tracer is attached to a molecule, such as a sugar, and injected into a patient. Because cancers are hungry and like to eat sugar, the molecule and its radioactive partner concentrate in those tumors. The scanner then picks up the radiation concentrations, detecting the cancer.

It's good technology, but Ramsey Badawi, director of nuclear medicine research, thinks it can be better.

"Current PET scanners only cover 15 to 20 centimeters at a time," says Badawi. "That means we can Before cancer can be treated, it must be detected. The earlier cancers can be detected, the better the patient's prognosis. That's where imaging comes in.

only image a small portion of the body at any one time, which slows the process and wastes radiation. However, if we build a scanner that's two meters long, we will see everything all at once, including smaller tumors. This will be great for patients, because it will work faster, require less radiation and detect cancer at its earliest stages."

The National Cancer Institute (NCI) has awarded Badawi a prestigious "Provocative Questions" grant to develop the technology. Of 700 applications, his project was one of only 57 to receive funding. The Badawi group is working with colleagues at Lawrence Berkeley National Laboratory, the University of Iowa and the University of Pennsylvania to make this happen.

First steps>>

A crush of data

Building such a large scanner brings a host of technical challenges. For example, with radiation coming from diverse angles, images can get blurred. Sophisticated software must be developed to determine where in the body the radiation originated and where it ended up.

The most significant challenge is the amount of data that will enter the scanner at once – not gigabytes, but terabytes. The researchers are taking their inspiration from websites like Facebook and Google, which use algorithms to instantly sort huge amounts of information. Badawi and his team are using similar algorithms and adjusting them to meet the large scanner's huge data-sorting needs. Better information-handling translates into sharper images.

A shopping list of benefits

The new scanner will be 30- to 50-times more sensitive than current scanners, allowing clinicians to detect tumors at their earliest stages. This added sensitivity brings other benefits. Scans can be completed in seconds, which is particularly helpful when imaging children.

Because of the scanner's increased sensitivity and speed, patients will require less radiation, allowing researchers to conduct studies they can only dream of now. If less radiation is used, physicians can use PET to scan high-risk patients before they develop symptoms. Volunteer study participants can also be safely scanned to study inflammation, obesity, even gut bacteria.

Seeing-eye molecules

While Badawi's team works to build a better scanner, Julie Sutcliffe and her team are working with Siemens to develop better tracers. PET scanning for cancer patients typically involves use of tracers inserted into the body. Current tracers generally combine glucose (a sugar) with radioactive fluorine (a chemical element). Since most tumors take up sugar at a higher rate than normal cells, they will light up on PET scans. The problem is that these tracers also light up the heart and brain, which

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"It's a difficult challenge. We're using everything from our chemistry toolkit to make this work."

~ Julie Sutcliffe

can muddy the picture and make diagnosis more difficult. That can muddy the picture and make diagnosis more difficult. Sutcliffe's group is developing new tracers that more precisely target cancers.

"Different cancers often have different biomarkers, and we're trying to target those biomarkers, much in the same way Herceptin targets HER2-positive cancer," says Sutcliffe. "We can do the same with an imaging agent. We can put the imaging agent onto a targeting molecule and it will light up in the areas that have that biomarker."

Sutcliffe's team is working with cell-surface proteins called integrins, prevalent in cancer cells, particularly metastatic ones. They are identifying molecules that will seek out these receptors and bring the radioactive payload with them. Specifically, they are interested in agents that will precisely target breast and pancreatic cancers. Breast cancer affects millions of women, while pancreatic cancer exhibits few symptoms and is notoriously difficult to detect.

In addition, a tumor-seeking molecule could do more than guide radiation particles to cancers; it could also guide treatments.

"Our long-term goal is to develop an imaging agent and a therapeutic at the same time," says Sutcliffe.

It's hard work. First, research using radioactive materials requires appropriate precautions. Second, the isotopes have very brief half-lives, in some cases just a few minutes. Scientists can't use normal slow chemistry to attach the isotope to the targeting agent because they simply don't have the time.

"It's a difficult challenge," says Sutcliffe. "We're using everything from our chemistry toolkit to make this work."

The big payoff

One of the biggest hurdles in developing new cancer therapies is that many drugs fail late in the process. By that time, hundreds of millions of dollars have been invested. Both Badawi and Sutcliffe believe the technologies they are developing

could profoundly improve this process, eliminating poorly performing drugs earlier in the pipeline.

"The earlier you can winnow out the bad ones, the more resources you can concentrate on the good ones," says Badawi. "Better PET technology could help us winnow out inferior drugs."

More sensitive scanning could allow researchers to measure where a drug goes in the body and how long it stays there. The scanner's enhanced sensitivity would also allow researchers to test compounds that would be toxic in larger amounts. A drug found to be toxic to the heart would be removed from the pipeline.

"You can attach any number of drugs with radioactive tags and find out what a drug does," Badawi says. "Does it go to the cancer, does it do bad things like go to the bone marrow or hang around in the liver too long? If you can do that, you can say ahead of time that it's probably going to be pretty toxic and move along to the next drug."

Patient focus>>



Bay Area patient embraces personalized approach

As a woman in her mid-forties who didn't smoke, Elizabeth Lacasia never expected to be diagnosed with lung cancer.

But in 2006, after she developed a persistent and serious cough, a chest X-ray and CT scan revealed several tumors in her lower left lung.

She was eventually diagnosed with stage IV lung cancer, a rare subtype called "bronchioalveolar carcinoma." Over the next 18 months, she underwent two surgeries followed by a tough combination of a targeted drug treatment and two chemotherapies. Yet the cancer continued to spread. As it turned out, the chemotherapy she was taking was later found to be ineffective against

her cancer, and it caused significant side effects.

Lacasia, who was an avid rollerblader, a snow skier and had a successful career with a biotech oncology company, was not a woman who gave up easily. She contacted David Gandara, a nationally recognized lung cancer expert and senior advisor for clinical research at the UC Davis Comprehensive Cancer Center.

Gandara is known for his emphasis on personalized treatment using information available through genetic testing of a patient's tumor to find the most effective therapies. Lacasia underwent a battery of molecular and genetic tests to help identify whether her cancer would respond to drugs designed to target specific genetic mutations in her cancer. These tests can also reveal which chemotherapies might be most effective in fighting a patient's tumor.

"The genetic testing panel I underwent at UC Davis was very cutting-edge, and it provided important information about how to effectively treat my cancer," Lacasia now says.

In Lacasia's case, the molecular and genetic tests revealed that her cancer was a "wild type," meaning it did not have the mutations that can cause some lung cancers to take hold and spread, and which can be effectively targeted by new state-of-the-art medications. So Gandara recommended a clinical trial, which used an approach that has now proven effective for people with Lacasia's "wild type" cancer.

Instead of just one medication, patients like Lacasia in the clinical trial received two drugs, which are usually considered antagonistic, or ineffective when used together. Yet in the clinical trial, Lacasia took the two drugs – erlotinib (Tarceva) and

"The **genetic testing panel** I underwent at UC Davis was very **cutting-edge**, and it provided important information about how to **effectively treat my cancer**."

~ Elizabeth Lacasia

pemetrexed (Alimta) – in a novel alternating schedule that Gandara knew from experience could help treat Lacasia's cancer.

"The novel schedule in which we give the drugs enables patients to get the greatest benefit from both therapies," Gandara says.

"By using this approach, we took two drugs that ordinarily just provide disease control – that is, the cancer stops growing – and made them much more effective," he says. This approach is now being used at hospitals worldwide, as well as in UC Davis' cancer clinical trials, chaired by oncology physicianscientist Tina Li.

The treatment Lacasia received in the clinical trial proved to be extraordinarily effective against her cancer. She had a "complete response" — meaning that there were no visible signs of lung tumors on screening tests, and the cancer has stayed in remission for more than two years.

"We hope my cancer can be managed more like a chronic disease, since I will be on treatment for the rest of my life," Lacasia says.

Now, Lacasia is able to do things she enjoys, such as gardening and creative writing. Married two years before her diagnosis, she lives in a house she and her husband designed and built together. She enjoys traveling and, for her birthday last year, she hiked to the top of one of the waterfalls at Yosemite National Park. She's involved in the Bonnie J. Addario Lung Cancer Foundation as a support group participant. She also finds solace through a group that helps cancer patients and survivors write about their experiences.

"I've learned to confront my fears about lung cancer and find peace, and also be an advocate for the best cancer treatment I can obtain," Lacasia says.

Through the genetic testing and the innovative treatment she received at UC Davis, Lacasia found renewed hope.

"I believe Dr. Gandara and the approach he took saved my life," she says.

At the same time, choosing to become an informed participant in her diagnosis and treatment – including genetic testing for her tumor and working with Gandara to try innovative approaches to therapy – has been crucial to her survival, she says.

"In fighting cancer you can't be passive," she says. "If I had not switched to an oncologist whose philosophy aligned with my own, I don't think I would be here today."

Unlikely collaborators

Research partnership yields prostate cancer biomarker

When the U.S. Department of Agriculture's Agricultural Research Service put its Western Human Nutrition Research Center on the UC Davis campus some 13 years ago, no one could have predicted that the decision would eventually lead to the development of a biomarker for metastatic prostate cancer.

But that's exactly what happened, due to a sequence of events that began in 2007, recently culminating with the results of a new study from the UC Davis Comprehensive Cancer Center.

The study focuses on what is called "castration-resistant" prostate cancer, the point at which the disease does not respond to a treatment that deprives the patient of the male hormone testosterone, which fuels prostate cancer growth. The research validates preliminary findings in castration-resistant prostate cancer

patients in which blood levels of proteins associated with bone turnover were found to be strongly associated with survival. Patients with high levels of these blood markers had a much shorter lifespan than those with low levels. However, and more importantly, patients with the highest marker levels – those with levels in the upper 25th percentile – appeared to preferentially benefit from an investigational bone-targeted therapy.

"The sooner the physician knows the level of this biomarker in the



"It was **very exciting** because we could – from one blood sample – **predict which patients** would be **progression-free the longest**."

~ Marta Van Loan

bloodstream, the sooner appropriate therapy can be provided, particularly for those who are destined to respond well," says Western Human Nutrition Research Center research physiologist Marta Van Loan, a key investigator on the study.

In a step toward personalized medicine, these measurements could soon be used in a more precise manner to predict an individual patient's response to a specific drug.

The Western Human Nutrition Research Center might at first seem like an unlikely partner for a prostate cancer study. It houses a dozen senior scientists conducting basic research on immunity, obesity and other nutritionrelated topics. Among them is Van Loan, who, like the other scientists at the center, also holds an adjunct faculty position at UC Davis.

It was her expertise in bone metabolism that led to her participation in the research project. Six years ago, Primo "Lucky" Lara, associate director for translational research at the UC Davis Comprehensive Cancer Center, began asking his peers for referrals to a bone expert, and those queries led him over the causeway to Van Loan.

Lara had been conducting a pilot study of a novel prostate cancer drug (BMS275291) in development that was reported to affect bone health. He needed an expert to help him monitor each patient's bone metabolism by measuring blood levels of proteins associated with bone turnover – that is, the body's natural process of bone removal and regeneration. High turnover ultimately results in a net loss of bone tissue; prostate cancer treatment contributes to the loss of bone integrity, as androgen-deprivation therapy often causes abnormally low bone density.

In translation>>

And so began the collaboration.
"It was coincidental that Lucky and
I got together on this," says Van Loan.
"He asked if someone could assist,
and he was referred to me."

Though BMS275291 failed to help the approximately 80 participants, Lara, Van Loan and their colleagues did find that patients with low turnover – meaning lower levels of bone-resorption enzymes –

tended to survive longer, and their disease was less likely to progress during the four-month study period. In contrast, patients with high bone markers – and therefore with higher bone turnover – had shorter survival times. In other words, the test could potentially predict who would respond to treatment and then help monitor the patient's response to treatment.



"These studies have led to a unique collaboration showing that co-location of science centers can coalesce in a way that has beneficial applications for patients, even when all the researchers work in seemingly disparate fields."

~ Primo "Lucky" Lara

"It was very exciting because we could – from one blood sample – predict which patients would be progression-free the longest," explains Van Loan.

Starting in 2009, the approach was tested as part of a much larger clinical trial on patients whose prostate cancer is resistant to castration therapy and has spread to bone.

More than 1,000 prostate cancer patients were enrolled in the nationwide double-blind study of a new cancer therapy and of the bone marker test. That trial was conducted by SWOG, a national cancer cooperative group supported by the National Cancer Institute. All patients in that trial received standard-of-care chemotherapy. Half of the subjects also were given atrasentan, an experimental bonetargeted pill, while the other half received a matched placebo. Nearly 900 patients in the trial consented to having their bone marker levels monitored to determine if the bone health measures correlated with response and outcomes. Lara and Van Loan hypothesized that patients with high bone marker levels would preferentially benefit from a bonetargeted drug such as atrasentan.

Over nearly three years, chemist Erik Gertz and a cadre of UC Davis graduate and undergraduate students analyzed 4,000 blood samples from more than 800 patients in the study. Each sample was analyzed using four different tests with an instrument called a spectrophotometer. The instrument allowed the scientists to determine the extent to which each sample absorbed light. Higher absorbance rates correlated with bone marker concentrations in each sample.

Lara presented the final results



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of this study, which was funded by a National Cancer Institute grant, at the 2012 American Society of Clinical Oncology meeting. Although the trial did not show a benefit for atrasentan in the overall patient population, the bone marker studies were clearly positive. The findings of the earlier study had been confirmed: the survival benefit from atrasentan could be predicted by measuring blood levels of bone turnover. Importantly, it showed for the first time that bone markers have utility in helping select patients for appropriate bone-targeted treatment.

The investigational agent in that trial (atrasentan) is no longer under development in prostate cancer. But the bone marker story is just getting started: orteronel, a new drug that inhibits androgen production, is currently being tested in metastatic

prostate cancer patients who are just initiating androgen deprivation therapy as part of a newly initiated Phase 3 SWOG trial. Together with other investigators, Lara is helping spearhead that trial and will again investigate the role of bone turnover biomarkers in this new patient population. He hopes that bone biomarkers in blood also will help predict which patients will benefit from a drug such as orteronel.

"This test could someday help us treat only those who are most likely to

benefit from specific therapies," Lara says. "That approach will obviously spare patients who are not destined to benefit from the side effects of ineffective therapy."

He adds, "An unexpected side benefit is that these studies have led to a unique collaboration between the cancer center and the Department of Agriculture, showing that co-location of science centers can coalesce in a way that has beneficial applications for patients, even when all the researchers work in seemingly disparate fields."

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Connections>>



"Truly exceptional"

Hsing-Jien Kung takes on new challenges in Taiwan

Hsing-Jien Kung retired earlier this year as UC Davis
Comprehensive Cancer Center's deputy director of basic science
and has taken on a new challenge as president of the National
Health Research Institutes in Taiwan, an organization similar in
function to the National Institutes of Health in the United States.

Fortunately, the emeritus professor's departure does not mean an end to his relationship with UC Davis. He already is looking toward expanding collaborations between the two countries to hasten the quest for cures for some of the world's most intractable diseases.

"I have been so very blessed at UC Davis with well-funded research and wonderful colleagues. No one in this position should be thinking of leaving," says Kung. "But I look forward to facilitating innovative, cross-disciplinary, integrative research in a country with limited resources but great potential."

A legacy of excellence

Kung arrived at UC Davis in 1998 when only a handful of laboratories throughout the campus focused on cancer research. As the cancer center's deputy director and chief of basic science, Kung oversaw the transformation of the cancer center into a world-class research institute, helping to achieve National Cancer Institute designation as a cancer center within only four years' time, and as a comprehensive cancer center last year – remarkable achievements for a relatively young institution.

Kung has a reputation as one of the most brilliant scientists at work on prostate cancer, with a particular interest in understanding the role of cancer-causing oncogenes and growth factors. He is also an enormously respected leader, mentor and colleague to all who have worked with him, as he is known to offer unfailing support along with his probing scientific questions.

"Hsing-Jien is special not just in his ability to do science – a lot of people can do science," says Ralph de Vere White, cancer center director.



He is also an enormously respected leader,
mentor and colleague to all who have worked
with him, as he is known to offer unfailing
support along with his probing scientific questions.

"It's his ability to bring everyone else along that is truly exceptional."

One of the individuals he brought along was 43-year-old David Boucher, now a biomedical engineering research scientist in the Sutcliffe Laboratory. Kung recruited Boucher 14 years ago when Boucher was an undergraduate. He says Kung's mentorship struck just the right tone.

"Dr. Kung gave us the independence

to really direct our own research,"
Boucher says. "But if there was something we thought would help us,
he would always support us. He gave
us the confidence that we could
do research."

A vision of crosscultural collaboration

Established in 1996, the National Health Research Institutes is a

Connections>>

nonprofit, autonomous organization under the supervision of the Taiwan Department of Health, dedicated to enhancing medical research and improving health care in the country. Kung, who was raised in Taiwan, will oversee all of its institutes, which include cancer research, cellular and system medicine, population sciences, biotechnology and pharmaceutical research, and infectious diseases and vaccinology. Research, developing technology and training are major thrusts of the institutes.

Kung is looking toward enhancing the research capabilities of both the Taiwan Institutes and UC Davis by combining their resources. For example, according to Kung, many cancers have important genetic and environmental factors that may best be discerned with large studies comparing different ethnic populations. He intends to combine

study populations across the ocean to create larger clinical trials and make use of the varied expertise from both institutions.

"I've learned over the years that collaborative research is the most productive," says Kung. "The whole often turns out to be greater than the sum of the individual parts."

Many of the Taiwan Institutes' researchers have trained under Kung at UC Davis, and, in his new position, he plans to expand exchanges between the two institutions. He will also maintain his own laboratory at UC Davis, continuing to do active research.

A beloved leader

In February, Kung's colleagues, students and friends came together to celebrate his career at a symposium and reception. Not surprisingly, research was a major



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~ Hsing-Jien Kung



focus of the afternoon, with older colleagues summarizing Kung's major contributions to cancer research and younger scientists presenting their current research under Kung's guidance. Topics ranged from basic research in virology and cancer cell biology to clinical trials for new breast cancer therapeutics.

All spoke with warmth and great respect for a mentor and colleague who was described as leading with a keen mind, hard work and unfailing kindness.

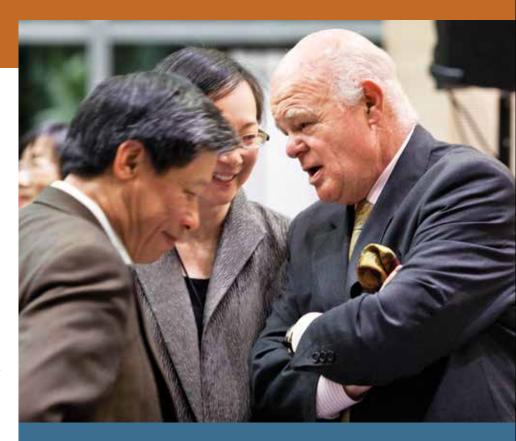
Colleen Sweeney told how she arrived at UC Davis feeling as if she were in the shadow of her husband, Kermit Carraway, who had been recruited to the Department of Biochemistry and Molecular Medicine. Sweeney – now associate professor in the same department and co-director of the breast cancer research program – expressed gratitude for Kung's role in her career.

"I want to thank you from the bottom of my heart for taking me under your wing and not doubting my abilities," she said in sentiments echoed by many of the researchers who spoke at the symposium.

In concluding the symposium, de Vere White offered the highest praise for the man he recruited 15 years ago to lead research.

"Hsing-Jien can be extraordinarily proud of what he is leaving behind – the cancer center is well known for wanting to do real science and doing it better," he said. "I don't think we could have recruited all the great scientists we have without Hsing-Jien and his enormous credibility. He led with kindness and with absolute passion that we should all be as good as we can be."

De Vere White concluded that he hoped Kung will be like the son that you're proud has launched, but you don't want to leave the nest. Only half-jokingly he added, "I hope he continues to come home for Sunday dinners."



"Hsing-Jien can be extraordinarily proud of what he is leaving behind... He led with kindness and with absolute passion that we should all be as good as we can be."

~ Ralph de Vere White

Outreach>>

Lending a helping hand

Supportive services introduces a new team, more resources

Tiffany White, 38, is a single mother of three young children who has advanced breast cancer.

In addition to dealing with her fears about the illness, she is grappling with numerous day-to-day, logistical problems such as finding adequate child care and financial resources to cover expenses related to her treatment.

"I need to relax sometimes and not be around the kids," says White. "A support group would be very good for me, but I need more help in the home."



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~ Tiffany White



The services offered through the program are **expanding** at UC Davis in coming months. They will include **social work interns** who will work directly with patients, a psychiatry clinic, a **volunteer coordinator** and possibly a spiritual resource, such as a chaplain.

Social workers with the UC Davis Comprehensive Cancer Center's support services work with White and other patients to help them solve some of the unexpected, and often daunting, logistical challenges of their illness. They also provide emotional support to patients throughout their cancer journey. Support services are a key part of the cancer center's commit-

ment to integrative, supportive care.

"Helping patients and their loved ones identify their next step is what I do at the UC Davis Comprehensive Cancer Center," says Angela Usher, one of two licensed clinical social workers who work in the cancer center's supportive services program. "The next steps may be applying for disability benefits, telling their

minor children they have cancer, asking for help from the community, figuring out what it means to finish treatment, or making quality-of-life decisions. I am there to help guide and coach them to their next best step in their journey."

Usher is working to assist White with a small grant to help her cover the cost of child care so that she can attend a support group.

Outreach>>



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The services offered through the program are expanding at UC Davis to include social work interns who will work directly with patients, a psychiatry clinic, a volunteer coordinator and possibly a spiritual resource, such as a chaplain. The team also works closely with the cancer center's WeCARE! Community-Based Cancer Peer Navigator program, which pairs newly diagnosed cancer patients with specially trained cancer survivors.

The expansion of offerings reflects a national trend of evolving standards for psychosocial care in oncology. The American College of Surgeons' Commission on Cancer developed standards of care that include supportive care. Development of the social services program also is an accreditation requirement for receiving National Cancer Institute (NCI) status as a comprehensive cancer center, as UC Davis did last year.

Part of the NCI requirement is that cancer centers offer all patients "distress screening," an expansive interview process in which a patient is asked generalized questions about their concerns and life changes related to their cancer. Questions delve into issues such as hair loss, changes in sexual functioning, sleep, weight loss and fears of dying. Social workers in the cancer center supportive services program hope to begin a pilot project of the distress

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screening in July and adopt a formal screening process by 2015.

"It allows us to look at how we can provide support and help before there is a crisis," says Usher.

Jena Cooreman, another licensed clinical social worker at the cancer center, says she sometimes feels "like a detective on the hunt for the perfect resource" for patients. Their needs are as varied as the clientele the cancer center serves, she says. Sometimes she helps arrange transportation for

patients; other times she helps them interact with their insurance companies or find resources through the state disability program.

"The overall goal is to help them cope with their illness and cope with the consequences of their illness, so they have the best life possible," she says.

"Sometimes patients' needs are concrete – they need someone to help cook their meals, or they need transportation assistance or information about co-pays for insurance," Cooreman adds, saying she and Usher then work to make referrals to outside programs for patients.

"Sometimes their needs are emotional. They need to be heard," Cooreman says. "They need a place to safely express their frustrations and their fears."

White says she has found the services to be extremely helpful.

"She was very informative on what to do for different benefits for cancer patients," White says of Usher's assistance. "She answered questions for me, and she told me about the programs she knew of."

It is typical of what the social workers try to accomplish for the patients.

"We are here so we can help bolster them and help them through their cancer journey," adds Cooreman.



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Building on basics>>

Breast cancer trailblazing

Stem cell discovery broadens treatment options

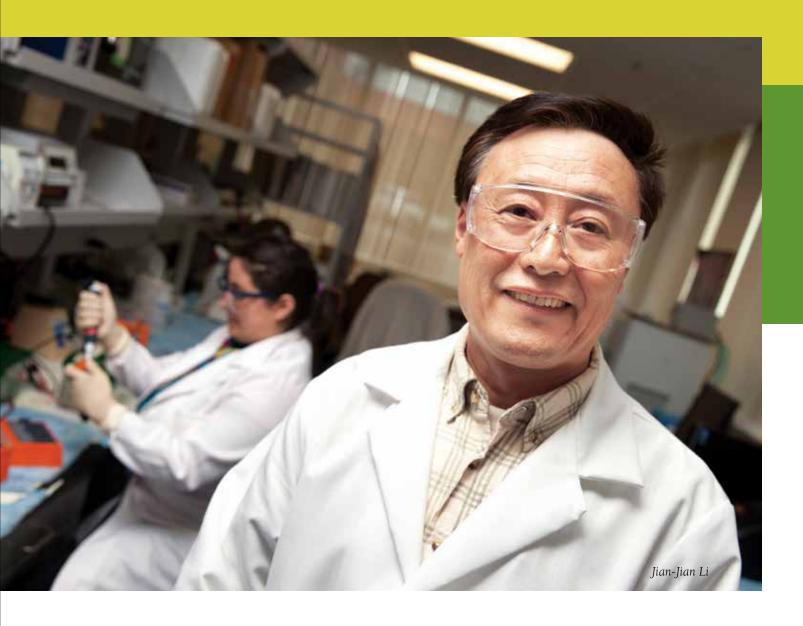
On its most fundamental level, cancer is chaos.

Tumors contain many parts, including healthy tissue and malignant cells with different mutations. This underlying chaos is one of the reasons cancer can be so difficult to treat. Even if the primary tumor is eradicated, smaller cell groups with different, sometimes treatment-resistant, mutations can bring it back.

Fortunately, researchers are beginning to get a handle on this chaos. Over the past few years, they have identified different tumor subgroups, recognized how they affect disease progression and, in some cases, developed treatments to combat them. They've learned that cancer is a highly personalized disease – tumors in the same types of tissue can differ substantially from patient to patient.

HER2-negative?

One success story is HER2, a cell surface protein that is overproduced in some breast cancers. A cancer's HER2 status can have a significant impact on the tumor's



aggressiveness, as well as patients' overall prognosis and their treatment choices. HER2-positive breast cancers are routinely treated with Herceptin or Tykerb, antibody drugs that inhibit the protein, with good results. However, until recently, there has been little reason to administer these targeted treatments to patients with HER2-negative cancer.

But that could change. A nationwide study led by UC Davis Comprehensive Cancer Center researchers found that HER2-negative tumors can contain a small, stubborn group of HER2-positive breast cancer stem cells (BCSCs). Prior to this research, most experts believed that

a breast cancer was either HER2 positive or negative – but never both. This finding underlines the chaotic environment in breast tumors and may change how these cancers are treated.

"These BSCSs are very resistant to traditional treatments, which can lead patients to relapse," says Jian-Jian Li, a professor in the Department of Radiation Oncology and the cancer center's director of translational research. "Despite chemotherapy, radiotherapy or even surgery, the cancer is still recurrent. These findings modify our concept of breast cancer, because now we believe HER2-negative breast cancers can be treated effectively with anti-HER2 treatments."

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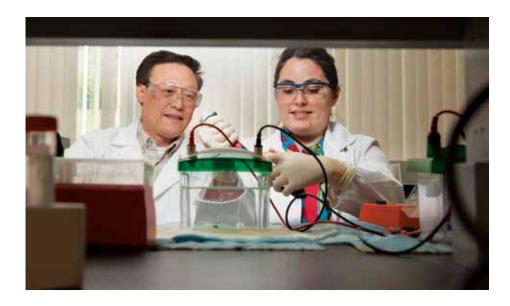
Building on basics>>

Hunting cancer stem cells

Regardless of where they come from, stem cells are recognized by their ability to divide, like fully mature cells, and differentiate into more mature cell types. While embryonic stem cells are known for their ability to become virtually any cell type, the body contains more specialized adult, or somatic, stem cells, which can regenerate brain, muscle and other tissue.

In recent years, biologists have hypothesized that some cancers may contain their own version of stem cells that are highly resistant to treatment and can therefore differentiate into new tumor cells. If the main tumor is destroyed by radiation, chemotherapy or surgery, the cancer stem cells can step in to generate a new tumor.

"We think there's a subpopulation of cells that has fundamentally different properties than the rest of the tumor," says Wolf-Dietrich Heyer, chair of Microbiology and Molecular Genetics. "These cells are dormant



and very resistant to treatment because they divide so slowly and may be responsible for recurrent cancer."

A needle in a haystack

The new study is providing ample evidence to back up this hypothesis. The starting point was a well-studied line of breast cancer cells known to be resistant to radiation. The team

wanted to figure out why that cell line is so radiation-resistant and whether a smaller subgroup of BCSCs was giving it those properties.

The group, which included researchers from the University of Michigan, University of Iowa, Emory University and MD Anderson Cancer Center, painstakingly isolated the cells they suspected were BCSCs. They were looking for cells that



"We think there's a subpopulation of cells that has fundamentally different properties than the rest of the tumor. These cells are dormant and very resistant to treatment because they divide so slowly and may be responsible for recurrent cancer."

~ Wolf-Dietrich Heyer

Also, by isolating this group of treatmentresistant cells in breast cancer, the team blazes a trail for scientists to pursue similar research in other stubborn cancers.

expressed the breast cancer stem cell markers CD44 and CD24. They found that cells that were CD44 positive and CD24 negative were more aggressive and particularly resistant to radiation. However, these cells also responded to Herceptin and other treatments.

In addition to identifying this previously hidden group of HER2-positive stem cells, the team also looked at how these BCSCs maintain their treatment resistance. They identified a complex group of proteins that control metastasis, programmed cell death and other functions. In particular, the power to inhibit cell death is a big deal, giving these tumors the ability to survive the gamut of traditional anticancer therapies.

"This research provides breast cancer patients with new information, especially for patients whose tumors are HER2-negative," says Li. "Patients could get second opinions or they could have their HER2 status rechecked after treatment. If the tumor does become HER2-positive, other treatments could be prescribed."



In addition to **identifying** this **previously** hidden group of HER2-positive stem cells, the team also looked at how these BCSCs maintain their treatment resistance.

Improving diagnosis and treatment

While this research may open up new treatment options for HER2-negative cancer, it also outlines a new approach to diagnose HER2-positive BCSCs in patients. Markers like CD44 could help clinicians identify these aggressive cells in cancers that appear to be HER2-negative, personalizing treatment to match each patient's needs. These findings may also advance treatment for other cancers.

"This may open the possibility of treating HER2-positive stem cells in bone, lung or brain cancers, which are all difficult to treat in the later stages," says Li.

Also, by isolating this group of treatment-resistant cells in breast cancer, the team blazes a trail for scientists to pursue similar research in other stubborn cancers. And while those studies are in the future, the results of this study could potentially influence clinical care today.

"This study has direct implications for the clinic," says Heyer. "Even if a cancer is HER2-negative, HER2 therapy might be helpful. Ultimately, we may begin treating cancers the way we currently treat HIV – by using a concurrent cocktail of therapies."

A lasting gift

Fund benefits women's cancer advocacy and research



Roberta Schneider, an expert aesthetician and trained chemist who developed her own natural skin care techniques and product line, was devoted to educating and mentoring people – within and beyond the skin care clinic she opened in Sacramento in 1967.

That dedication and compassion led her to establish the R.J. Schneider Trust for Women's Health Care, a legacy that, under the care of Bobbi Little, will help women with cancer.

Schneider and Little met in 1991. Although Schneider hired Little to be her personal trainer, Schneider eventually became Little's "adopted mom," and Little became her business partner's health advocate.

Schneider's cancer story began around 2003, when she began experiencing abdominal pain and belly bloating. But she wasn't diagnosed with ovarian cancer until 2006. She underwent surgery at Sutter Health in Sacramento and had additional treatment at Stanford University. Eventually, the cancer returned.

In 2010 Schneider transferred her medical care to UC Davis Comprehensive Cancer Center, where she received treatment from gynecologic oncologist Susannah Mourton, who has since left UC Davis.

Schneider was stoic, and an easy patient, Little recalls.

"Every doctor loved her and her drive, tenacity and passion for learning," she says. "She was just a wonderful, intelligent, caring woman with a great sense of humor."

That same blend of tenacity and compassion strengthened Schneider's desire to advocate for and help other women with cancer, even as her own health waned. She wanted to use her own experience with cancer to give back.

She and Little established the trust in 2011. Through Schneider's estate and fundraising efforts, including a bike ride, the trust donated \$250,000 to the UC Davis Comprehensive Cancer Center to support ovarian cancer research. (Another fundraising bike ride is tentatively scheduled for this summer.)

Early cancer detection – particularly for ovarian cancer – remains a vital theme. "Roberta wanted to create a place where women can learn about cancer and are taught to recognize signs and symptoms," Little says. "We learned through her cancer. It's a shame we didn't catch it quick enough. She would still be here."

"It is unfortunate that most women with ovarian cancer will be diagnosed with advanced-stage



"Every doctor loved her and her drive, tenacity and passion for learning. She was just a wonderful, intelligent, caring woman with a great sense of humor."

~ Bobbi Little

disease," says Gary Leiserowitz, professor and chief of gynecologic oncology at UC Davis. "The symptoms and signs of ovarian cancer are often non-specific or confused with conditions other than ovarian cancer, both by patients and their physicians."

He adds that although there are no currently effective screening tests for ovarian cancer, earlier detection is feasible if patients and their doctors consider the diagnosis as a possibility and investigate with a pelvic exam and pelvic ultrasound.

A devoted and astute businesswoman for 45 years, Schneider had many talents. She loved dining out and gardening as well as music, particularly the violin, which she had to give up in the later years of her illness, due to neuropathy.

"Roberta was stubborn; she wanted to fight it until the end," Little says. "No wheelchairs, no walkers, and no oxygen!"

When the wheels finally fell off, as Little puts it, Mourton helped them with palliative care for Schneider. During that time, Little hosted a stream of Schneider's clients, each of whom got about five minutes with Schneider to say their goodbyes.

Schneider died in her home, exactly as she wanted, in March 2011. One month later, Little threw a celebration of life party, attended by about 400 people.

Shortly after Schneider's passing, Schneider's trust began building steam. Little set up a cozy meeting area in the J Street location where Roberta J. Schneider Inc. is housed. Little's preparation is paying off, continuing to bolster the trust. She hopes to make the trust a nonprofit organization and a haven for women living with cancer by offering resources, education and support as well as bringing in educators – doctors, nurses, and other experts – on a regular basis to discuss prevention and detection.

"We lost a good woman," Little says.
"But her legacy lives on. And that's our goal, for the R.J. Schneider Trust for Women's Health Care and UC Davis Comprehensive Cancer Center to find common ground in helping educate all women on all forms of cancer, not just ovarian."

"Ovarian cancer research is an important focus of our investigations at UC Davis," says Leiserowitz.
"Current projects include developing a potential diagnostic blood test for ovarian cancer, investigating clinical and molecular factors associated with long-term survival, and contributing to cooperative group clinical trials to evaluate the best therapies."

Michele Steiner, associate director of development for the cancer center, says that philanthropic support like Schneider's is essential to advancing the cancer center's mission to provide excellent patient care and innovative research.

"We are truly grateful," Steiner says, "that Roberta recognized the importance of establishing the Roberta J. Schneider Memorial Fund to benefit advocacy and research on women's cancers."

News briefs>>

Researchers discover promise in soybean extract for prostate cancer

A natural, nontoxic product called genistein-combined polysaccharide, or GCP, which is commercially available in health stores, could help lengthen the life expectancy of certain prostate cancer patients, UC Davis researchers reported in *Endocrine-Related Cancer* in February.

Men with prostate cancer that has spread to other parts of the body, known as metastatic cancer, and who have had their testosterone lowered with drug therapy are most likely to benefit. Lowering of testosterone, also known as androgen-deprivation therapy, has long been the standard of care for patients with metastatic prostate cancer, but life expectancies vary widely for those who undergo this treatment.

Paramita Ghosh, an associate professor in the UC Davis School of Medicine, led the pre-clinical study.

Study co-author Ralph de Vere White is now pursuing funding to begin GCP human clinical trials.

"We want to see up to 75 percent of metastatic prostate cancer patients lower their PSA levels, and GCP holds promise of accomplishing this goal," said de Vere White. "If that happens, it would probably be a greater therapy than any drug today."

Chong-xian Pan wins national investigator leadership award



Chong-Xian Pan

Chong-xian Pan has been recognized by the National Cancer Institute (NCI) with a Cancer Clinical Investigator Team Leadership Award. Pan, associate professor of medicine and leader of the cancer center's urothelial carcinoma initiative, was one of 11 award recipients for FY 2011.

The leadership awards recognize mid-level clinical researchers

at NCI-designated cancer centers throughout the U.S. who participate extensively in collaborative clinical trials.

Pan's current collaborative translational research efforts include: development of a drug delivery system that allows administration of higher doses of chemotherapy for advanced bladder cancer without increasing toxicity; a micro-dosing trial to determine efficacy of chemotherapy for bladder cancer; targeting alternative signaling pathways to treat prostate cancer; and a drug delivery system to eradicate leukemia stem cells.

New radiation oncology device reduces treatment times, increases safety

With radiation oncology treatments, the goal is to hit the tumor with as much ionizing X-ray energy as possible, while sparing adjacent, healthy tissue. The UC Davis Comprehensive Cancer Center has taken a major step toward that goal as one of the first sites in North America to install a sophisticated new multileaf collimator (MLC) system on its medical linear accelerators.

The MLC system, installed last November, precisely focuses high-energy, megavoltage X-ray beams that increase doses to tumors and minimize doses nearby. The 160-leaf collimator also allows radiation oncologists to customize the therapeutic beams to conform to a tumor's shape and size. The new system is used to treat a wide variety of diseases, including prostate, breast and lung cancers, as well as for highly specialized treatments such as stereotactic body radiosurgery.

"This system is safe, reliable, accurate and fast," said Stanley Benedict, chief of clinical physics in the UC Davis Department of Radiation Oncology. "It's great technology for our patients."

Multi-leaf collimators act like high-tech lenses, focusing radiation beams and conforming them to the shape of an individual's unique tumor. The collimator's high speed is



Stanley Benedict

ideal for radiation dose control and for arc-based treatments, in which a linear accelerator gantry rotates around the patient while simultaneously conforming to the tumor from different angles and continuously shaping the radiation beam.

Experts recommend closer scrutiny of radiation exposure from CT scans

Amid increasing fear of overexposure to radiation from CT scans, a panel of experts has recommended more research on the health effects of medical imaging and ways to reduce unnecessary CT tests, as well as industry standardization of CT machines.

The recommendations, published in the November 2012 issue of *Radiology*, were developed at the Radiation Dose Summit, organized by the National Institute of Biomedical Imaging and Bioengineering. The proceedings, held in Maryland in early 2011, covered currently understood risks of radiation exposure from CT scans, set priorities for future research and called for changes to industry practices.

"The number of CT exams in the U.S. has increased by about 10 percent each year over the past decade," said John Boone, UC Davis professor of radiology and lead author of the *Radiology* article. "This trend under-



John Boone

scores the importance of developing a better understanding of the health risks of radiation exposure versus the benefits of enhanced diagnosis."

The University of California recently provided grants to all five of its medical schools to develop methods for more accurate measures of radiation exposure from CT scans

and to build protocols that improve diagnostic information and reduce radiation risks. According to Boone, the tools under development are very powerful and will move the UC system toward achieving the goals outlined during the Radiation Dose Summit.

WeCARE! program expands to Central Valley

The UC Davis Comprehensive Cancer Center's WeCARE! Cancer Peer Navigator program is coming to Modesto's Memorial Medical Center, a Sutter Health hospital.

The program provides special support on a one-toone basis, matching newly diagnosed cancer patients with trained cancer survivors. The program is available to any newly diagnosed cancer patient, regardless of where the patient receives treatment.

The program was founded by Marlene von Friederichs-Fitzwater, director of the cancer center's Outreach Research and Education Program. Since the program began in 2009, it has expanded to Gene Upshaw Memorial Tahoe Forest Cancer Center in Truckee, Fremont-Rideout Cancer Center in Marysville, Feather River Hospital Cancer Center in Paradise and the University of Nebraska Medical Center Cancer Program in Omaha, Nebraska.

A new WeCARE! program recently trained caregivers to offer peer coaching to other cancer caregivers who may suffer their own health issues while taking care of loved ones during cancer treatment.



Marlene von Freiderichs-Fitzwater

UC Davis Cancer Care Network News

San Joaquin Community Hospital joins network

Residents of Kern County will now have access to the expertise and experience of UC Davis Comprehensive Cancer Center researchers and clinicians.

The hospital's affiliation links
San Joaquin Community Hospital's
new AIS Cancer Center with
UC Davis through the university
health system's Cancer Care Network.
The partnership represents the network's first affiliation with Adventist
Health, a faith-based, not-for-profit
health-care delivery system.



"We are incredibly excited to partner with a very dynamic and growing organization that has clearly committed time and energy and considerable resources to developing a state-of-the-art cancer program," said Scott Christensen, a professor of hematology and oncology and network medical director.

Rideout Cancer Center expands

Rideout Cancer Center, in partnership with the UC Davis Cancer Care Network, held a public tour and ribbon cutting at the newly expanded Rideout Cancer Center in January. The 42,000-squarefoot cancer center integrates care management, radiation oncology, PET/CT services, medical oncology,



hematology and clinical trials with a team of highly trained board-certified physicians, oncology-certified nurses and certified radiation therapists.

Gene Upshaw Tahoe Forest Cancer Center gains accreditation

The Commission on Cancer of the American College of Surgeons has granted three-year "accreditation with commendation" to Gene Upshaw Memorial Tahoe Forest Cancer Center in Truckee. The accreditation was awarded following an on-site evaluation by a physician surveyor during which the facility demonstrated a "commendation" level of compliance with standards that represent cancer committee leadership, cancer data management, clinical services, research, community outreach and quality improvement.

News briefs>>

UC Davis scientists identify new target for lung cancer treatment

A team of UC Davis investigators has discovered a protein on the surface of lung cancer cells that could prove to be an important new target for anti-cancer therapy. A series of experiments in mice with lung cancer showed that specific targeting of the protein with monoclonal antibodies reduced the size of tumors, lowered the occurrence of metastases and substantially lengthened survival time. The findings were published in the November 2012 issue of Cancer Research.



Joseph Tuscano

"Lung cancer continues to be one of the biggest killers in the United States, and very few treatments directly target it," said Joseph Tuscano, co-principal investigator of the study and professor of hematology and oncology in the UC Davis Department of Internal Medicine.

The UC Davis investigation focused on CD22, a cell adhesion molecule, a protein located on the surface of a cell. Its function is to bind with other cells or with the extracellular matrix, the non-cellular environment surrounding cells.

The research group has worked on CD22 for many years since finding that B lymphocytes carry CD22, making it a potential target for the treatment of non-Hodgkin's lymphoma, a disease that usually involves an abnormal proliferation of B cells. They developed a monoclonal antibody — known as HB22.7 — to target CD22, and it was found to successfully treat non-Hodgkin's lymphoma in mouse models.

Furthermore, mice treated with the antibody had significantly longer survival: more than 90 percent were still alive at the end of the 84-day trial, while most of the untreated mice had died by the 14th day, and all of them had died by day 40.

"The results of the metastasis experiments were really dramatic," said Tuscano. "They indicate that CD22 may play a significant role in the development of lung-cancer metastasis."

UC Davis part of Stand Up To Cancer and Prostate Cancer Foundation research dream team

Stand Up To Cancer (SU2C) and the Prostate Cancer Foundation (PCF), along with the American Association for Cancer Research, SU2C's scientific partner, formed a second Dream Team project dedicated to prostate cancer research — "Targeting Adaptive Pathways in Metastatic Treatment-Resistant Prostate Cancer" in late 2012.

Among the six principal investigators on the \$10 million grant is Hsing-Jien Kung, UC Davis emeritus distinguished professor of biochemistry and molecular medicine.

"This puts UC Davis on the map of elite prostate cancer research teams in the nation," said Kung.

The SU2C-PCF Prostate Dream Team Translational Cancer Research Grant will be led by researchers at the University of California, San Francisco, and the University of California, Los Angeles.



Chris Evans

The Stand Up To Cancer Dream Team will explore the idea that resistance is a result of the prostate cancer cells using common cellular responses, called adaptive pathways, to escape current therapies.

"The objectives of the Dream Team align very well with our strengths in prostate cancer translational science," said Chris Evans, professor and chairman of the UC Davis Department of Urology and one of the Dream Team researchers.

Synthesis is published twice each year by the UC Davis Comprehensive Cancer Center.

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Ralph de Vere White and Leslie Snyder were part of the cancer center team that raised more than \$8,000 at this year's St. Patrick's Day event for pediatric research.

COMPREHENSIVE CANCER CENTER

Designated by the National Cancer Institute



A special message to Synthesis readers

Each year, the UC Davis Comprehensive Cancer Center publishes two issues of *Synthesis*, which is distributed to thousands of subscribers and also provided free to our patients and visitors at the cancer center and its affiliates. Every new issue also can be found on the UC Davis Comprehensive Cancer Center website, cancer.ucdavis.edu.

For more than 10 years, each of our issues has highlighted a blend of new and ongoing cancer research, outreach and education efforts, as well as feature stories about our patients and donors.

We would like to know how we are doing, and we need your help. You can share your opinions about *Synthesis* by completing a brief survey. The survey can be accessed online on our website at cancer.ucdavis.edu. Or, use your Smartphone to scan the QR code below to find and complete the survey.

Each survey participant will be entered into a drawing to win a dinner for two at de Vere's Irish Pub in Sacramento with Cancer center director Ralph de Vere White.

We appreciate your helping us make *Synthesis* better. Thank you for your continued readership.

Dorsey Griffith | EDITOR

