

SYNTHESIS

THE MAGAZINE OF UC DAVIS COMPREHENSIVE CANCER CENTER

VOL 17 • NO 2 • FALL/WINTER 2014

A woman with dark hair, wearing a dark blue textured blazer over a patterned top, stands in a pharmacy aisle. She is surrounded by shelves filled with various medications and pill containers. She is looking directly at the camera with a slight smile.

An extra layer of attention

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Relieving pain, reviving spirits

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From bedside to bench

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Making cancer care dollars count

| A DIRECTOR'S PERSPECTIVE

RALPH DE VERE WHITE
*Director, UC Davis
Comprehensive Cancer Center*
*Associate Dean
for Cancer Programs*
*Distinguished Professor,
Department of Urology*

treatments, and in the community-based work to eliminate health disparities bring value to every patient.

These investments fund the creation of new knowledge, which translates into better care and better cancer outcomes — not just for the people we treat, but for anyone counting on a determined search for advanced cancer cures.

Without the resources of a National Cancer Institute-designated comprehensive cancer center like UC Davis, these advances simply won't happen.

For example, we have been awarded three major grants to conduct clinical trials of novel therapies at phases I, II and III, and we lead two of the three trials nationally. These trials not only

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Health-care costs in the United States consume a staggering 18 percent of the nation's gross domestic product, and the United States spends more on health care per capita than any other industrialized country. Critics often cite academic medical centers, in particular, as excessive consumers of health-care dollars.

It is fair to ask whether the public is getting value for the expense. Is there a legitimate return on the investment in academic medical centers, generally, and comprehensive cancer centers like UC Davis, specifically?

I argue that the costs associated with these NCI-designated cancer centers are justified. The investments made here help create new knowledge about a disease we do not yet fully understand. This knowledge can only evolve from basic scientific investigation, and the researchers and clinicians who work for a comprehensive cancer center are driven to ensure they bring this knowledge to their patients, improving survival for them and others affected by cancer.

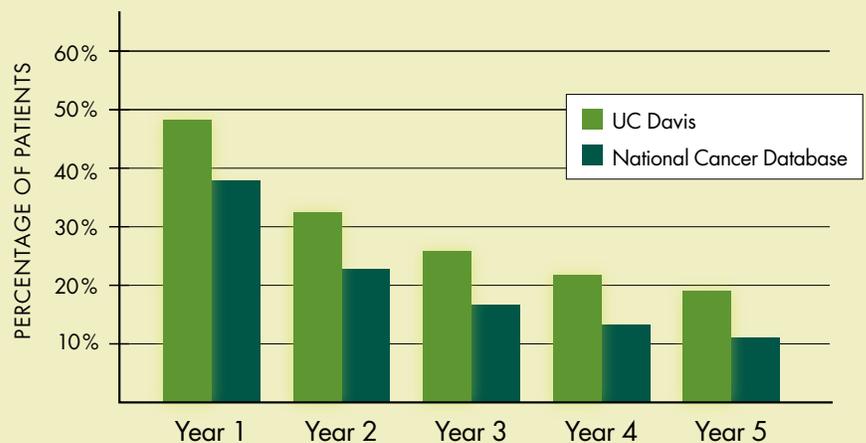
This issue of *Synthesis* explores many of the ways we are using these investments to break

barriers to beat cancer, and bring value to our patients.

The investments made in the education of our cancer researchers and clinicians, in technologies that help us find tumors sooner, in our laboratories hunting for new drug targets, in clinical trials of innovative

Without the resources of a National Cancer Institute-designated comprehensive cancer center like UC Davis, these advances simply won't happen.

Survival Rates for Patients with Stage IV Solid Organ Cancers*



*Excludes lymphoma, leukemia, brain, bone and eye tumors

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Breaking Barriers to Beat CancerSM

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UCDAVIS
COMPREHENSIVE
CANCER CENTER

*A National Cancer Institute-designated
comprehensive cancer center*

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An extra layer of attention

Pharmacy program personalizes cancer care

Pedro Nieves takes 12 different medications every day. One to relieve swelling and bruising, one to regulate blood pressure, one to help manage his diabetes, and a blood thinner, among others.

From heart disease to renal failure, the petite, soft-spoken 71-year-old from Santa Clara County has had his share of health problems over the years and, in 2009, life got even more complicated. Nieves was diagnosed with late-stage kidney cancer. His daily medication regimen now also includes oral anti-cancer drugs — three pills in the morning and three in the afternoon.

“Sometimes I forget to take them all,” he says, as he gets settled into a chair for rehydration therapy at the UC Davis Comprehensive Cancer Center after a long day of running errands and helping out with his eight grandchildren. He says he feels lucky to have help from cancer center staff.

Nieves is one of many patients enrolled in the Medication Adherence Pilot Program, a specialty pharmacy program created in 2013 by the UC Davis Departments of Pharmacy and Internal Medicine, and the Division of Hematology and Oncology. The program is designed to ensure patients on any kind of oral anti-cancer drug stick to their treatment regimens to safely maximize their effectiveness and minimize or manage side effects.

Oral anti-cancer agents include targeted therapies (drugs designed to target specific genetic mutations), as well as oral chemotherapy prescriptions that target individual genes involved in tumor growth.



Josephine Lai

“The wider availability of orally bioavailable anti-cancer agents has increased the need for better coordinated cancer care,” says Primo Lara, a medical oncologist and the cancer center’s associate director for translational research. “These oral agents span the spectrum of hormonal therapies, molecularly targeted therapies and cytotoxic chemotherapy.”

In addition, many traditional chemotherapy drugs are being developed in oral formulations, allowing for continuous exposure of the drug in the patient over time, which can be more effective and

Through **education, monitoring and one-on-one counseling**, the **specialty pharmacy program** helps oncologists determine the effectiveness of prescribed cancer treatments. For Nieves, it has helped him **stick to his drug regimen and manage debilitating side effects**.

less toxic, says Ted Wun, a medical oncologist and chief of the Division of Hematology and Oncology.

Lara prescribed an oral drug for Nieves because it represents “state-of-the-art” care for his patient. Oral

therapy also has the advantage of being more convenient and less invasive.

When oral treatment is prescribed exclusively, patients require fewer office visits and may have a greater sense of control over their treatment.

But along with the benefits, the drugs pose new challenges.

Unlike traditional drug therapy, which takes place in special infusion centers with intensive nursing care, patients taking oral anti-cancer drugs without the information or support they need may experience potentially life-threatening side effects.

While on the drug sunitinib, Nieves was at risk for a host of serious side effects — an uneven heartbeat, seizures, liver problems — and needed careful monitoring, for example.

“Patients are monitored when they’re here, but when they go home, they are harder to monitor,” says Josephine Lai, the cancer center’s pharmacy supervisor, who has been assessing adherence rates of anti-cancer drugs since 2012. She says harsh side effects are one of the primary reasons patients often stop taking the drugs.

Having endured extreme fatigue, vomiting and diarrhea so severe he’s needed multiple sessions of intravenous rehydration, Nieves admits he’s skipped some pills.

That can lead to other problems, says Wun. Stopping the medication

Stopping the medication or **not following the directions correctly can affect treatment efficacy, produce misleading results and cause higher mortality.**

or not following the directions correctly can affect treatment efficacy, produce misleading results and cause higher mortality.

“When patients don’t respond to the drug, we wonder if they’re taking it. Intravenous administration means we know they got the drug, but with oral drugs we don’t typically measure drug levels in the blood, so we just have to take it on faith,” he says. “It’s important we have confidence the drug is being taken.”

Through education, monitoring and one-on-one counseling, the specialty pharmacy program helps oncologists determine the effectiveness of prescribed cancer treatments. For Nieves, it has helped him stick to his drug regimen and manage debilitating side effects.

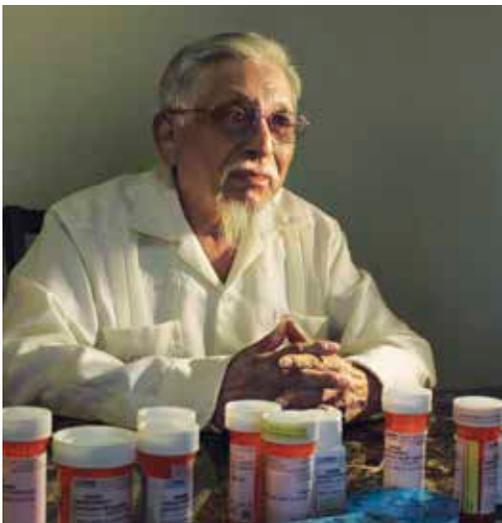
“For the past year, they’ve been calling me from the pharmacy,” he says, smiling. “They want to know

how I’m feeling and if I’m taking my pills correctly.”

After sunitinib stopped working, Nieves was prescribed other targeted therapies. He says the phone calls have been a perfect way for him to communicate new health issues that come up.

“They put me on 10 mg of axitinib recently, and the diarrhea was intolerable,” he says. “I told the pharmacist on the phone, and they immediately talked to my doctor. The dose was changed.”

The program gives patients “a consistent way to complain about their side effects,” says Laura Brennan, a cancer center nurse practitioner who provides one-on-one patient counseling. Patients are often hesitant to talk about side effects, she says, because they think it’s a necessary part of the cancer treatment, but



“For the past year, they’ve been calling me from the pharmacy. They **want to know** how I’m feeling and **if I’m taking my pills** correctly.”

~ Pedro Nieves



Helen Chew and Nanette Osborn

Living far from the Cancer Center, Osborn says she **appreciates the constant connection** she has to her UC Davis care team through the program, and her oncologist Helen Chew **welcomes the extra monitoring.**

I'll be back to UC Davis to get more, and if I can't come down, they arrange for the drugs to be mailed."

Living far from the cancer center, Osborn says she appreciates the constant connection she has to her UC Davis care team through the program, and her oncologist Helen Chew welcomes the extra monitoring.

"Because we have more oral treatment options for a variety of tumors, compared to a decade ago, it's helpful to have a program that contacts patients to review the correct dosing and reinforce important information about the expected side effects," she says.

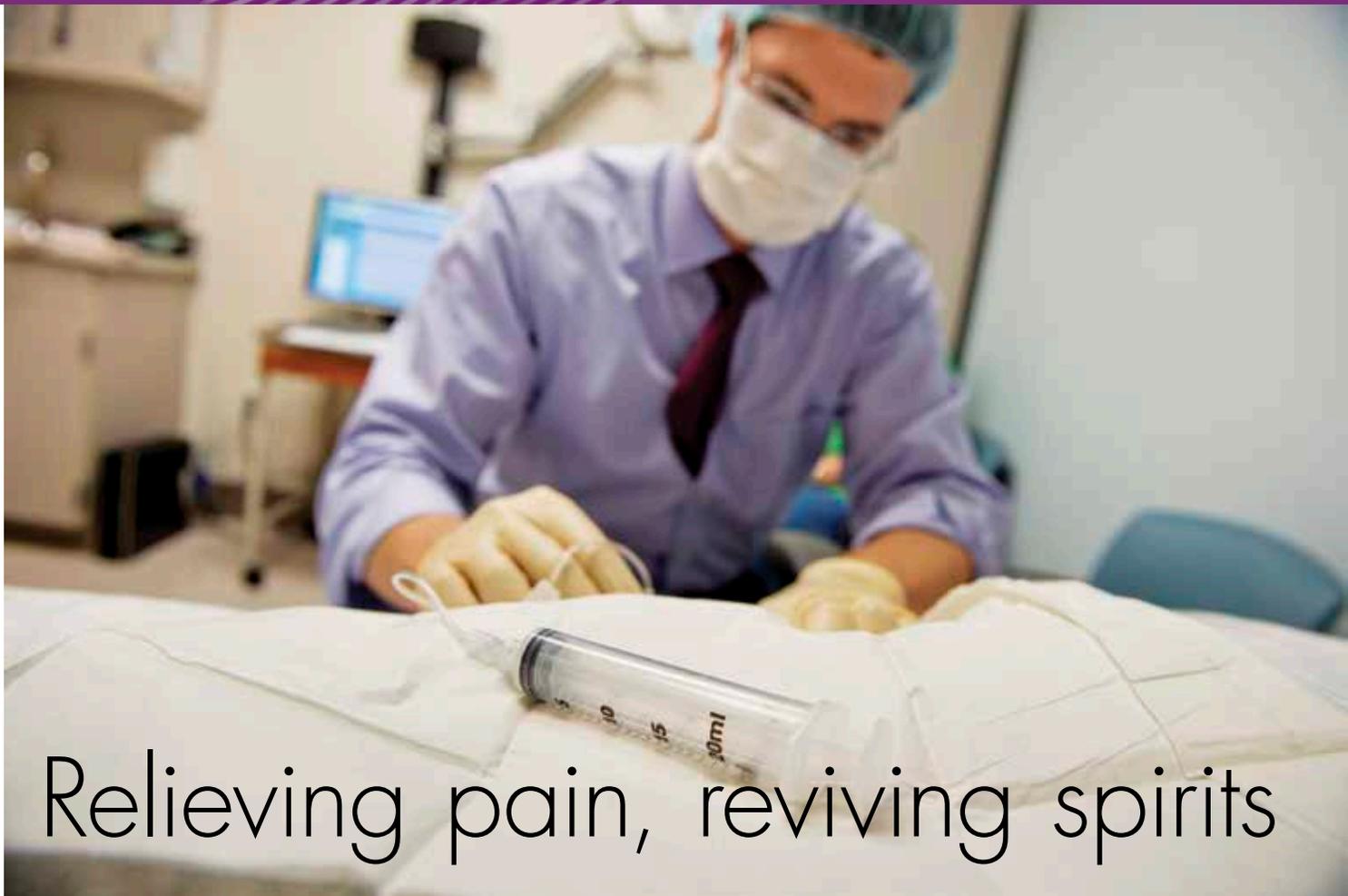
Nieves and Osborn were two of 44 patients enrolled in the pilot program, and preliminary assessments show 92 percent of participants adhered to their regimens. Today, 80 cancer center patients are enrolled and, beginning this fall, a full-time pharmacist will operate the program, which will be offered to all UC Davis cancer patients.

"we want them to tell us because there are ways we can make it better."

Patients enrolled in the program can make an appointment with a pharmacist or a nurse practitioner anytime they have side effects or a question about their drug regimen. In addition to calling regularly to monitor patients' progress and notify oncologists of any issues, pharmacists go over regimens and offer practical

tips, such as how to maintain a medication calendar or handle a missed dose.

"Just knowing someone is checking up on me is comforting," says Nanette Osborn, who has metastatic breast cancer. Osborn, 80, lives in Pollock Pines and is treated exclusively with oral chemotherapy. "They ask me how many pills I have left, how soon



Relieving pain, reviving spirits

Clinic takes on patient suffering

Donald Tweet was running low on hope. Battling late-stage colon cancer was one thing, but the pain that accompanied it? That was almost impossible to endure.

By early 2014, Tweet was taking so much oral pain medication that the gregarious UPS driver could not get out of bed and was “totally out of it all the time,” his wife, Krystalon, recalls. And even at those high levels the morphine and Dilaudid brought little relief.

“It was horrible,” she says, “just horrible.”

But deliverance came last April when Tweet's oncologist referred him to the UC Davis Cancer Pain Management and Supportive Care Clinic — and the clinic's director, David Copenhaver.

Among other changes, Copenhaver recommended implantation of an intrathecal pump to deliver medication via catheter into Tweet's spine and, thus, directly to his central nervous system. Dispensing the drug this way not only reduces the medication's side effects but dramatically increases its potency as well.

Tweet passed away in early July at age 53, but the pump transformed his final weeks, allowing him to attend church, visit with friends, even ride his beloved motorcycle.

"It was a miracle," his wife says. "It was the first time in two years that he actually found relief and was able to participate in life."

For Copenhaver, Tweet's experience illustrates the essence of his core clinical mission: to use all means possible to help patients manage cancer-related pain, thereby preserving quality of life.

It sounds like a no-brainer. But Copenhaver says pain management in cancer patients still rarely receives the specialized attention it deserves. The National Cancer Institute (NCI) agrees, reporting that despite the availability of a wide range of pain control therapies, undertreated cancer pain is a serious and neglected public health concern.

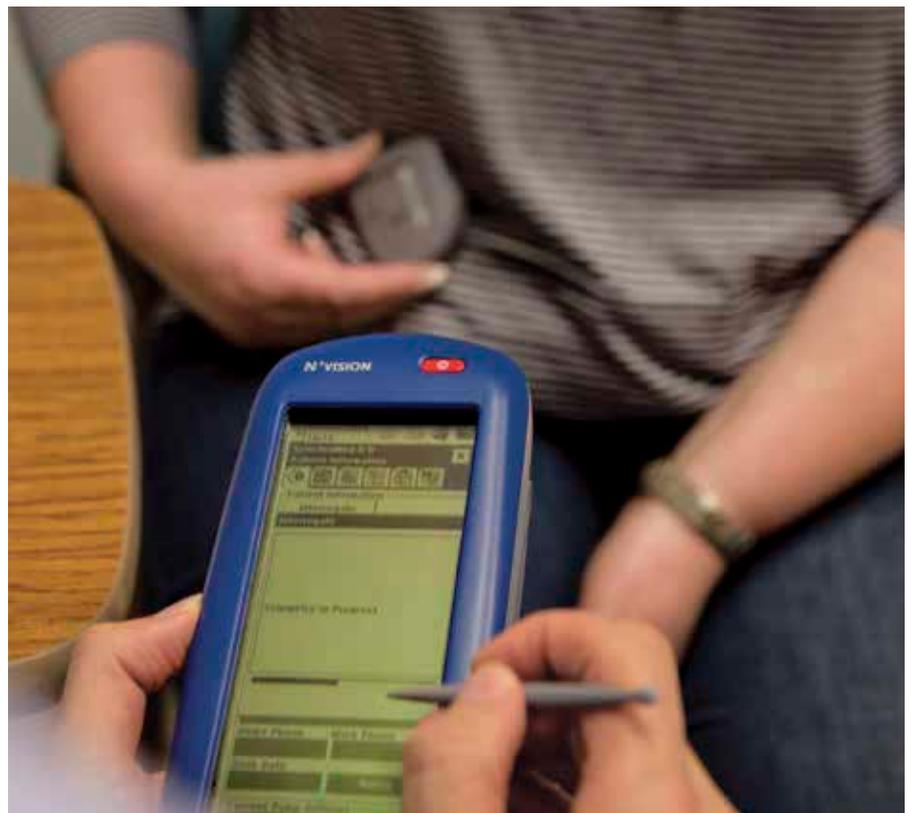
"We've become very accomplished at curing cancer and extending the quantity of life, but when it comes to the quality of life measures that are so important to patients, there are definitely gaps in care," says Copenhaver, whose professional priorities were shaped by serving as

caregiver to his grandfather, who suffered pain while battling multiple myeloma.

Statistics illustrating the incidence of pain afflicting cancer patients prove his point. Among those with advanced cancer, as many as 80 percent of patients report

experiencing pain. For patients in active treatment and undergoing chemotherapy, up to 70 percent of patients experience pain.

Barriers to effective pain management are many, the NCI reports. Clinicians may lack expertise in assessing pain and prescribing



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suitable therapies, or may be concerned about side effects or patient addiction.

Patients, meanwhile, may be reluctant to report pain, fear side effects or feel concerned about being viewed as a “bad patient” or addict, especially in an era of rampant prescription drug abuse. The health-care system itself often hinders cancer pain management too, either through restrictive regulations, supply issues, or high costs coupled with low insurance reimbursements.

“The statistics show that we’re not doing enough to help patients manage pain,” Copenhaver says. “It’s no one’s fault, but as health professionals, we need to work together and tackle this because it’s a major issue.”

At the UC Davis Comprehensive Cancer Center, Copenhaver and his colleague Scott Fishman from the Division of Pain Medicine are working on multiple fronts. They now see patients at regular weekly clinics in the cancer center, as well as daily at their offices.

They are also reaching out to oncologists and others across the

health system, emphasizing their availability to help and the importance of recognizing pain control as an integral aspect of cancer treatment.

Because cancer cases are complex, involving multiple diagnoses and side effects, the clinicians draw on a broad therapeutic repertoire. Copenhaver, board certified in anesthesiology and pain medicine, helps patients through the use of everything from the intrathecal pump to regional blocks and other injections, pharmacologic compounding to maximize relief, and a careful focus on nutrition and strategies to improve sleep.

Psychiatric and psychological interventions are another critical component, as mood plays a significant role in how patients experience and tolerate pain.

Copenhaver’s patients typically fall into one of three groups along a continuum — those undergoing active treatment and coping with side effects, those with advanced cancer facing the end of life, and a middle group of patients who have completed treatment and are left

with residual pain, such as neuropathy.

This middle group, Copenhaver explains, has historically “fallen off the radar a bit,” with their pain often going undertreated. The NCI estimates that as many as one-third of patients will experience pain post-treatment.

“As we get better and better with our chemotherapy, we have more patients in remission, and survivors grow in number,” Copenhaver says. “But many are left with exquisite pain problems.”

Jeanna Smith, 29, is not scheduled for chemotherapy until later this year but is already battling intense pain related to her metastatic carcinoma cancer, which involves tumors in the gastrointestinal system. Smith, an emergency room nurse, says it varies from “aching to sharp, dull and stabbing pain so bad I can barely breathe.” She also suffers from nausea, vomiting and diarrhea.

With oral medications providing little relief, Smith was referred to Copenhaver, who “recognized right away that I had zero quality of life and needed to get my pain under



“The statistics show that **we’re not doing enough** to help patients **manage pain**. It’s no one’s fault, but as health professionals, we need to work together and tackle this because **it’s a major issue**.”

~ David Copenhaver

control before my body was hammered with chemo.”

In late May, Copenhaver implanted an intrathecal pump. Roughly the size of a hockey puck, the battery-powered, programmable pump is surgically implanted in a patient’s abdomen. A catheter is then tunneled under the skin and inserted in the spine where the cerebrospinal fluid lives, and medication is delivered in a controlled stream according to each patient’s needs.

In addition to morphine, the pump can dispense local anesthetics and other medications to reduce pain and help with symptoms such as bowel dysfunction.

Smith says that while Copenhaver is still adjusting the drug dosage, the pump has already made a difference. Just as important, she says, is the comfort she draws from Copenhaver’s optimism.

“He is so positive, so reassuring and so obviously determined to do whatever it takes to help manage my pain,” Smith says. “He has been an absolute blessing. I truly, truly hit the jackpot when I got Dr. Copenhaver on my team.”

Tweet was among those patients who faced pain as cancer reaches its most advanced stage. At age 50 he underwent surgery to remove parts of his liver and stomach, and was treated with chemotherapy as well. Test results initially indicated that he was cancer-free, but last year he began experiencing stomach problems and other symptoms, and oncologists said there were no remaining surgical options.

What did remain was the pain, and Tweet was forced to consume ever greater quantities of pills to cope. Once an outgoing man who



“He is so positive, so reassuring and so obviously determined to do whatever it takes to help manage my pain. He has been an absolute blessing.”

~ Jeanna Smith

loved to socialize and build model airplanes, Tweet became crippled by his pain, virtually unable to function.

Then came the intrathecal pump and, gradually, Tweet’s curtain of pain began to lift.

“All I can say is, Dr. Copenhaver was a star,” Tweet’s widow says. “He even made house calls to adjust the dosage, if needed. He promised us he would ease my husband’s pain, and that’s what he did.”



All in a day's work

Allen Gao: Finding new tools against prostate cancer

As most late-stage prostate cancer patients know, androgens stimulate prostate cancer cells to grow.

If these hormones, which include testosterone, successfully bind to receptors on prostate cancer cell linings, they can prompt proliferation. Hormone therapy to lower androgen levels, coupled with therapies that shut down the receptors themselves, can shrink or slow the growth of prostate cancers.

There's just one problem. Such therapies alone do not cure prostate cancer and, eventually, stop helping.



That's primarily because, sooner or later, the body finds alternative ways to get the androgen receptors working again.

That's where the work of Allen Gao comes in. The director of urologic research and the Ralph de Vere White Professor at the UC Davis Comprehensive Cancer Center is dedicated to extending the lives of late-stage prostate cancer patients whose cancer has metastasized, typically despite the best of early care.

With success on a variety of fronts, Gao and his laboratory seek to better understand the molecular changes associated with the progression of prostate cancer cells, with an emphasis on the mechanisms of aberrant activation of androgen receptors. The goal: identification of diagnostic markers and therapeutic targets for patients who are running out of options to stop the progression of late-stage prostate cancer.

As Gao puts it, "We're researching the reasons why androgen deprivation stops working, and we hope to use that research to develop new ways

"We're researching the reasons why androgen deprivation stops working, and we hope to use that research to develop new ways of making co-targets to improve hormone therapy effectiveness."

~ Allen Gao

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His team's latest research finding, published in the journal *Clinical Cancer Research*, demonstrates that niclosamide, a medicine commonly prescribed to fight tapeworms, dramatically enhances the efficacy of androgen-suppressing drugs such as enzalutamide.

As it turns out, some patients taking enzalutamide — often referred to as a second-generation treatment of last resort — develop a resistance to the drug due to the development of genetic variants that essentially

re-activate their androgen receptors. Gao's research in animal models showed that, when taken concurrently with enzalutamide, niclosamide successfully eroded proteins essential to a key genetic variant called AR-V7, thus staving off resistance to enzalutamide in subjects who have this variant. Furthermore, niclosamide inhibited prostate cancer cell growth and induced death of prostate cancer cells. Human trials are now in the works.

Growing up in the Sichuan province of China, best known as

the home of the giant panda bear, Gao didn't necessarily set out to become an expert in this relatively arcane field. After earning his medical degree from the Sichuan University West China Medical Center, he went on to pursue a Ph.D. in molecular biology at the University of Texas M.D. Anderson Cancer Center, followed by a post-doctoral fellowship at Johns Hopkins University in Baltimore.

Narrowing his research focus to the molecular mechanisms of late-stage prostate cancer, he went on to serve as an assistant professor at the University of Pittsburgh and professor at the Roswell Park Cancer Institute at SUNY at Buffalo. In 2007, he relocated to UC Davis, where he also co-leads the Prostate Cancer Program at the cancer center.

Today, he oversees the center's urological research lab, whose staff of postdoctoral fellows, graduate students, and researchers is funded by major grants from the National Institutes of Health, Department

of Defense, and Veterans Administration, augmented by the center's own endowment program. Rounding out the staff are several young volunteers seeking to broaden their training in this field.

As evidenced by his work on niclosamide, Gao's research increasingly blends genetics with biology as he simultaneously explores both the genetic and molecular pathways that lead cancer-related genes to turn on and off. DNA sequencing — the process of determining the precise order of nucleotides (organic molecules that play central roles in metabolism) within a DNA molecule — is an important tool for Gao and his team as they seek to understand the alterations that occur during late-stage prostate cancer progression.

Last year, the group published a paper in the journal *Molecular Cancer Therapeutics* pinpointing overexpression (over-production) of a protein called p52 in prostate

cancer cells, leading to the promotion of cell growth and the aberrant activation of androgen receptors. In turn, these cells become resistant to enzalutamide.

In a paper published early this year in the journal *Endocrine-Related Cancer*, Gao and his team built on the findings, using analysis of DNA arrays to show that these p52-over-expressing cells also overexpress glucose, a form of sugar. Since these cells apparently depend on this extra glucose and are sensitive to its deprivation, their growth can potentially be stopped through the deprivation of glucose, which in turn could re-sensitize prostate cancer cells to enzalutamide treatment. This suggests a potential therapeutic approach for late-stage prostate cancer patients experiencing resistance to enzalutamide.

A paper that Gao and his group published early this year in the journal *The Prostate* identified a different potential therapeutic approach. They had earlier established that expression of a cytokine (a category of small proteins important in cell signaling) called Interleukin 6 in prostate cancer cells can cause resistance to enzalutamide. In this paper, they found that Interleukin 6 activates a protein called Stat3 and, most importantly, that application of a Stat3 inhibitor reversed enzalutamide resistance in prostate cancer cells.

"The current therapy for late-stage prostate cancer patients provides some improved care and extension of life, but eventually resistant mechanisms will occur," says Gao. "There's reason for hope, however, because researchers around the world are exploring

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Lakshmi Nadiminty and Allen Gao

new drugs and other therapeutic interventions to improve survival.”

He adds, “At the UC Davis Comprehensive Cancer Center, we have a state-of-the-art laboratory and a cross-disciplinary team of clinicians and researchers dedicated to improving therapies and patient care. I am optimistic that, in the foreseeable future, we can not only identify but also move into clinical practice a variety of effective tools to further extend the lives of late-stage prostate cancer patients.”

“At the UC Davis Comprehensive Cancer Center, we have a **state-of-the-art laboratory** and a **cross-disciplinary team of clinicians and researchers** dedicated to **improving therapies** and patient care.”

~ Allen Gao

The digital revolution

Cell signaling insights for cancer therapies

[Digital technologies have changed how we live.

Smart phones, computers and broadband Internet let us transmit and receive astoundingly complex information. The key is multiplexing: the ability to send many different signals through a single conduit.

However, while digital signaling is a great human achievement, it may not be an original idea. Research by UC Davis assistant professor John Albeck and others has shown that cells have been using similar mechanisms for eons. As happens so often, nature may have beaten us to the punch.

Uncovering a secret code

Cell signaling is essential to life. Using complex protein networks, cells communicate with each other and respond to changes in their

surrounding microenvironments. These responses can govern hundreds of fateful decisions, some of which can lead to cancer and other diseases.

One of the most important signaling pathways revolves around the epidermal growth factor receptor (EGFR). When functioning normally, EGFR helps drive cell proliferation, survival, migration and other functions. When mutated, EGFR can go into overdrive, fueling cancer.

“EGFR controls many different processes in the cell,” says Albeck, “but how does it know which ones to turn on?”

Albeck wanted to understand how EGFR and other cellular switches pull off this multitasking. Scientists had thought that signaling was a one-to-one relationship:

a protein, lipid or other ligand attached to a receptor and a single pathway was activated. But cell behavior was just too complicated. For example, genetically identical cells were responding differently in similar environments. There had to be more going on.

“There seemed to be a code that could allow a single signaling pathway to control different outputs independently,” says Wolf-Dietrich Heyer, professor and chair of microbiology and molecular genetics. “Different signals could turn on one protein, or a different

protein or an entire set of proteins.”

In other words: multiplexing.

Biological cryptography

Recognizing that cell signaling was more complex than previously thought was just a start. Albeck and colleagues wanted to know why. While working at Harvard, he

helped customize a technology to illuminate these networks. Fluorescence resonance energy transfer (FRET) allows researchers to observe energy conduction between molecules, a handy tool when measuring protein-protein interactions, the basis for cell signaling.

“EGFR controls many different processes in the cell, but how does it know which ones to turn on?”

~ John Albeck



Building on basics>>

The Albeck lab has combined FRET, which narrowly focuses on individual cellular components, with automated microscopy, which can observe many cells at once. These complementary technologies allow them to record cell behavior in real time.

“We wanted to be able to look at a cell and then come back five minutes later and see what’s changed,” says Albeck. “Now we can observe an individual cell and understand what happened yesterday that is making it proliferate or go into apoptosis today.”

These observations have produced some amazing results.

“We used to think the amount of activity inside the cell would reflect the amount of EGF binding to the receptor,” says Albeck. “But the pathway is converting EGF into a series of digital blinks that are controlling activity in the cell. The frequency encodes information.”

This insight helps explain how cells respond to an ever-changing microenvironment. Proportional or analog signals don’t have the horsepower to transmit all this data. But

a digital code, in which different sequences generate varied responses, could give cells the information they need to make the right choices.

Optimizing treatments

Albeck’s EGFR research could have big implications for clinical care, as EGFR mutations are known to drive lung cancer, neurodevelopmental disorders and other conditions. Understanding how these receptors communicate could change how we approach them.

“Dr. Albeck’s basic research ties in nicely with the translational side,” says Heyer. “It’s helping us understand how cell signaling influences cancer, which may ultimately help us find better ways to treat it.”

For example, EGFR inhibitors have been used for years to treat lung cancer, but are these important drugs being delivered effectively?

“We’ve been using cancer drugs like antibiotics,” says Albeck. “We just apply the largest and longest dose the patient can tolerate. But cancer is a very different condition. Linear doses may not be the best approach because of the toxicity and the way cancer cells learn to respond.”

Albeck and others believe that EGFR inhibitors, and perhaps other anticancer drugs, could be delivered in pulses. This approach could maximize drug effectiveness while minimizing both toxicity and a tumor’s ability to develop resistance.

“We’re learning that it may be better to deliver these drugs during defined windows and give the cells a break,” says Albeck. “We just need to figure out what those windows are.”

Translating basic discoveries

While Albeck has been with UC Davis for only a year, he is already finding collaborators working to improve lung cancer therapies. Associate professor



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“We want to **translate** these laboratory **strategies** into **improved patient care**. The better we understand these events at the **molecular level**, the more likely we’ll be able to **use drugs in the right combinations**, schedules and concentrations to **make the tumor respond**.”

~ Philip Mack

Philip Mack has been investigating new drug combinations for more than 15 years. Now, he is using advanced genomics to identify mutations in individual tumors and match treatments that target those mutations. He also has a keen interest in EGFR.

“A small subset of tumors are particularly dependent on EGFR for growth and survival,” says Mack. “Blocking that signaling will cause the tumor to stop growing and die.”

While this strategy often works in patients — for a time — cancer

evolves mutations to escape the inhibitors. Mack hopes that the added insights into EGFR signaling might help clinicians and patients avoid this pitfall.

“We want to translate these laboratory strategies into improved patient care,” says Mack. “The better we understand these events at the molecular level, the more likely we’ll be able to use drugs in the right combinations, schedules and concentrations to make the tumor respond. We can also use these tools, in real time, to

evaluate how a patient is responding to a particular therapy.”

The wider landscape

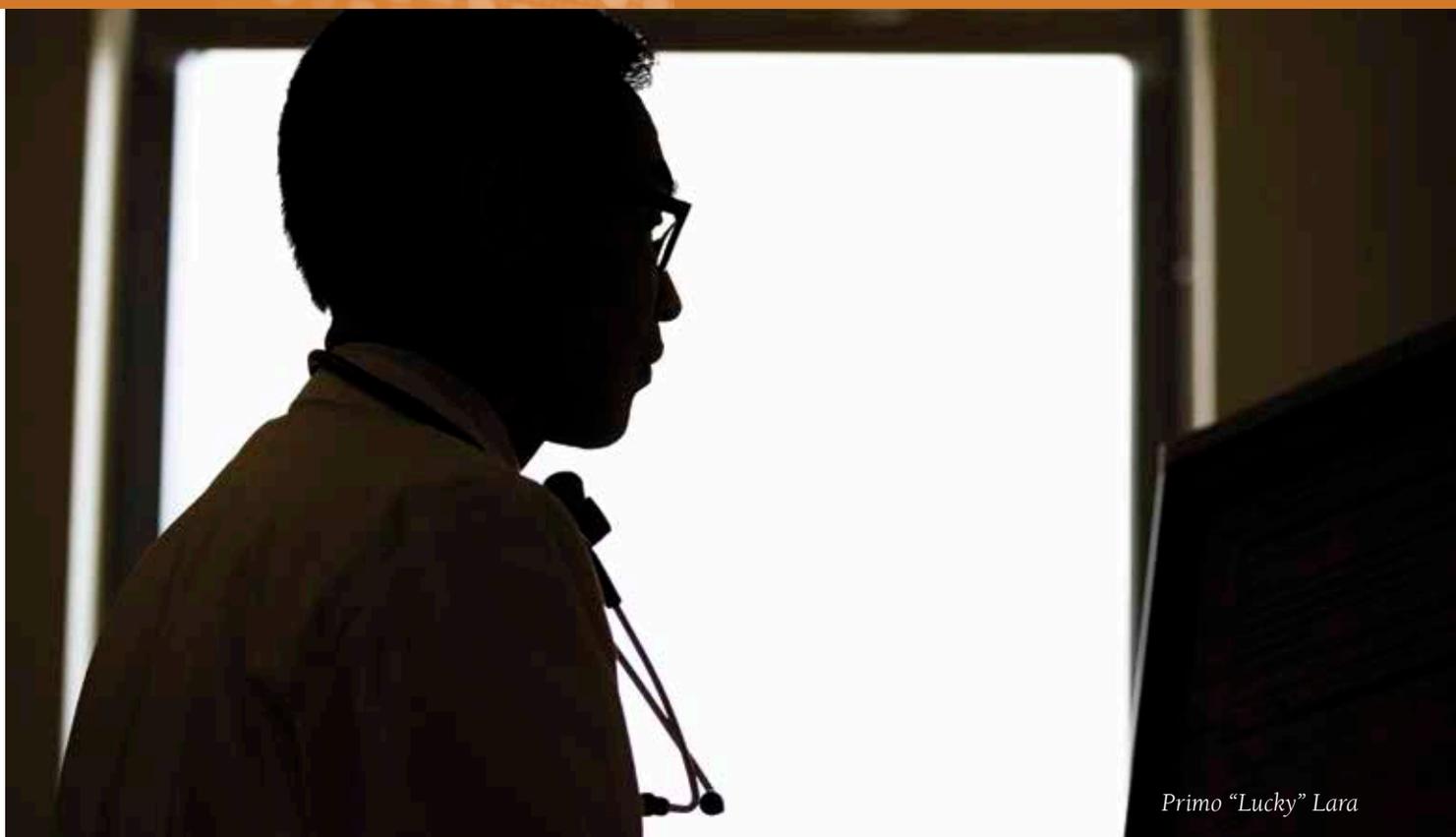
EGFR is an important signaling pathway, but it’s one of many. For example, signals conducted by the enzyme AMPK also may have a digital signature, a finding that could enhance our understanding of diabetes and other metabolic conditions.

“We don’t think this behavior is confined to the EGF pathway,” says Albeck. “It just happens to be the first one we looked at.”



“Dr. Albeck’s basic **research ties in nicely** with the translational side. It’s **helping us understand** how cell signaling influences cancer, which may **ultimately help us find better ways to treat it**.”

~ Wolf-Dietrich Heyer



Primo "Lucky" Lara

From bedside to bench

Grooming next generation clinician-researchers

Primo "Lucky" Lara is optimistic about the future of cancer research.

As principal investigator of the Paul Calabresi Career Development Award for Clinical Oncology (K12), the professor of medicine and associate director of translational research at the UC Davis Comprehensive Cancer Center leads the selection committee that chooses bright young faculty members to pursue promising research. Awarded in 2011, the five-year \$3.5 million

grant is now funding the third group of young investigators.

"We look for junior faculty members who have a strong commitment to undertake clinically oriented cancer investigations," Lara says. "Thanks to the grant, we are supporting an outstanding group of researchers who are poised to find cures for cancer."

“Pancreatic cancer is **notoriously difficult** to treat. That’s what attracts me — there’s the **opportunity** to really **make a significant impact.**”

~ Edward Kim



The Calabresi Award provides at least 75 percent protected time for the scholars to conduct cancer research. The program also offers a rigorous curriculum that includes training in a variety of essential research elements — from bench techniques in cancer molecular biology to designing clinical trials and analyzing data. Each investigator is assigned to both a clinical and basic science mentor, with an emphasis on rapidly turning findings into clinical applications.

“The program promotes learning and research results at a much faster pace than if the investigators were working on their own,” Lara says. “We are so fortunate that UC Davis has resources to provide such significant support for promising researchers at an early stage in their careers. It bodes well for

the future of cancer diagnosis and treatment.”

THE CALABRESI SCHOLARS

Tackling pancreatic cancer

Edward Kim, assistant professor of medicine and a gastrointestinal oncologist, is often frustrated by the treatment options available for his patients with pancreatic cancer.

“Pancreatic cancer is the only cancer with increasing mortality in both men and women,” says Kim. “No clinically significant advances have been made in novel agents to fight it in the last 15 years.”

He points out that although recent new treatment regimens — different combinations of standard drugs — have helped improve survival, they tend to have many side effects because of the cumulative toxicity of multiple drugs that are all designed to kill rapidly

dividing cells, not just cancer cells.

“Combining standard drugs can be more effective but also compounds toxicity,” he says.

Kim is hopeful that this bleak picture will change soon. He is focusing on a protein called aurora kinase A expressed by cells during the cell cycle phase of mitosis. Because cancer cells express it in much greater numbers than do healthy cells, inhibiting aurora kinase A and thereby stopping cancer cell proliferation is a promising new approach for cancer therapy. In the laboratory, he is testing different potential partners to enhance the efficacy of aurora kinase A inhibition.

At the same time, Kim is involved in a phase I clinical trial testing an aurora kinase A inhibitor called alisertib. This trial, open to patients with any solid tumor, combines the standard chemotherapy drug gemcitabine with escalating doses

First steps>>

of alisertib and is designed to establish the maximum tolerated dosage of the new drug. Once the dosage is determined, patients with pancreatic cancer will be specifically recruited to evaluate efficacy. It is anticipated that the two drugs in combination will work synergistically, with greater effects but lower toxicity than standard combination therapy.

“Pancreatic cancer is notoriously

difficult to treat,” says Kim. “That’s what attracts me — there’s the opportunity to really make a significant impact.”

Recruiting immune cells to fight solid tumors

Most people think of stem cells — the early undifferentiated cells that have the capability to grow into many cell types — as helpful cells in the developing fetus and the bone

marrow of adults. But stem cells also exist in tumors, and many believe that they are the source of metastasis and relapse after treatment.

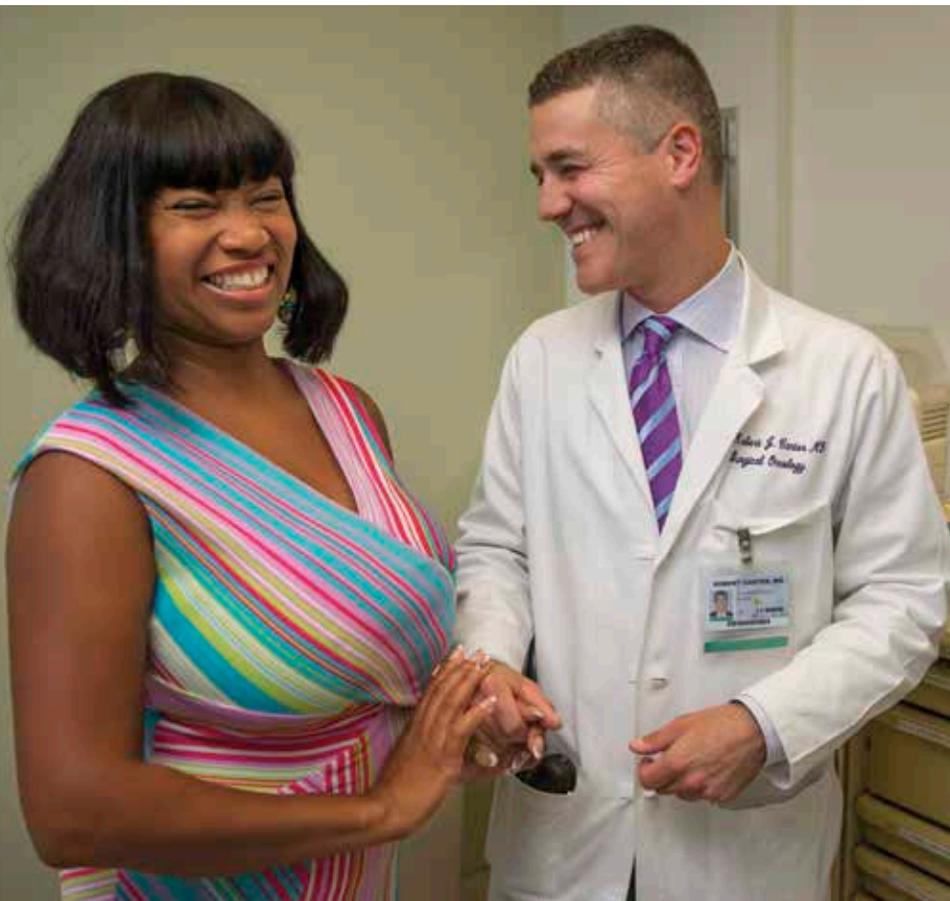
“Cancer stem cells appear to do the ‘dirty work’ for tumors,” says Robert Canter, associate professor of surgery and a Calabresi investigator. “And, unfortunately, chemotherapy and radiotherapy tend to leave them behind.”

Working with William Murphy, professor and acting chair of the Department of Dermatology, Canter is exploring immunotherapy to target stem cells in tumors. To do this, he is recruiting natural killer cells — a type of lymphocyte in the blood that when “activated” can recognize and destroy cancer cells. Immunotherapy with natural killer cells has demonstrated success in the treatment of some blood cancers, but has been less effective against solid tumors because of the inability to deliver large enough numbers of activated cells against the tumors.

Canter’s work involves isolating natural killer cells from the blood of patients or donors, increasing their numbers and activating them so that they are primed to recognize and better attack cancer stem cells, and then infusing them back into the patient.

“The goal is that the expanded and activated population of natural killer cells will go in and more effectively fight the tumor, especially the cancer stem cells,” Canter says. “We hope that combining this technique with standard therapies will completely destroy solid tumors such as sarcomas.”

Canter expects to begin trials soon to test what they have learned from their laboratory findings. One will be in collaboration with the School of Veterinary Medicine, using dogs that develop sarcomas similar



“The goal is that the **expanded and activated population of natural killer cells** will go in and more effectively **fight the tumor**, especially the **cancer stem cells**.”

~ Robert Canter

“I believe that a **personalized approach to cancer therapy** will be **key to success**. The Calabresi award gives me dedicated time to really explore this **promising avenue** to fight cancer more effectively.”

~ Jonathan Riess



to those seen in people, especially in the pediatric population.

“While helping people’s pets, we expect to pave the way to start trials with children and adults,” Canter says. “This research offers a promising new approach that may be a game-changer in curing these hard-to-treat cancers.”

Personalizing cancer therapy

When it comes to cancer therapy one size does not fit all, says Jonathan Riess, assistant professor of medicine and a Calabresi Award recipient. His research interest is non-small cell lung cancer, which comprises about 85 percent of lung cancers. Riess is homing in on a special mutation of a protein called the epidermal growth factor receptor (EGFR), which is found in non-small cell lung cancers of about 10 percent of patients in the United States. EGFR controls a signaling pathway important for cell division; the mutation keeps the receptor in the “on” position, resulting in continuously active and dividing cells.

Riess is investigating erlotinib,

The **Calabresi Award** provides at least **75 percent protected time** for the scholars to conduct cancer research.... Each investigator is assigned to both a **clinical and basic science mentor**, with an emphasis on **rapidly turning findings into clinical applications**.

a drug that specifically targets EGFR. While traditional chemotherapy drugs attack all cells in the body that are dividing quickly, erlotinib specifically blocks EGFR signaling. In people who have tumors with the EGFR mutation, erlotinib inhibits tumor growth but leaves the rest of the body pretty much alone. As a result, side effects are fewer compared with standard chemotherapy agents.

According to Riess, the new approach can be very successful in patients who have tumors with the EGFR mutation — until resistance develops. Why does this happen, and what to do then?

“The more we learn about cancer, the more we realize that you usually

can’t be successful by treating everyone alike,” says Riess. “Cancer is a lot more complicated than that — it is different among individual patients and often changes in the same person.”

Working with David Gandara, professor of internal medicine and director of the thoracic oncology program, and others as his mentors, Riess is exploring these questions using unique mice models from Jackson Laboratory. The mice are specially developed to incorporate cancer cells taken from individual patients, so that experiments can be designed to study mechanisms of tumor growth and effectiveness of different therapies in a very patient-specific fashion. He is working to

First steps>>

design clinical trials to find optimal combinations of targeted and standard therapies.

“I believe that a personalized approach to cancer therapy will be key to success,” Riess says. “The Calabresi award gives me dedicated time to really explore this promising avenue to fight cancer more effectively.”

Unraveling drug resistance

Thomas Semrad is fascinated by the phenomenon of tumors responding well to a therapy then, after a period of time, ignoring the killer drugs they’re being bombarded with.

“Why do drugs work, then stop working?” he asks. “It’s a problem common to many different cancers. I want to be able to put together a story to explain it.”

The assistant professor of medicine in hematology and oncology is focusing on angiogenesis — the ability of tumors to recruit the host’s blood supply for

their own nourishment. Although several drugs are available that specifically inhibit aspects of tumor angiogenesis, cells often become resistant to these agents.

Semrad is involved in two ongoing clinical trials testing new anti-angiogenic drugs: one at UC Davis for patients with lung or colon cancer, and the other that involves five cancer centers across the United States for patients with kidney cancer. When a patient does well with a standard anti-angiogenic drug, then shows signs that treatment has stopped working — the tumor starts growing, or more tumors appear — Semrad steps in.

He obtains biopsy material from the tumor and compares it to a baseline biopsy sample taken from the patient when he or she was first diagnosed.

“What has changed?” he wonders, as he runs the samples through a

battery of tests. Semrad is hopeful he will find signals common to a variety of cancers cells use to recruit blood vessels. Such signals could potentially be used as biomarkers to detect whether a patient’s tumor has become resistant to an anti-angiogenic agent and a different therapy is needed.

“I think that the way to help people is to target the process early and delay progression,” he says.

All the Calabresi Award investigators expressed abundant gratitude for the opportunity to pursue research in such a dedicated fashion and to work closely under high-caliber senior mentors.

“This kind of work requires a tremendous amount of resources, time, learning and organization,” Semrad says, echoing the words of all the award recipients. “Without a program like this that provides formal training and experience with talented mentors, how would we develop the next generation of researchers?”



“Why do drugs work, then stop working? It’s a problem common to many different cancers. I **want to be able** to put together a story **to explain it.**”

~ Thomas Semrad

Patient and benefactor leaves deep legacy

IN MEMORIAM

VIRGIL TRAYNOR

1937 – 2014



Virgil Traynor first stepped through the doors of the UC Davis Comprehensive Cancer Center in 1995, as a prostate cancer patient of Dr. Ralph de Vere White. Grateful for the care he received and eager to give back, he later launched a movement in his Auburn community that helped build the cancer center's research program into a powerhouse.

Virgil, who passed away at age 76 on September 20, was the engine behind the Auburn Community Cancer Endowment Fund, begun in 2001 with a handful of supporters in the Gold Rush town. Fueled by barbecues, golf tournaments, motorcycle rallies, fun runs and a few large individual donations, the fund hit \$1.5 million in 2006 — enough to establish an endowment in basic research at the cancer center.

A beloved veterinarian with deep ties to his community, Virgil never let up on his determination to reach the goal. With potential donors, he was forthright: “You just ask people,” he said at one point,



Ralph de Vere White and Virgil Traynor

and the effort “just snowballed.”

Income from the fund has since paid for dozens of basic science projects helping to unravel cancer's most perplexing mysteries. Today, the fund stands at \$2 million.

Over the years, Virgil became an important and inspirational member of the UC Davis Comprehensive Cancer

Center family, inspiring several other community philanthropies and forging lifelong friendships. One of those friends, de Vere White, noted that while the quietly resolute donor would object to being singled out for his contributions, everyone would agree that their mentor, their inspiration and driving force was Virgil Traynor.

A gift that keeps on giving

Endowed professorship seeks lymphoma cure

[The promise has been kept, so the giving is far from over.

What started in 2006 as a \$313,000 donation from the family and friends of Norman deLeuze and a promise to raise more money to fund research into lymphoma blossomed into an endowment of more than \$1 million. Now, that money is being used to fund The deLeuze Family Endowed Professorship to Find a Non-Toxic Cure for Lymphoma — a professorship that will allow focused, continued lymphoma research at UC Davis.

A promise kept, indeed.

“We saw the endowment as a long-term effort,” says Brett deLeuze, Norman’s son. “We’ve never really let up. Now, we’re in the process of converting the endowment to an endowed professorship with the goal to find a non-toxic cure for lymphoma.”

Norman deLeuze, 75, the family patriarch, was a Napa winemaker who lost his battle with mantle cell lymphoma in 2007. During his

illness, he was committed to finding a non-toxic cure for lymphoma, eschewing the traditional path of radiation and chemotherapy as too toxic. As fate would have it, deLeuze was treated by UC Davis oncologist Joe Tuscano. The two hit it off — as patient and physician — as well as through their mutual interest in non-traditional treatments.

“They developed a relationship,” says the younger deLeuze, “not just as doctor to patient, but on a research basis.”

Tuscano remembers deLeuze as a “very smart man” who took an active role in his treatment.

“He investigated it and read about it,” Tuscano says of deLeuze’s research into lymphoma. “He would come to me and say, ‘What about this?’”

That relationship, and Tuscano’s continued commitment to alternative lymphoma treatments, has spawned some interesting research. Specifically, Tuscano has investigated the efficacy of Avemar, a natural product made from fermented wheat germ extract. Norman deLeuze took Avemar during his lymphoma treatment, and his tumors shrank. Tumors also shrank in mice injected with Avemar during tests conducted in Tuscano’s lab.

Tuscano continues to pursue



“The **funding environment** is **very difficult**, and it’s even more difficult to get funding for the **non-traditional approach.**”

~ Joe Tuscano



Jill, Brandon and Brett deLeuze

“We saw the endowment as a long-term effort. We’ve never really let up. Now, we’re in the process of converting the endowment to an endowed professorship with the goal to find a non-toxic cure for lymphoma.”

~ Brett deLeuze

the Avemar treatment with vigor. He and his colleagues have identified 17 proteins in Avemar that appear to be effective against lymphoma. The research team has submitted a patent application and has agreed to collaborate with Avemar maker BioScience Inc. to continue work on developing the product as a lymphoma treatment. The deLeuze Family Endowed Professorship to find a Non-Toxic Cure for Lymphoma will go a long way toward continuing the research.

“The funding environment is very

difficult, and it’s even more difficult to get funding for the non-traditional approach,” says Tuscano. “Hopefully we can prove it is effective so we can get more funding.”

As deLeuze’s physician, Tuscano initially counseled his patient to stick with traditional therapies with proven track records, such as chemotherapy and radiation. But deLeuze, a determined man who launched his now hugely successful winery as a side venture while working at Aerojet, was adamant

that he avoid the toxicities of those treatments.

Brett deLeuze and the other members of his family appreciated Tuscano’s willingness to consider his patient’s wishes.

“My father was sick, and he couldn’t find anybody to listen to him,” says Brett deLeuze. “Dr. Tuscano listened to him.”

The deLeuze family, which runs ZD Wines in Napa, has continued its relationship with Tuscano since Norman’s deLeuze’s passing. Each year, the family hosts a dinner in Davis for staff at UC Davis Health System, Tuscano included. The family is also co-sponsoring a fundraising bike ride in Napa in October called the Crush Challenge. Co-sponsored with the Patrick Dempsey Center for Cancer Hope & Healing in Maine and Amgen, proceeds will be split among the endowment, Dempsey Center and Amgen’s Cancer research fund, Breakaway from Cancer. Tuscano, an avid cyclist, will ride with the deLeuzes.

“He’s a total match for us, a neat guy,” said Brett deLeuze of Tuscano.

Since the deLeuze endowment launch in 2006, Brett deLeuze, along with his brother Robert, mother Rosa Lee and niece and nephew Jill and Brandon continue to raise money for the endowment.

Sunny Mason, director of development for the UC Davis Comprehensive Cancer Center, says the deLeuze family’s support is a huge boost to the health system and its cancer research.

“We are so grateful to the deLeuze family for their unwavering and visionary support for cancer research,” says Mason. “By funding an endowed professorship, their support will have a profound effect on the future of cancer research, patient care and clinical services.”

Canines join the UC Davis cancer team

The UC Davis Comprehensive Cancer Center's pediatric infusion center has added some four-legged members to its team.

The dogs are key participants in a novel clinical trial, called the "Canines and Childhood Cancer Study," examining the effects of animal-assisted therapy on patients, their families and the therapy dogs themselves.

UC Davis is one of five children's hospitals in the United States participating in the 12-month study, pioneered by Zoetis Inc., an animal pharmaceutical company, and the American Humane Association (AHA).

Focusing on newly diagnosed children who receive regular outpatient chemotherapy, researchers are studying how animal-assisted therapy affects stress levels of patients, their parents and the animals, and how it contributes to patients' overall quality of life.

Based on pediatric oncology and animal-assisted therapy research, Zoetis and AHA determined that children with cancer and their families are prone to psychological problems, including stress, anxiety, trauma, depression and loneliness.

"As providers, we are always looking for anything we can do to help alleviate stress for these children, and it's anecdotally known that dogs can help with stress in any condition," said pediatric hematologist/oncologist Anjali Pawar, principal investigator of the study at UC Davis.



U.S. News ranks UC Davis first for cancer in the Sacramento area

UC Davis is ranked the #1 hospital for cancer in the Sacramento area and 34th in the nation based on the annual *U.S. News Best Hospitals for Cancer* rankings. **The national *U.S. News* rankings recognize hospitals for cancer with exceptional survival rates, advanced technologies, high nurse-to-patient ratios, special patient services and that treat difficult cases. The cancer center at UC Davis is the only National Cancer Institute-designated Comprehensive Cancer Center in the Sacramento area and one of only two such centers in Northern California.**



"This honor tells us we are fulfilling our mission by creating new knowledge and delivering the best possible care to our patients," said Ralph de Vere White, cancer center director.

UC Davis Medical Center was ranked one of the nation's best hospitals for 2014–15 in 10 adult medical specialties. UC Davis Children's Hospital was also ranked among the nation's best.

For 2014–15 rankings, *U.S. News* evaluated hospitals in 16 adult specialties and ranked the top 50 in most of the specialties. Just 144, or 3 percent, of the nearly 5,000 hospitals analyzed for Best Hospitals 2014–15 earned national ranking in even one specialty.

Forum set for young adults and adolescent cancer survivors

Young people living with cancer and young adult cancer survivors are invited to a special forum November 8 in the UC Davis Comprehensive Cancer Center Auditorium.

The event, hosted by the Cancer Crusaders, the Adolescent and Young Adult Cancer Advisory Board, will tackle issues such as infertility, body image, sexuality, legal and employment issues associated with a cancer diagnosis, treatment and survivorship.

Called "Pushing Past Cancer," the forum targets all young survivors and current cancer patients in Northern California, ages 15–39, their friends and caregivers. Admission is free.

Learn more about Pushing Past Cancer on the UC Davis Cancer Center and Cancer Crusaders Nor Cal Facebook pages and on Twitter @Cancer_Crusaders.

For more news stories, visit cancer.ucdavis.edu, click on "Newsroom."

Pan awarded grant to test “smart” chemotherapy drug on bladder cancer

UC Davis genitourinary oncologist Chong-Xian Pan, who leads the cancer center’s bladder cancer research initiative, received a \$650,000 grant from the VA Northern California Health Care System to conduct the first human clinical trial of a unique chemo-delivery drug on bladder cancer patients.

Bladder cancer is among the 10 most common cancers in the United States, and there has been little improvement in treatment outcomes over the last three decades. Researchers hope the trial will change that.

Sixty percent of patients who get standard treatment for the disease experience a recurrence within two years. Additionally, valrubicin, the only FDA-approved drug used to treat recurrent bladder cancer, only works in 20 percent of the patients.



Chong-Xian Pan

To improve this, Pan and Kit Lam, study co-investigator and chair of the UC Davis Department of Biochemistry and Molecular Medicine, developed a bladder cancer-targeting micelle, a first-of-its-kind nanotherapeutic drug formulation designed to find and kill bladder cancer cells.

The drug targets bladder cancer cells and loads them with Paclitaxel, a chemotherapy agent. The drug is coated with a PLZ4 ligand — a sequence of amino acids that only binds to bladder cancer cells, enhancing its delivery capabilities. The micelle itself is crucial to facilitating the drug’s effectiveness because it not only acts as a nanocarrier of Paclitaxel, but has been shown to decrease toxicity.

Fighting lung cancer with a purple pedicure

A UC Davis cancer patient’s purple toenails have sparked a national and international movement, raising awareness and research funds for lung cancer, the number-one cancer killer in the United States.

It started when Valerie Brosdal’s husband, Ralph Kaposstins, decided to cheer his wife up by getting the same purple pedicure she had. Brosdal, 53, of Pleasanton, had recently been diagnosed with late-stage lung cancer.

They shared their moment with friends on Facebook, and invited others to paint their toenails purple and send a snapshot. For each of the first 50 photos they received, the couple would make a \$20 donation to the Bonnie J. Addario

Lung Cancer Foundation. Word spread, and the Purple Toes Campaign, Smiles for Val was born.

As promised, the couple donated money to the Addario foundation, which seeks to transform lung cancer treatment through education and research. The foundation also helped connect Brosdal to David Gandara, a renowned UC Davis lung cancer specialist.

The couple has received photos of more than 500 individuals, groups, even cats and dogs — all wearing purple polish on their toenails. The effort garnered national media attention, and nail care giant OPI Products Inc. donated 500 bottles of polish — Purple with a Purpose — to the cause. In partnership with the Addario organization, the campaign has raised more than \$15,000 for patient services, lung cancer awareness and research.

For more information or to submit a photo, e-mail purpletoes@lungcancerfoundation.org.



Making cancer care dollars count

A DIRECTOR'S PERSPECTIVE CONTINUED, FROM INSIDE FRONT COVER

give our patients at every stage of their disease more treatment options, but advance the field of drug development generally, which benefits all cancer patients.

Similarly, because our clinicians also conduct research, our patients immediately benefit from the findings that continue to improve how we treat each individual cancer. A recent example: UC Davis thoracic surgeon Tom Cooke recognized that many late-stage lung cancer patients do not get surgical biopsies, which are usually necessary to obtain sufficient tumor tissue for genetic testing. The testing allows scientists to determine if the patient would benefit from an available targeted drug treatment. Cooke studied the problem and found that for carefully selected patients, surgical biopsy is safe, after all. His findings will change the game for late-stage lung cancer patients in search of new treatment options.

Value in cancer care also is evident in the improved survival rates of patients at our cancer center. The American College of Surgeons' Commission on Cancer, which accredits and sets standards for cancer centers across the country, released outcomes data for all 1,500 accredited cancer centers. The recent data demonstrate that UC Davis Comprehensive Cancer Center had dramatically better survival rates in several types of cancer, when compared with all other accredited centers.

For solid organ cancers (excluding lymphoma, leukemia, brain, bone and eye tumors), five-year survival rates of stage IV cancer patients treated at UC Davis were nearly double that of all other ranked programs. In prostate cancer, specifically, 58.6 percent of stage IV patients at UC Davis were alive after five years, compared with 37.6 percent of stage IV patients at other centers.

Our hard work on behalf of patients and the larger community has not gone without notice. *Becker's Hospital Review* just listed ours as one of 100 hospitals and health systems with "great oncology programs." *U.S. News and World Report* recently ranked us 34th among 50 of the best hospitals nationally for cancer care.

Of course we don't rest on our laurels. There is much to do in the ongoing challenge that is cancer. Rest assured that we will not put down our tools until the job is done and every life we touch experiences a full return on the investment.

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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Spencer Serratos, 14, celebrates his end of treatment for a rare form of bone cancer with nurse Becca Billings and oncologist Jo Chung. The celebrations are made complete with a cake and gifts from the Keaton Raphael Memorial, a Roseville-based foundation supporting pediatric cancer research, patients and their families.

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Synthesis

Synthesis—the art of bringing together distinct elements in a way that makes them whole—

is a particularly relevant name for the magazine of UC Davis Comprehensive Cancer Center, which is distinct in its commitment to team science.

Our research program unites clinical physicians, laboratory scientists, population specialists and public-health experts from

throughout UC Davis and Lawrence Livermore National Laboratory with the goals of making cancer discoveries and delivering

these advances to patients as quickly as possible. We are also dedicated to sharing our expertise throughout the region,

eliminating cancer disparities and ensuring all Californians have access to high-quality cancer care. *Synthesis*—linking the best

in cancer science toward the united goal of improving lives—is the name of our magazine, and our promise as your National

Cancer Institute-designated comprehensive cancer center.