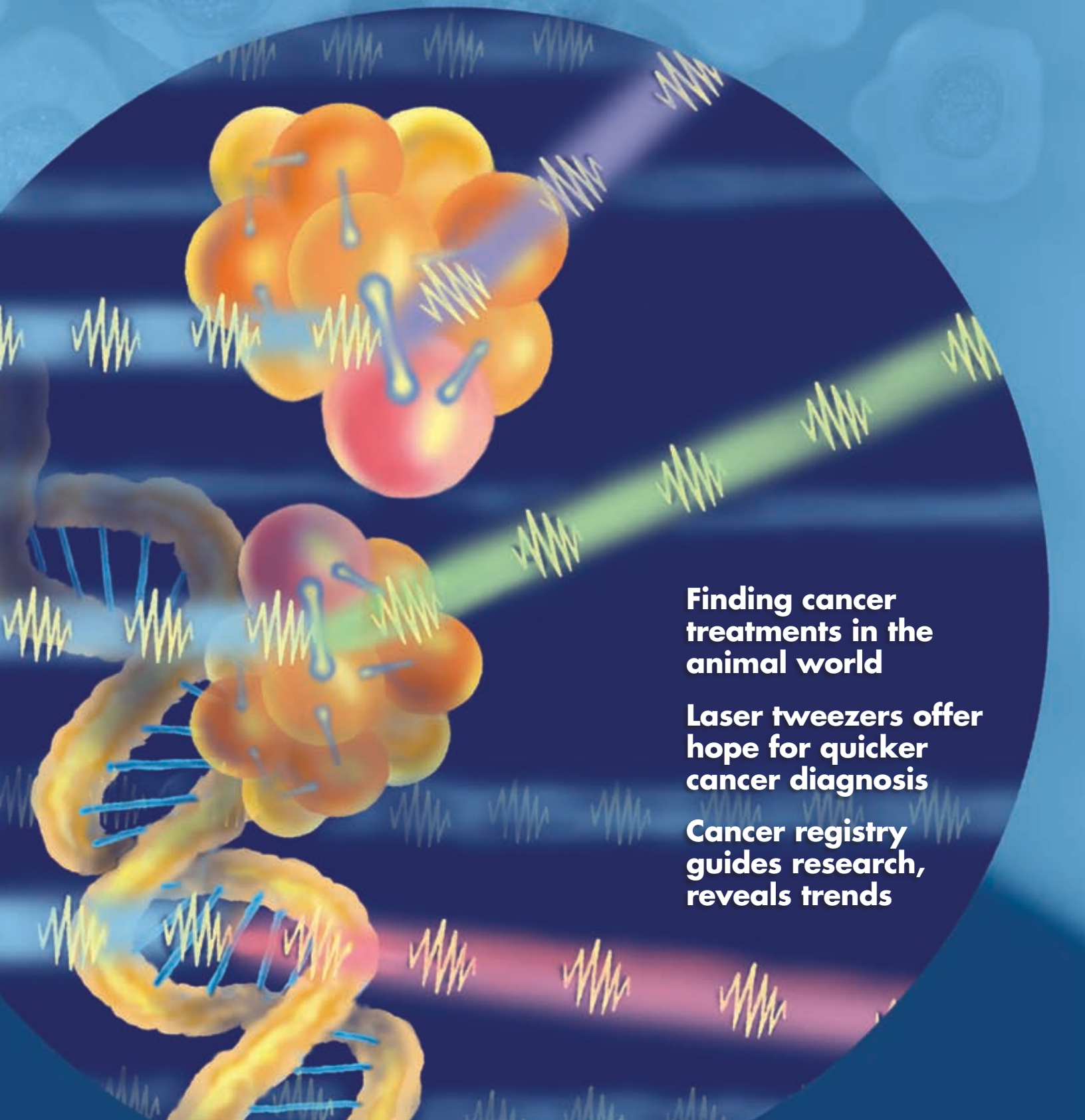
SYNTHESIS

A PUBLICATION OF **UC DAVIS CANCER CENTER** VOL 11 • NO 1 • WINTER 2008



Finding cancer treatments in the animal world

Laser tweezers offer hope for quicker cancer diagnosis

Cancer registry guides research, reveals trends

Dear Reader,

All cancer centers designated by the National Cancer Institute share the expectation that they deliver the world's best available care to their patients and their communities. But we each also look for areas that make our centers unique. In this edition of *Synthesis,* we touch on three special features of UC Davis.

First, the university's School of Veterinary Medicine, one of the best in America and the leader in research funded by the National Institutes of Health, makes our work on cancer distinctive. The goal of its veterinary oncologists is to prevent and cure cancer in their animal patients. The goal of the UC Davis Cancer Center is to do the same for our human patients. The question we are asking is, "How can we work together to help all of our patients?" A major step in this direction was the joint recruitment of Xinbin Chen by the veterinary school and the medical school to lead a collaborative effort in cancer research called "comparative oncology." I believe once you have read about him, you will understand what a wonderful choice we have made.

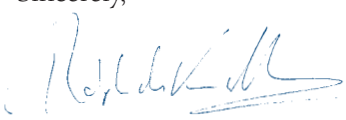
The second unique characteristic of our cancer center is its integration with Lawrence Livermore National Laboratory. Among other activities, researchers from both institutions collaborate on the Sacramento campus at the Center for Biophotonics Science and Technology. In this issue, you will read about one result of this partnership: the development of a laser Raman cystoscope to improve treatment of children with leukemia. A key figure on the team is Douglas Taylor, the pediatric oncologist leading the clinical portion of the project. In a previous *Synthesis* we introduced you to Thomas Huser, a Lawrence Livermore physicist on this project who has recently joined the UC Davis faculty.

Our cancer center's third special feature is its proximity to and relationship with the California Department of Health Services in Sacramento, and especially its California Cancer Registry. The registry is considered one of the finest of its kind in the world because of its 20-year collection of records and its extraordinarily high level of data integrity. Rosemary Cress, who heads up the registry's research programs, will tell you that the partnership with oncologists at the UC Davis Cancer Center is yielding new clues about cancers that burden women.

We are also pleased to bring you the stories of two patients. Norman deLeuze was an engineer-turned-winemaker determined to help researchers find a non-toxic cure for lymphoma. He and his family set up an endowment to support his determination. The other patient you'll read about, Mike Zawilski, received a groundbreaking new treatment for liver cancer that extended his life beyond initial expectations. Both patients passed away in October. What we learned – and will continue to learn – thanks to Norman and Mike will benefit all others dealing with tough cancers.

I thank you again for your interest in the UC Davis Cancer Center and I hope that this edition of *Synthesis* will show you how we use your support and trust to the very best of our ability.

Sincerely,



Ralph W. deVere White, M.D.
Director, UC Davis Cancer Center
Associate Dean for Cancer Programs
Professor, Department of Urology

Synthesis is published by UC Davis Cancer Center. If you receive multiple copies of this publication, please share them. If you need to change your mailing address, please call (916) 734-9064.

Ralph deVere White
Director
UC Davis Cancer Center

Carole Gan
Executive Editor

Jenifer Warren
Editor

Pat Grind
Art Director

Jodi Adkins
Graphic Designer

José Luis Villegas
Photographer

Camille Rey
Karen Schmidt
Julie Sly
Writers

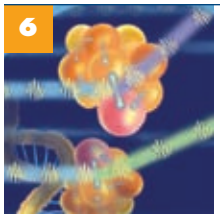
On the cover:
Illustrator ***Nelva Richardson*** *brings to life Raman spectroscopy, a technology that accurately identifies cancer cells and speeds diagnosis and treatment. Read the story on page 6.*

UC DAVIS CANCER CENTER

SYNTHESIS

VOL 11 • NO 1 • WINTER 2008

CONTENTS



Xinbin Chen leads the new Veterinary Oncology Laboratory, where research on cancers in companion animals can lead to answers for human cancers.

Answers from the animals

Studying cancer in pets benefits human patients, too

The gleaming two-story building on the UC Davis campus looks like a typical medical clinic, but with subtle differences. The parking lot has a dog walk area, and in back there's a bucolic horse stable. Inside, portraits of bulldogs, kittens and goats adorn the walls. The suite where technicians administer radiation treatment has a dry-erase board listing scheduled appointments with Sheba, Sassy and Taco.

This state-of-the-art hospital is the Center for Companion Animal Health, where it's common to see a black lab sauntering down a hall or a Persian cat resting on a lap in the waiting room. People bring their sick pets here for life-extending treatments. What many don't realize is that these animals may in turn help extend human lives – particularly in the fight against cancer.

"Our goal is to do something mutually beneficial," says Professor Xinbin Chen, 45, who holds appointments at the UC Davis Cancer Center and the School of Veterinary Medicine. "We can help the companion animals and, meanwhile, use the animals to learn more about human cancer."

"Why are certain breeds of horses more susceptible to melanoma? This is veterinary medicine, but it may in the future apply to human melanoma."

~ Xinbin Chen

Chen joined UC Davis in March to establish and direct the new Veterinary Oncology Laboratory in the center. His work is an outgrowth of the Cancer Biology in Animals program, one of six core areas of emphasis at UC Davis' National Cancer Institute-designated cancer center. The program focuses on bridging the gap between human and animal medicine.

Chen and his team will conduct research that draws on UC Davis' rare combination of resources: the renowned cancer center and its School of Veterinary Medicine. That powerful collaboration gives the university one of the nation's leading comparative oncology programs, says Chen.

With graying hair and a quick smile, Chen moved west after serving as co-director of the University of Alabama Cancer Center's Tumor Biology Program. Although he began studying veterinary microbiology and clinical medicine in China, it was during his graduate study in the United States that he realized there were strong connections between cancers in people and domestic animals.

One such connection surfaced in the 1990s with the gene p53.

Murals decorate the courtyard beside the Center for Companion Animal Health. Inside, researchers study links between pets and human patients.

In the long term, the comparative oncology program could yield entirely new treatments for melanoma, osteosarcoma and lymphoma.

The subject of thousands of research papers in that period, p53 is a gene encoding a protein that was found mutated in half of all human tumors. Given that, like humans, cats, dogs and horses also develop cancer, Chen wondered: Would mutant p53 be present in their tumors as well? A review of the sparse veterinary literature revealed the answer – yes – and Chen's fascination with the molecular similarities between animal and human cancers was born.

Studying cancer in domestic animals makes good scientific sense, Chen says. Pets live in the same environment as people do, often sharing the air, water, food and sleep patterns of their owners. Like humans, these animals develop tumors that arise spontaneously, grow fairly slowly and are associated with old age. And dogs, cats and horses are more closely related genetically to humans than are the laboratory mice typically used in research.

"It's puzzling," the bespectacled Chen says with a chuckle. "Cancer in mice has been cured many times. But often the drugs that work in mice don't work in humans. We need some new animal models."

That's the idea behind comparative oncology, which UC Davis researchers began exploring many years ago. In the 1960s, for instance, scientists studied dogs in order to develop tumor radiation protocols for human patients. More recently, the UC Davis Cancer Biology in Animals program tested a range of new anti-cancer drugs in cats and dogs. Chen is now broadening the program to include horses and aims to focus studies on three kinds of cancer common in companion animals: melanoma, osteosarcoma and lymphoma.

To get the new program and laboratory up and running, Chen has been busy assembling and training a team of veterinarians to study and treat cancer in domestic animals. He also has hired a drug trial coordinator – the first ever for the veterinary school – to track data on how animal patients respond to experimental therapies. Ultimately, he hopes to learn more about the role of p53 and other genes in tumor growth and use that knowledge to develop more effective cancer treatments for people and their pets.

Already his team is testing a drug that might one day be deployed against non-Hodgkin's lymphoma, a cancer of the immune system that each year strikes about 60,000 Americans and kills 18,000. The compound is a small peptide that appears to inhibit the progression of the disease. Kit Lam, chief of the Division of Hematology and Oncology at the UC Davis Cancer Center, is now giving the promising drug to cats and dogs with lymphoma and collecting data on the results.

Humans, as well as dogs, cats and horses, benefit from the research at the Center for Companion Animal Health.

"When we use cats and dogs to test drugs – instead of lab mice – it's much more likely that they will work in humans," Chen says.

This advantage is not lost on drug companies, notes Chand Khanna, director of the comparative oncology program at the National Cancer Institute's Center for Cancer Research in Bethesda, Md. "New tools for studying cancer in companion animals are now helping us to find out why cancer goes away with some therapies and doesn't go away with others," he says. "That information is very valuable to the pharmaceutical industry."

The UC Davis program, he adds, will contribute research data to a national Comparative Oncology Trials Consortium made up of 14 university research centers. The consortium collaborates with the U.S. Food and Drug Administration and with pharmaceutical companies. "The goal," Khanna explains, "is to learn more about new therapies and to use that information to develop the best human clinical trials possible."

Chen's particular interest is to find new drugs that can be used in combination with radiation therapy to prevent metastasis – the spread of cancer throughout the body. That's what kills patients with osteosarcoma, a bone cancer that is the second major cancer in children, and also is common in dogs. Chen is testing compounds that bind to mutant p53 and can restore its normal function as a tumor suppressor. "If this works well in dogs, then maybe we'll have better justification to try it in kids," he says.

In the longer term, the UC Davis program on comparative oncology could yield entirely new approaches for treating these three cancers, as clues reveal discoveries about other key genes besides p53. Chen already sees a golden opportunity to learn more about melanoma – the most lethal form of skin cancer – by studying the genetics of the disease in horses.

"Why are certain breeds of horses more susceptible to melanoma?" Chen asks. "This is veterinary medicine, but it may in the future apply to human melanoma."

Because horses tend to be inbred, their pool of genes shows limited variety. Information about their breeding is also readily available. By examining DNA from horses with and without melanoma, Chen hopes to find new genes associated with the disease. Then, he'll search the human genome for comparable genes and investigate whether these might be good targets for new kinds of melanoma treatments.

In the meantime, animal patients should benefit from the research, as Chen's team tries some of the latest therapies for humans on ailing pets. Animals with melanoma and osteosarcoma, for example, will be given an antibody-based treatment to see if the drug helps prevent metastasis, as it does in cases of human breast cancer.

"We may not be able to cure someone's pet now, but in the future someone else's pets will get better care," says Chen. And there's an indirect benefit, too. "When a pet lives longer, it increases the owner's lifespan," he notes. "Animal health is part of human health." UCD

Cancer in the crosshairs

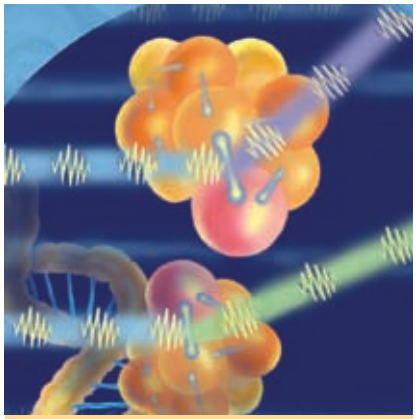
Laser tweezers promise better, faster cancer screening

If anything comes close to the anguish accompanying the news that a child has cancer, it's the agony of waiting for a precise diagnosis – and the start of treatment to attack that disease. At UC Davis, oncologists meet every day with families struggling with such circumstances. And they are working in earnest to ease their distress.

In a laboratory near the UC Davis Cancer Center, researchers are striving to develop a quick and reliable diagnostic technique to identify all types of cancer from a small blood sample.

Ultimately, they hope their technology – based on a new application of Raman spectroscopy – could help doctors choose the most suitable drug for a particular cancer and assess the effectiveness of treatment within hours or days.

The work is in the early stages, and the scientists caution that many possible stumbling blocks stand in their way. But if they achieve their goal, cancer patients could get answers – and treatment – far more quickly than they do today.



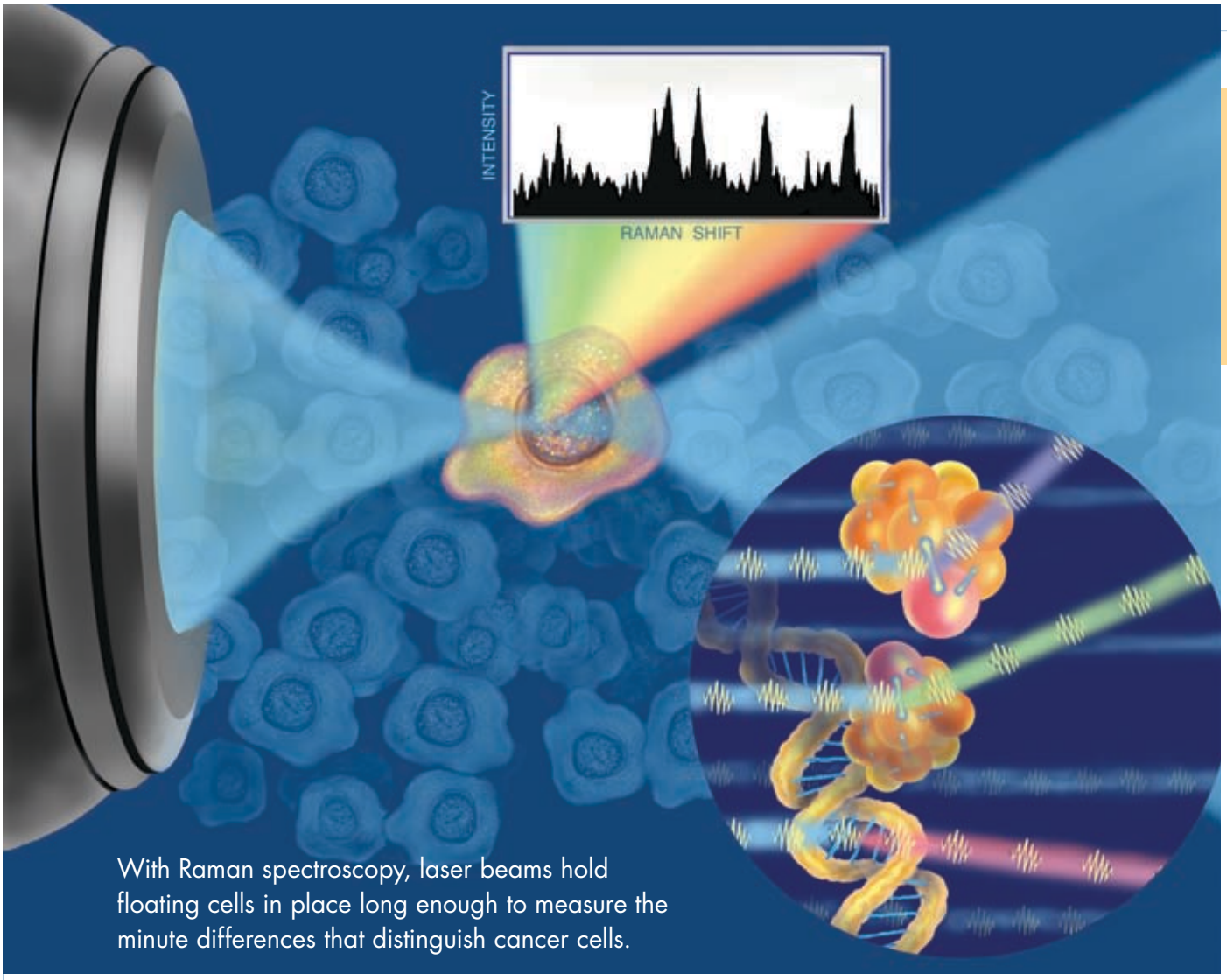
It can sometimes take days or weeks to arrive at a precise diagnosis. The wait is agonizing for patients and their families.

"Making diagnoses now is not always the simplest process on the planet, despite what you see on TV," says pediatric oncologist Douglas Taylor, one of two faculty members leading the research. "It involves often archaic technologies and multiple technicians. And it can often take days or occasionally weeks to figure out exactly what type of malignancy someone has."

Taylor has teamed up with physicist Thomas Huser to make his cancer-diagnostic machine a reality. They are developing a novel application of a technique called laser tweezers Raman spectroscopy. The breakthrough application involves using laser beams to hold floating cells in place, measuring the light scattered by their nuclei and, based on these measurements, accurately identifying them as cancer cells.

In January 2006, Taylor, Huser and their colleagues published a paper in the *Biophysical Journal* showing that they could use the technology to distinguish normal white blood cells from cells taken from

Thomas Huser (left) and Douglas Taylor use a breakthrough application – laser tweezers Raman spectroscopy – to identify cancer cells earlier than conventional diagnostic methods.



With Raman spectroscopy, laser beams hold floating cells in place long enough to measure the minute differences that distinguish cancer cells.

Despite significant gains in cancer treatment, cancer screening still relies heavily on a method developed in the late 1800s.

leukemia cell lines used in cancer research. Since then, they have successfully repeated those experiments using cells taken from actual leukemia patients.

"Each type of cell has its own biomolecular signature and we were able to use that to distinguish the cancer cells from the normal ones," Taylor explains. Publication of these newer results is pending.

The unique collaboration between Taylor and Huser was made possible by the Center for Biophotonics Science and Technology, a National Science Foundation facility based at UC Davis. Formerly employed at Lawrence Livermore National Laboratory, Huser now serves as chief scientist for the center and is a UC Davis associate professor in the Department of Internal Medicine. Taylor is director of the UC Davis pediatric stem-cell transplant program and an associate professor of pediatrics.

The center's goal is to spawn partnerships that lead to the application of the physical sciences to medical problems. In this case, the problem is the need for a better, faster and cheaper method for diagnosing cancer. Despite numerous advances in the treatment of cancer, the cornerstone of modern cancer screening is a method developed in the late 1800s. And not all cancers can be identified by

" In the future, we hope not only to screen for the presence of cancer, but also to quickly determine whether patients are responding to treatment and detect residual disease. That's the diagnostic nirvana."

~ Douglas Taylor

the fastest current method, flow cytometry, Taylor says.

The technology behind laser tweezers Raman spectroscopy is not new. Raman spectroscopy was invented in the 1920s, while laser trapping of cells was first developed about a quarter-century ago. It wasn't until spectroscopy could be fine-tuned and lasers became smaller, less expensive and more precise that these technologies could be applied to biological samples.

"The marriage of the two technologies only happened in the last five to six years," Huser says. "Now we can use lasers to optically suspend a cell within the laser focus and then determine its chemical signature."

The amount of laser light that is scattered by the nucleus of a cell depends on the amount and configuration of the biomolecular compounds it contains, such as DNA, RNA and proteins. More specifically, the number, density and type of molecular bonds determine the shift in the wavelength of the scattered light. Although minute, these differences are measurable and so unique that each cell type has its own spectroscopic fingerprint, Huser says.

Using these biomolecular fingerprints to find and define cancer in a blood sample, or elsewhere, would be a huge improvement over many current screening methods. Some diagnostic tests, for example, require patients to ingest radioactive materials and undergo CT scans. All the while, patients and their families are waiting – and worrying.

"I think the most distressing part is the waiting, because until the complete problem is known, the complete solution cannot be discussed," Taylor says. "Once the cancer is identified, and folks are marching toward a solution, there's security in that, and an element of solace."

Huser predicts that it will take four to five years for the team to show that the technology is not only safe and effective for widespread use as a diagnostic tool, but also faster than current methods.

"We have shown that Raman spectroscopy works to distinguish cancer cells," Huser says. "Now we just need to show that we can do it ten thousand times faster. At that point, it becomes interesting."

The group's ongoing experiments include automating the technology. They are working toward developing a high-throughput instrument and exploring other applications that promise advancements in patient care.

"In the future, we hope not only to screen for the presence of cancer, but also to quickly determine whether patients are responding to treatment and detect residual disease," Taylor says. "That's the diagnostic nirvana."

As a physician treating leukemia patients, Taylor's biggest hope is to one day use laser-trapping Raman spectroscopy technology to remove cancer cells from a patient's blood and then return the disease-free blood to that patient. While this and the other applications remain at best a distant reality, "in theory, the technology lends itself to these possibilities," Taylor says.

At UC Davis Children's Hospital, Medical Director Anthony Philipps is cheering on his colleagues' work, and waiting hopefully. When it comes to cancer diagnosis, he says, time is of the essence, and Raman spectroscopy could vault the process forward.

"If so, that will mean we can determine a course of treatment quicker, and that's beneficial to the patient," says Philipps, who is also the chair of pediatrics.

In the short-term, Philipps already sees a payoff. By bringing together physical scientists from the Livermore lab and UC Davis physicians, the project has created a fertile environment for collaboration that can only benefit cancer patients.

"It's fun to see it happen," says Philipps, who anticipates more collaboration in the future. "We knew it was going to work. But still, it's great to see the results." UCD

Data on California cancers housed in the California Cancer Registry help researchers like Gary Leiserowitz resolve disparities in cancer diagnosis and care. The registry's partnership with the university was initiated by its research director, Rosemary Cress.

California Cancer Registry

A gold mine for researchers studying women's cancers

Twenty-two years ago, California legislators gave researchers a long-coveted tool, requiring state health officials to gather detailed information on the incidence and treatment of cancer. Today, the California Cancer Registry is a vast gold mine, containing demographic data and other nuggets of information on more than 2.5 million cancer cases.

UC Davis researchers have been quick to pounce on the voluminous files. Now, in a unique collaboration with registry staff, the university's oncologists are targeting cancers that strike women.

Powered by the registry's richly detailed data, researchers are documenting cancer trends, illuminating disparities in treatment and unearthing a string of findings that are helping to guide patient care.

They have produced sometimes provocative reports on ovarian, cervical and endometrial cancers, and published a series of papers investigating the outcomes of cancers in pregnant women. In one high-profile study, appearing in a 2005 issue of the journal *Cancer,* UC Davis researchers dispelled the long-held view that pregnant women with melanoma fared worse than those who were not carrying a child.

The registry is a powerful guide-book, helping illuminate cancer trends, disparities in treatment and other findings that are improving patient care.

"There was a belief that the pregnancy milieu made the melanoma progress faster, and, in some instances, pregnant women diagnosed with the cancer were even advised to abort the fetus," says Rosemary D. Cress, research program director for the registry. "So the study showing there was actually not a difference in how pregnant women fared was really significant."

The collaboration on women's cancers was launched in 1999, when former California Sen. Debra Ortiz (D-Sacramento) and other lawmakers set aside about $300,000 for the work.

"While quite a lot of money has been dedicated to studying breast cancer, some of the other women's cancers had not been as heavily investigated," says Cress, who sparked the partnership with UC Davis oncologists. "The grant was intended to help us close that gap. And, fortunately, I found researchers at the cancer center who were as excited about the prospects as I was."

One of the earliest enthusiasts was Gary S. Leiserowitz, professor and chief of the UC Davis Division of Gynecologic Oncology.

"The collaboration has been terrific, and there is so much more that could be done. The projects are limited only by the imagination of the scientists."

~ Rosemary Cress

Partnership payoffs

Using data housed by the California Cancer Registry, researchers have been able to uncover new information about cancers that affect women. Significant discoveries that have driven new approaches to patient care include:

- Ovarian masses during pregnancy are relatively common, but not usually malignant, allowing women to avoid surgery during pregnancy.
- About 20 percent of women under age 55 with early stage ovarian cancer do not receive chemotherapy treatments that may improve survival.
- Ovarian cancer is not the "silent disease" it was once thought to be. Early symptoms are reported but can be easily misinterpreted by physicians.
- When diagnosed around the time of pregnancy, cancer of the cervix increases the risks of premature births or stillbirths.
- Less-invasive laparoscopic surgery for endometrial cancer yields at least as good as survival rates as open abdominal surgery, which requires much longer recovery time. UCD

Leiserowitz calls the work rising from the registry's population data a vital report card on patient treatment.

"The cancer registry is a great and powerful guidebook," he says. "It can illustrate disparities in treatment and patterns of care that might not meet our expectations. And then we can do something about that."

Housed in a nondescript office building in Sacramento, the registry first began collecting data in 1988, three years after the Legislature required health officials to establish a statewide cancer reporting system. Each year, more than 140,000 new cases of cancer are added to the registry's files.

The database includes information on patient demographics, cancer type, extent of disease at diagnosis, treatment and survival. In authorizing its creation, lawmakers hoped the availability of information on cancer statewide would help researchers tease out geographic, ethnic, occupational and other differences, providing clues about risk factors. The data also helps shape policy, revealing where early detection, educational or other cancer-related programs should be directed.

In addition, the registry publishes reports each year summarizing statewide cancer case rates and deaths, changes in rates over time and differences according to age, race/ethnicity and types of cancer. Because of California's multi-ethnic population, more is now known about the occurrence of cancer in diverse communities than ever before, making the registry a cornerstone of a substantial amount of research.

The registry's size makes it particularly valuable. Covering more than one-tenth of the United States population, the registry allows researchers to identify associations that might not be apparent in smaller samples, such as an individual cancer center.

"It's a very broad sweep," Leiserowitz says. "The law requires hospitals and radiation oncology centers to report on their cases, and compliance is very high, approaching 100 percent. So we really are capturing most of the data about patients in California, and there is rich detail about the kinds of cancers and their outcomes."

For Leiserowitz, the registry provides a "reality check" for oncologists and policymakers by documenting disparities in cancer treatment in the community. Those disparities, he says, may relate to income or education level, ethnicity or other cultural factors. Findings can then be used to guide political decisions about where to allocate health-care dollars.

Because the registry's data is relatively unfiltered, researchers must be careful not to overreach,

Lloyd Smith's research showed that detecting ovarian cancer early can happen more frequently as long as physicians listen carefully for patient reports of symptoms like abdominal swelling and pain when they are still mild. His patient, Sharon Ogden, was diagnosed when her ovarian cancer was at stage 1, allowing her to begin treatments when they can be most beneficial.

Leiserowitz says. In some instances, he notes, two experts could look at the same records and draw very different conclusions about what it all means.

"It's easy with these population-based studies to see things that may not be there," Leiserowitz acknowledges. "And sometimes the explanations for what we see aren't as nefarious as we initially believe."

One ongoing series of reports anchored in registry data centers on the outcomes of cancers in pregnant women. The work was spearheaded by Lloyd Smith, professor and chair of the Department of Obstetrics and Gynecology at UC Davis.

Smith had the novel idea of linking registry cases with a database of hospital deliveries. That approach has led to a variety of reports – including the study on melanoma during pregnancy – that have illuminated the incidence and risks of these cancers. Leiserowitz, for example, used the data to show that although ovarian masses are relatively common during pregnancy, they are not typically malignant, allowing many women to avoid surgery while pregnant.

In perhaps the most widely noticed of these studies, Smith and Cyllene Morris, a registry research scientist, helped dispel the long-held myth that ovarian cancer is a "silent disease," announcing itself only at the late stages when prognosis is poor. Instead, the study found that patients with ovarian cancer were more likely than two groups of other patients to report symptoms such as abdominal swelling and pain. The symptoms were reported at least four months – and, in some instances, as long as a year – before the patients with ovarian cancer were diagnosed.

"Dr. Smith showed that these women do in fact have symptoms that are often misinterpreted by their physicians, often leading to a delay in diagnosis," Leiserowitz says. "Ovarian cancer, he found, is really not a silent disease at all."

For Cress, such findings are a gratifying payoff from the partnership between the registry and the cancer center. Moreover, she notes, they are merely the start of what researchers may find as they comb through the registry's ever-expanding files.

"The collaboration has been terrific, and there is so much more that could be done," Cress says. "The projects are limited only by the imagination of the scientists." UCD

A combination of creative treatment options has given Mike Zawilski the chance to take a trip to Kauai with his wife, Kim, coach his daughters' swim team and cook gourmet meals.

Teaming up for Mike

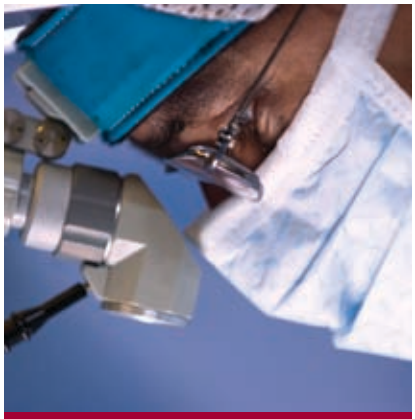
Doctors blend an array of aggressive treatments for liver cancer

The ordinary moments are the ones that mean the most to Mike Zawilski: leisurely conversations over dinner, poolside cheering at a daughter's water polo match, preparing his signature feast of seared ahi for relatives.

In early 2004, Zawilski faced a future without such treasured everyday events. Lying on the exam table after a colonoscopy, he was told he had colon cancer, and later learned the disease had spread to his liver.

The prognosis for such patients is typically poor. But, thanks to an aggressive, integrated approach to his care by doctors at the UC Davis Cancer Center, Zawilski's cancer is for now under control, allowing him to continue enjoying life as a married father of two teenaged girls in Cameron Park, Calif.

"I still have challenges, but the quality of life is there," says Zawilski, 52, a retired information technology manager who worked in state government for 25 years. "It's a cliché, but I'm taking it one day at a time and cherishing the good times with family and friends."



Four years after his diagnosis, Mike Zawilski stays strong for his family and cherishes the good times with family and friends.

Zawilski's doctors say his relatively strong condition nearly four years after diagnosis proves that a multidisciplinary treatment approach to such cancers can yield encouraging results. Vijay Khatri, the surgical oncologist on the team, says Zawilski's case was challenging because his colon cancer had spread to both sides of his liver. With chemotherapy alone, about half of such patients would be expected to survive 21 months, studies show.

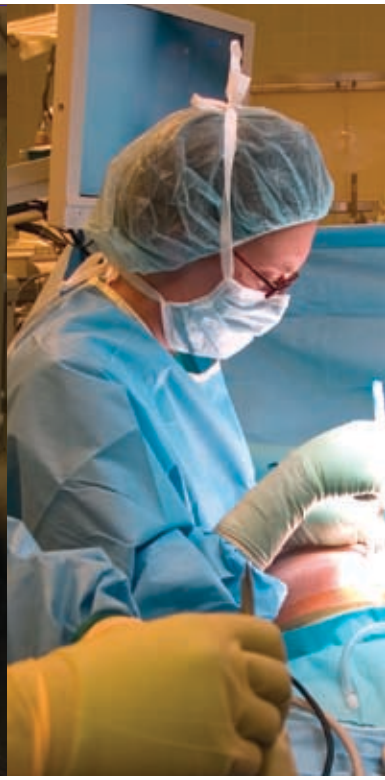
Surgery can significantly extend that timeframe, Khatri says, with some patients living as long as 10 or 20 years. But Zawilski's cancer had invaded his liver to such an extent that surgery was initially not possible – and also too risky.

That meant it was time to get creative.

Step one was to address the cancer in his colon, and then begin an intensive course of chemotherapy provided by Zawilski's medical oncologist, Tsuong Tsai of Cameron Park.

Doctors turned next to the liver, where they combined several treatments in a novel

In a series of procedures, a team led by UC Davis surgical oncologist Vijay Khatri attacked the tumors that had invaded both sides of Zawilski's liver.



fashion to allow Zawilski to undergo removal of the liver tumors. First they used radiofrequency ablation to burn the tumors on the left side of the liver. Increasingly common for small liver and kidney tumors, the procedure is performed with a thin needle inserted into a tumor with the help of computer tomography or ultrasound.

Radiofrequency energy channeled through the needle then super-heats and destroys the tumor. Handling that segment of the treatment was UC Davis radiologist John McGahan, who pioneered this technique.

Zawilski was then ready for portal vein embolization. Performed by Daniel Link, a UC Davis radiologist who specializes in interventional vascular care, the procedure involves blocking blood flow to one side of the liver in order to enlarge the other side. The goal is to increase the size of the organ to the point where surgery to remove the remaining cancer lesions is safe. In Zawilski's case, the plan was to block blood flow to the right side to allow the left side, which had more healthy tissue, to grow. If all went according to plan, the right side of his liver could then be removed safely.

The results were impressive.

"When we went back and repeated the CAT scan a month later, we found the left side of the liver had increased in size by almost 30 percent," recalls Khatri, a UC Davis professor of surgery. "That gave me a great advantage, and we were then able to take him to surgery and remove the right side of the liver. In fact, the left side of the liver had grown enough to enable us to safely remove even the tumors on the left side that had been previously ablased by Dr. McGahan. If we had not taken these innovative steps, removal of all the tumors would not have been possible without resulting in liver failure."

Khatri adds that, under ordinary circumstances, expanding the left side of the liver through portal vein embolization would also have caused the tumors there to grow. "But burning them with radiofrequency ablation beforehand prevented that," Khatri says. "That's why it is such a crucial part of our approach."

Once he recovered, Zawilski again was given a course of chemotherapy. Through it all, he says, Khatri's upbeat assessment of the treatments kept his family's spirits high.

"Dr. Khatri's demeanor and confidence in the procedures gave us a high degree of trust," says Zawilski. "It's amazing the technology they use nowadays. And I'm still here, so I certainly recommend it."

In the months since his treatments, Zawilski has managed a family trip to his favorite destination – Kauai – and a few other vacations. Mostly, though,

he's savored time spent with his wife, Kim, and daughters, Alexandra, 17, and Katherine, 14.

Over the summer he devoted countless hours to the girls' swim team, managing the computer system that tracks race times at meets. At the season-ending championship event in July, the Suburban Swim League honored Zawilski for his contributions, awarding him a thank-you plaque.

"That meant a lot to him, and to me," Kim Zawilski recalls. "He has been able to stay so strong for the kids and to stay very involved in their activities – not just as a spectator, but as a board member of the swim team, guiding how that institution runs. He's been through a lot, but he never falls into the pity pot, and that's an inspiration to a lot of us."

Zawilski continues to receive chemotherapy to manage some tumors that have resurfaced in the liver area. "This is an aggressive cancer, but we're keeping a handle on it with my special chemotherapy concoction, and maybe a cure will come along," he says. "In any case, I have no complaints."

Khatri says Zawilski's "positive outlook is inspiring," and an asset to his health. He also hopes other patients will find solace in the fact that Zawilski, a patient whose cancer had metastasized to both sides of the liver, is faring well thanks to a unique combination of treatments.

"If this case sends a message to the community, it is that they have these experts at their disposal, and that we can work in a multidisciplinary fashion with one goal – optimal outcomes for our patients," says Khatri, who published an article on the treatments used in Zawilski's case in a 2005 issue of the *Journal of Clinical Oncology*. "At a minimum, we can provide people with more time without tumors or improve their quality of life." UCD

After battling a persistent infection in recent months, Mike Zawilski passed away on Oct. 10, 2007. His wife, Kim, expressed thanks to his medical team for their life-extending treatment.

"Their combined efforts gave Mike 42 months after diagnosis to enjoy his family and friends, which was twice as long as the initial prognosis. Mike fought the disease valiantly until the end, and he remained deeply involved in our daily lives until just before he passed away."

A memorial service was held Oct. 27, 2007.

Norman deLeuze left a career in engineering to pursue his dream to be a full-time vintner. Finding alternative treatments for lymphoma is a dream that his family is still supporting. From left to right are Rosa Lee, Norman, their grandson, Brandon, and their children, Julie, Robert and Brett.

In pursuit of options

Norman deLeuze fuels the hunt for a nontoxic cure for lymphoma

A Napa winemaker sees great promise in alternative medicine and works with a UC Davis oncologist to study these approaches.

Norman deLeuze is a man accustomed to chasing big dreams. In 1968, the engineer teamed up with a colleague at Aerojet General in Rancho Cordova, Calif., to pursue a lifelong goal – the production of world-class wine. Before long, their business, ZD Wines, was born in a rented Sonoma farm building and the partners were producing 350 cases of wine from their first crush.

Now deLeuze is focusing his unbridled determination on another dream – the discovery of a nontoxic cure for lymphoma. Toward that goal, the vintner and his family have established an endowment supporting what they call "the outstanding research approach" of UC Davis oncologist Joseph Tuscano.

The fund was launched in December 2006 with a donation of $313,000 by the deLeuze family, their winery and their friends. DeLeuze is continually seeking outside support for the UC Davis endowment, and hopes it will break the $1 million mark by the end of this year.

For deLeuze, 75, the search for a cure is a highly personal cause. In January of 2004, the UC Berkeley graduate was diagnosed with mantle cell lymphoma, a subtype of non-Hodgkin's lymphoma. Originating in the body's white blood cells, known as lymphocytes, lymphoma kills more than 24,000 Americans every year.

For a health nut who took scrupulously good care of himself, the diagnosis was a shock, deLeuze's son, Brett, recalled.

"My father used to say he wanted to live to 120, and he followed a very healthy, nutrition-conscious lifestyle," said Brett deLeuze, who helps manage the winery along with his mother, Rosa Lee, and two siblings, Robert and Julie.

"Then he was diagnosed with cancer and told he was going to die within eight months without chemotherapy or radiation."

Despite that stark forecast, deLeuze said he was "not interested in those conventional medical approaches because of their toxicity." Instead, he began researching – and trying – a host of alternative treatments to fight his cancer, including high doses of intravenous vitamin C and a

When a product containing fermented wheat germ extract appeared effective against his patient's lymphoma, UC Davis researcher Joseph Tuscano began the search for the active ingredient.

wide variety of other nutritional supplements.

Using his scientific background, deLeuze has done his best to distinguish the promising approaches from the dubious ones. But a lack of solid data has been a constant frustration.

"There are a lot of options out there but none of them has gone through clinical trials," deLeuze said. "Basic research that can help people make a careful evaluation and decide what to try is missing."

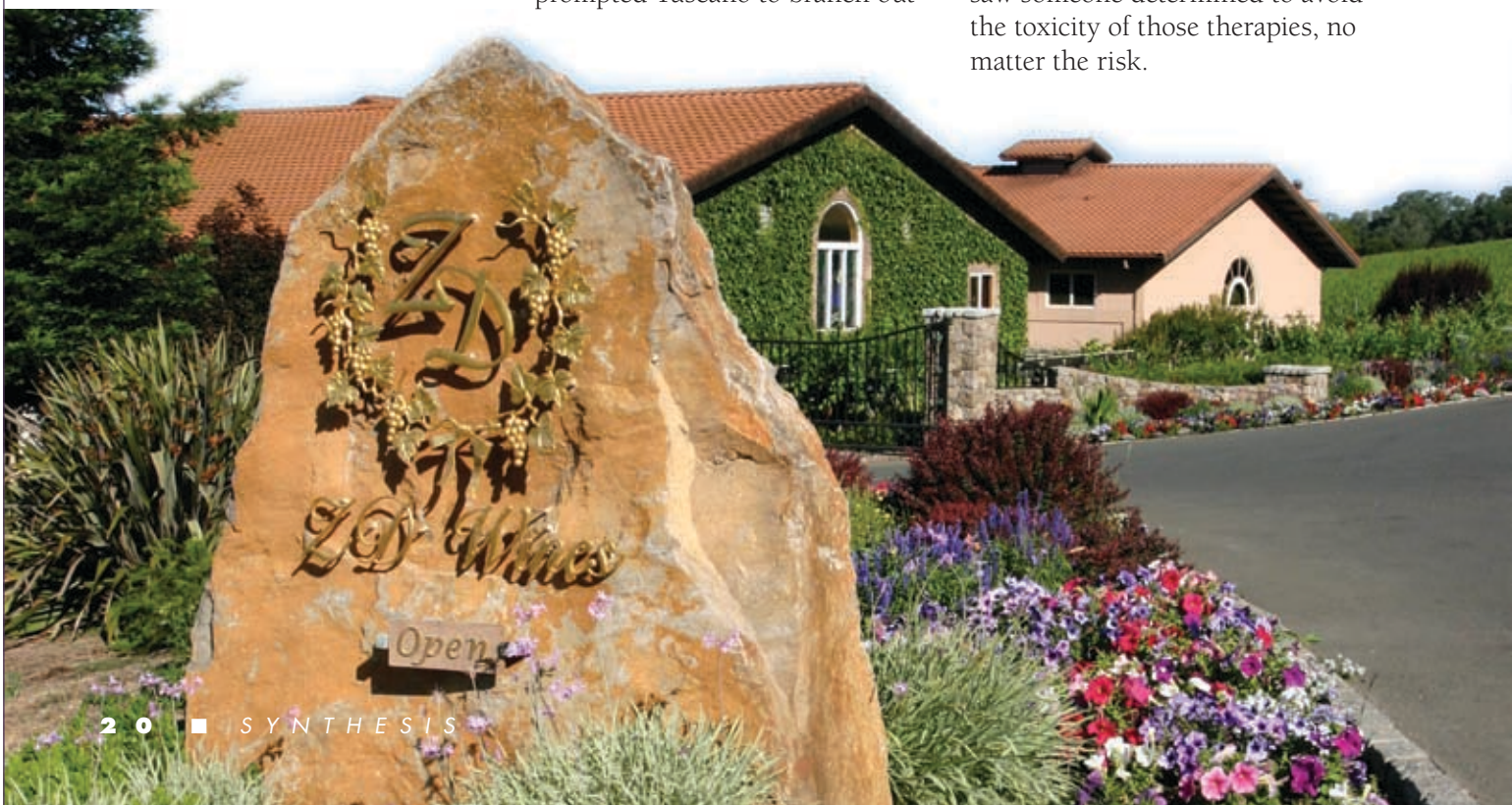
At UC Davis, Tuscano is seeking to close that gap. Now the primary oncologist for deLeuze, Tuscano has been developing novel, immune-based therapies to treat lymphoma, including the use of monoclonal antibodies. He has also studied a variety of natural, homeopathic compounds, including fermented soy products, in collaboration with two cancer center colleagues, molecular geneticist Philip Mack and urologic oncologist Ralph deVere White, the UC Davis Cancer Center director.

About a year ago, deLeuze prompted Tuscano to branch out and take a look at another natural product – fermented wheat germ extract. Rarely used here but more common in Europe, the compound, known in one form as Avemar, has not been studied in formal, preclinical or clinical studies, Tuscano said. But lab tests have shown promising results in a few human cancers.

When deLeuze began taking Avemar, Tuscano observed him and concluded that his patient's lymphoma appeared to be shrinking.

"I then tested the product in the laboratory, and found that in fact it was very active for the treatment of lymphoma, both in the test tube and in animal models," Tuscano said. "Based on this surprising and significant result, we've begun a search for the active ingredient."

As an oncologist, Tuscano typically advises that his patients take a traditional approach to their cancer, using proven strategies such as radiation and chemotherapy. But in deLeuze, the doctor saw someone determined to avoid the toxicity of those therapies, no matter the risk.



With the competition intense for federal research grants, gifts such as those from the deLeuze endowment are more critical than ever.

UC Davis oncologist Joseph Tuscano has been developing novel, immune-based therapies to treat lymphoma.

"He understands the consequences of avoiding the traditional therapies and is willing to accept those risks to try to identify less toxic treatments," Tuscano said. "He has outlived everybody's expectations for patients who forgo standard cancer care, so he must be doing something right."

With his training, research record and interest in nontraditional responses to cancer, Tuscano was a perfect candidate for the deLeuze family endowment, Norman deLeuze said.

"He's pursuing some very nonconventional approaches, and I've really enjoyed working with him," deLeuze said. "He's at least open-minded about the possibilities out there, and he's willing to listen, to have a two-way conversation."

Tuscano called the deLeuze Family Endowment for a Nontoxic Cure for Lymphoma a substantial and critical boost for the search to find nontoxic treatments for lymphoma. He noted that despite a resurgence of interest in this type of research by the federal government and other groups, funding is highly competitive, making gifts such as those from the deLeuze endowment even more important.

DeLeuze has no illusions that the campaign to find the nontoxic weapon he seeks will be easy. But he is not one to shy away from a long-odds challenge. For 10 years, he and his partner ran their wine business as a part-time concern while holding full-time jobs. By 1978, ZD Wines was crushing a staggering 41 tons of grapes from the 1977 vintage, and it was time for deLeuze to leave engineering behind.

"He built an amazing winery," son Brett said, "but now he is devoting all his energy to his new dream – finding a cure for lymphoma. Our partnership with UC Davis is a great way for us to get there."

For more information or to contribute to the fund, please call Ann Pridgen at (916) 734-9675. UCD

While Norman deLeuze lost his battle with lymphoma on Oct. 26, 2007, his family continues to honor his commitment to finding alternatives to chemotherapy and radiation treatments.

"What we learned together could have great outcomes for others who are seeking alternative treatments for lymphoma and other cancers," said Tuscano, who spoke at the memorial service. "Norman was a man of great pride, intelligence and conviction. It was an honor to care for him and to know him. He was not only my patient but also my friend and collaborator. He will be missed, but his spirit will live on as inspiration for my research."

Gene variations may affect how chemotherapy drugs are metabolized

David Gandara

When given the same chemotherapy treatment, why did a group of Japanese lung cancer patients survive longer – yet with a higher rate of side effects – than their U.S. counterparts? A study spearheaded by the Southwest Oncology Group and led by David Gandara, director of clinical research at the UC Davis Cancer Center, suggests that the reasons lie in subtle variations in genes that govern how the body metabolizes chemotherapy drugs.

The discovery that Japanese and U.S. patients, matched in age, gender and other respects, had differences in key metabolism-related genes is the latest result from a seven-year collaboration between the Southwest Oncology Group and two clinical trials groups in Japan.

Researchers found that patients with a certain variation in the CYP3A4 gene responded more favorably to the chemotherapy drugs paclitaxel and carboplatin and that their lung cancers progressed more slowly. A variation in another gene, ERCC2, seemed to interfere with how well patients responded to treatment.

The study breaks new ground by exploring the possible role of ethnic patterns in the emerging science of pharmacogenomics, in which drug regimens are tailored to a patient's genetic profile.

The differences in outcomes corresponded with the patients' genetic makeup, rather than their ethnicity, because some individuals in each group possessed genetic variations not typical of their group. The study suggests that in the future, therapies need to be tailored to each individual based on analysis of their genetic makeup, not simply their ethnicity.

Accuracy of mammograms reduced?

Computer-aided detection (CAD) software designed to improve how radiologists interpret mammograms may actually make readings less accurate, according to new research conducted by investigators at UC Davis.

CAD was approved by the U.S. Food & Drug Administration in 1998 and has been incorporated into many mammography imaging practices.

"Within three years of FDA approval, 10 percent of the mammography facilities in the country were using CAD," said lead researcher Joshua J. Fenton, assistant professor of family and community medicine at UC Davis. "There had been no large-scale, community-based review of CAD efficacy despite the rapid adoption of this technology."

The new study, funded by the National Cancer Institute, the U.S. Agency for Healthcare Research and Quality and the American Cancer Society, showed that women who received screening mammograms at centers using CAD software were more likely to be told their mammograms were abnormal and thus more likely to undergo biopsies to rule out breast cancer. The authors of the study estimate that for every additional woman diagnosed with breast cancer on the basis of CAD, 156 women were falsely recalled for more tests and 14 had unnecessary biopsies to exclude cancer.

Resources and support for adolescent and young adult cancer patients

Board members include (left to right) Lisa Massi Lindsey, Marlene von Friederichs-Fitzwater, Danny Cocke, Nichole Becker and Kimberly Hicks.

Kimberly Hicks knows firsthand what it's like to be a teen and young adult cancer survivor – three times over. She was first diagnosed at age 15 with Ewing's sarcoma. Four years later, doctors discovered cancer in her lung. Three years after that, she was diagnosed with an entirely different form of cancer – renal cell carcinoma. Today, Hicks is cancer-free and a UC Davis graduate with a bachelor's degree in human development and psychology.

As a member of the UC Davis Adolescent and Young Adult Cancer Advisory Board, Hicks participates in a variety of programs and events designed to boost awareness and increase support for teens and young adults with cancer.

The board was formed to bring issues of teen and young adult survivors of cancer to the forefront of research and support services. For instance, at the most recent National Cancer Survivor's Day on June 1, board members displayed creative collages about their cancer experiences. They are currently overseeing a new Healing and Performing Arts Program for children with cancer. And they are evaluating computer software that can help with problem-solving and coping skills.

With her positive attitude, Hicks will no doubt be an inspiration to adolescent patients. As she says, "Because I've had cancer, I'm pretty confident. I mean, what else can you throw at me?"

Upcoming Events

INTRODUCING THE

HEALING AND PERFORMING ARTS PROGRAM

Free music, art and writing therapy for all children with cancer and their siblings

Beginning in 2008 at the UC Davis Cancer Center

- Writing and Performing as Healing
- Making a Mark Art Therapy
- Songs of Hope Music Therapy
- And companion sessions for siblings

For more information, call Patti Robinson (916) 734-0823 or e-mail patricia.robinson@ucdmc.ucdavis.edu.

thecelebration
reaching for a cure for cancer

presented by Comcast

FEBRUARY 29, 2008

CANCER CENTER CELEBRATION GALA

Presented by Comcast
Hyatt Downtown Sacramento
Information: (916) 734-9675 or
ann.pridgen@ucdmc.ucdavis.edu

Compact proton therapy machine enters development

Proton therapy is considered the most advanced form of radiation therapy available, but, until recently, size and cost have limited the technology's use to only six cancer centers nationwide. That is about to change, as the first compact proton therapy system for use in a clinical setting entered development in June.

The result of defense-related research, the compact system was originally developed by scientists at Lawrence Livermore National Laboratory. The project was jointly funded by the laboratory and UC Davis Cancer Center, and the technology has been licensed to TomoTherapy Inc.

TomoTherapy will fund development of the first clinical prototype, which will be tested on patients at UC Davis Cancer Center. If clinical testing is successful, TomoTherapy will bring the machines to market. The compact system will be designed to fit into any major cancer center and will cost a fifth as much as a full-scale machine.

"We have taken proton therapy and achieved major advances toward what we were told was impossible – to scale it down to a size and price that will bring it in reach of every major cancer center," said Ralph deVere White, director of the UC Davis Cancer Center and associate dean for cancer programs.

Conventional radiation therapy kills cancer cells using high-energy X-rays that deliver energy to all the tissues they travel through, from the point they enter the body until they leave it. Doctors therefore must limit the dose delivered to the tumor in order to minimize damage to surrounding healthy tissue. In contrast, proton beams deposit almost all of their energy on their target, with a low amount of radiation deposited in surrounding tissues. This enables doctors to hit tumors with higher, potentially more effective radiation doses.

10-year-old cancer survivor named ambassador for children's hospitals

Francesca Arnaudo, 10, a two-time cancer survivor from Ripon, Calif., has been chosen as California's representative in the Champions Across America tour, an awareness campaign designed to highlight the work of the nation's 170 Children's Miracle Network hospitals. "I'm excited to have the opportunity to help other children who've had traumatic experiences in their lives, and to help doctors find a cure for me and other kids," Arnaudo said.

Francesca Arnaudo

Arnaudo was diagnosed at age six with osteosarcoma, a bone cancer, and at age eight with acute myeloid leukemia, a white blood cell malignancy. Today, following four years of treatment at UC Davis Children's Hospital, Francesca is cancer-free.

"We're thrilled that Children's Miracle Network has selected one of our patients to represent California on its awareness tour," said Anthony F. Philipps, medical director of UC Davis Children's Hospital. "The network is absolutely vital in supporting the extraordinary variety of programs, projects, equipment and people who make UC Davis Children's Hospital the important resource that it is for young patients in our region. For cancer patients like Francesca, for instance, Children's Miracle Network supports the research efforts of Dr. Douglas Taylor to eliminate leukemia recurrences."

After an exciting and emotional send-off from UC Davis Children's Hospital, Arnaudo joined 49 other young "champions" from around the country in Washington, D.C. There, the children shared their stories of triumph during a press conference at the White House. Then, it was on to Walt Disney World in Orlando, Fla., where they participated in the taping of a television show to be broadcast nationally.

Fred Meyers

UC Davis awarded grant for Latino/a palliative care cancer study

The American Cancer Society has awarded a two-year, $144,000 grant to UC Davis researchers to develop and test a Spanish-language educational program for Latino/a cancer patients and their caregivers. The program is designed to help monolingual, Spanish-speaking patients improve their coping skills and quality of life.

"In any chronic illness, stress increases," said Fred Meyers, professor and chair of Internal Medicine at UC Davis and principal investigator for the new grant. "If we can improve people's coping strategies and problem-solving skills, we can enhance their quality of life."

Meyers and his co-investigators will enroll 60 monolingual Spanish-speaking cancer patients in the study. They will be evaluated for health literacy, the meaning their illness has for them, their immigration experiences, religion, social stressors and social support networks. Educators will then provide the participants with culturally tailored coaching in Spanish using a problem-solving approach known as COPE (Creativity, Optimism, Planning and Expert information).

''We hope to be able to cut through perceptual barriers and lift veils of social and cultural misunderstanding, improve patients' abilities to communicate with their physicians and other health-care providers, and alleviate stress experienced by both cancer patients and their families," Meyers said.

UC Davis and Turtle Health Foundation expand partnership

The UC Davis Cancer Center has formalized and expanded a partnership with the nonprofit Turtle Health Foundation to improve cancer education, research and training for American Indian tribes and tribal communities.

"The partnership is a natural one," said Marlene M. von Friederichs-Fitzwater, director of the outreach research and education program at the UC Davis Cancer Center. "California is home to the nation's largest population of American Indians, who unfortunately have the poorest cancer survival rate in the United States."

The partnership will spawn a variety of initiatives designed to strengthen cancer education outreach and increase health education awareness among American Indians while focusing on cancer prevention, early diagnosis and treatment options.

Linda D. Navarro

The collaboration will also provide educational opportunities for American Indian undergraduate and graduate students, including scholarship programs in nursing, physical therapy, health science, therapeutic recreation, medical social work, speech pathology, pre-med and medicine.

"We are looking forward to an increased level of collaboration in the areas of research, education and prevention for the benefit of the American Indian community," said Linda D. Navarro, chief executive officer of Turtle Health Foundation.

UC DAVIS
CANCER CENTER

A National Cancer Institute-designated cancer center

SYNTHESIS

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

www.ucdmc.ucdavis.edu/cancer

UC DAVIS CANCER CENTER
4501 X STREET
SACRAMENTO, CA 95817-2230

ADDRESS SERVICE REQUESTED

NON-PROFIT ORG.
U.S. POSTAGE
PAID
UC DAVIS