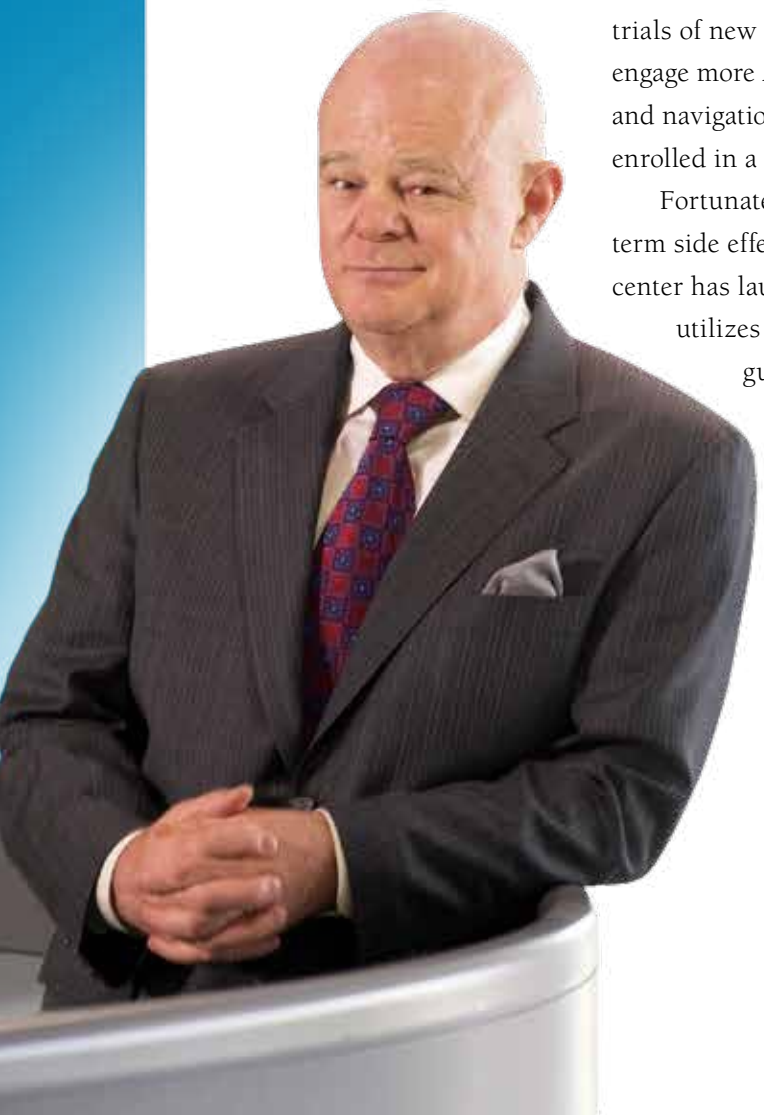
SYNTHESIS

THE MAGAZINE OF **UC DAVIS COMPREHENSIVE CANCER CENTER** VOL 16 • NO 2 • FALL/WINTER 2013



Dear Reader,

Cancer is not a single disease. We now know that every tumor is as complex in its molecular makeup as the person diagnosed with the disease. That's why our work in cancer prevention, diagnosis, treatment and follow-up care must be tailored to the individual patient and tumor.

In this issue of *Synthesis*, we explore these efforts from the basic science in our laboratories to the clinics where we care for our patients.

New technologies that quickly analyze human samples for cancer-causing genetic mutations are increasingly helping us understand cancer but also improving cancer control through targeted prevention and treatment.

Building on his study of homogeneous populations in South America, Luís Carvajal-Carmona is using genetic analysis techniques to quickly screen human genomes for new mutations that may be targets for new treatment. In another laboratory Jeff Gregg and Clifford Tepper will soon sequence individual patient tumors to identify mutations and hasten effective treatment.

The cancer center is working equally hard to build participation in clinical trials of new therapies. In this issue you will learn about an approach to engage more Asian-Americans in clinical research through patient education and navigation. And you will meet a 9-year-old leukemia patient who is enrolled in a trial that informs future treatment options for other children.

Fortunately, childhood cancer is relatively rare, but for survivors, long-term side effects of treatment can be a great burden. That's why the cancer center has launched a clinic dedicated to childhood cancer survivors that utilizes an Internet-based program to track each patient's treatment and guide clinicians in preventing or responding to potential late side effects. It's another way we are breaking barriers to beat cancer.

We hope you enjoy this issue of *Synthesis*. Thanks for reading.

Ralph de Vere White

Director, UC Davis Comprehensive Cancer Center
Associate Dean for Cancer Programs
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Breaking Barriers to Beat Cancer℠

INSIDE THIS ISSUE

UCDAVIS COMPREHENSIVE CANCER CENTER

A National Cancer Institute-designated comprehensive cancer center

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It's GREAT!

New clinical support for childhood cancer survivors

When Shannon and Gary Whisenant were absorbing news of their child's grim prognosis, the potential side effects of her cancer treatment were not high on their what-if list of immediate concerns and overwhelming fears.

The couple's 5-year-old daughter, Evan, was gravely ill. She would require an extremely tough treatment regimen involving numerous rounds of intensive chemotherapy followed by a bone marrow transplant. As part of the transplant, she would have total body radiation with extra doses to the brain, and additional intensive chemotherapy. Even if a good transplant match were found, the Whisenants were told, the odds of Evan surviving five years with hypodiploid acute lymphoblastic leukemia were just one in two.

"We said, 'just fix her,' " says Shannon Whisenant, Evan's mother. "And then we powered through it."

Evan bravely survived the treatments. Now 10, she is in the fourth grade at Dudley Elementary School in Antelope. With her peace-sign decorated jeans, purple hair bow and painted pink fingernails, the thoughtful, inquisitive girl appears and behaves like any other her age. But five years after so many therapies and the transplant, Evan is not a normally developing child. Like many children who have endured cancer treatment, she copes with multiple late effects, including problems with her vision, diminished lung capacity, disrupted hormone production and other complications — many of which will be with her for the rest of her life.

Fortunately, the family has had ongoing support and care from the UC Davis Comprehensive Cancer Center's "Getting Regular Evaluations After Treatment" clinic, or GREAT clinic, for short. While the cancer center has long monitored patients after treatment for signs of late effects, a $75,000 grant from Hyundai's Hope on Wheels this year has enabled a more formal, coordinated clinical approach.

Kathryn Wells, a pediatric oncology nurse practitioner, is leading the effort. She sees GREAT patients on Friday mornings. Most are at least four years out from their cancer treatments. Wells explains that while not all pediatric cancer patients suffer late effects, many do because childhood malignancies are treated very aggressively.

"They need very intensive treatment to be cured, and they can tolerate the treatment, even more than many adults can," she says.

Wells explains that while not all pediatric cancer patients **suffer late effects,** many do because childhood malignancies are treated very aggressively.

"And because we are treating them when they are going through growth and development, we need to assess what kind of damage that treatment may or may not have caused."

The childhood cancer survival rate has surged to 80 percent over the past several decades, but more than 70 percent of the 350,000 survivors will develop adverse health effects, and 25 percent to 40 percent of those effects will be

severe or life threatening, according to a 2006 study in the *New England Journal of Medicine*.

Evan has osteoporosis. She takes vitamin D and drinks milk to maintain and, hopefully, rebuild her bone density. Because of the radiation treatments she received, the 10-year-old has had three melanomas, skin cancers that must be caught and treated quickly. Radiation to her head caused cognitive delays, making reading more difficult. And treatment-related cataracts eventually will require eye surgery.

Radiation therapy and some chemotherapy agents also can cause infertility by directly damaging the ovaries or the testes. In addition to infertility, Evan likely will require hormone therapy to reach puberty.

Fortunately, some post-treatment problems have improved. Her liver has regained full function, and her kidneys are working well. While Evan's limited lung capacity hampers her participation in school physical education, she loves to practice holding her breath while swimming in her backyard pool, and running around an expansive park near her Antelope home.

The long list of challenges would seem an overwhelming burden to most, but, as Shannon Whisenant says, "It's who we are. It's who she is. But we are blessed. She is here."

The family also feels relief knowing that Wells has logged everything in Evan's "Passport for Care," an Internet-based tool that facilitates the comprehensive follow-up medical care for child and young adult cancer survivors.

At Evan's GREAT clinic visit recently, Wells carefully goes through Evan's record, checking to ensure she has received the **follow-up care** she needed from **endocrinology, dermatology and ophthalmology,** and that her blood and bone density tests are **up to date.**

Marc Horowitz, professor of pediatrics at Texas Children's Cancer Center, led development of the tool in collaboration with Baylor College of Medicine and the nationwide Children's Oncology Group. He says Passport for Care addresses many problems confronting childhood cancer survivors including: the absence of good post-treatment care plans; the survivor's limited understanding of their disease, treatment history and late effects risks; survivors' frequent changes in medical providers, and the fact that most general practitioners are not trained to deal with late effects of cancer treatment.

Passport for Care works by assembling individualized survivor-care recommendations based on the survivor's treatment history. It also provides end-of-treatment care summaries and customized educational resources. Horowitz says that 105 institutions now use Passport for Care, with more than 10,000 patients enrolled.

"I can input the therapy the patient has received and, based on the (treatment) exposures the patient has had, it lists the different sorts of health problems he or she may be at risk for," says Wells. "It guides us in what kinds of questions we should ask, what sorts of physical findings we should look for, and which kinds of diagnostic tests we should consider."

At Evan's GREAT clinic visit recently, Wells carefully goes through Evan's record, checking to ensure she received the follow-up care she needed from endocrinology, dermatology and ophthalmology, and that her blood and bone density tests are up to date. She talks with Evan and her mother about special education classes, her weight and diet, and tests Evan's balance and listens to her heart. A social worker drops by to talk about a free camp for children with cancer diagnoses.

Wells hands Shannon Whisenant a printed summary of Evan's treatment history and educational materials on each of the areas of concern. The thorough documentation and follow-up is a tremendous comfort.

"The (cancer center and Kay Wells) guide me **step-by-step** through everything she needs. They make sure we are OK."

~ Shannon Whisenant

"When you are going through it, the worst thing would be to feel abandoned — to not know everything," Shannon Whisenant says. "The (cancer center and Kathryn Wells) guide me step-by-step through everything she needs. They make sure we are OK."

Evan seems pleased with the attention, too. She presents Wells with three carefully sealed envelopes, each containing a hand-painted watercolor. Wells assures her young patient that she will proudly display each one of them on her office walls.

Hunting genes

Isolated villagers offer cancer clues

When Luís Carvajal-Carmona left his Colombian village to study in London and Oxford, he didn't suspect that clues to some of the world's most vexing health problems had surrounded him all along.

In remote regions of the Andes live people who have been relatively isolated for more than 500 years. This, combined with some intermarriage and large families, makes them genetically more similar than populations almost anywhere else in the world — and a gold mine for a "gene hunter" like Carvajal-Carmona.

"Homogeneity and long lines of ancestors make it easier to find genetic mutations — or differences between individuals," says Carvajal-Carmona, who joined the faculty last year as assistant professor in the UC Davis Department of Biochemistry and Molecular Medicine. "Few other places in the world offer the opportunity for such productive medical research studies."

Luís Carvajal-Carmona

Using **blood samples** collected from the **Andean villagers,** Carvajal-Carmona and his laboratory at the UC Davis Genome Center use a variety of high-throughput **genetic analysis techniques** to screen for **genetic differences** between individuals.

Carvajal-Carmona says knowing that a specific mutation can signal a higher risk for cancer or another disease provides valuable information that researchers anywhere in the world can use to develop genetic screening tests for cancer risk, for example, or to explore new avenues for development of targeted therapies.

Using blood samples collected from the Andean villagers, Carvajal-Carmona and his laboratory at the UC Davis Genome Center use a variety of high-throughput genetic analysis techniques to screen for genetic differences between individuals. Plans are in place to validate relevancy of the discoveries through partnerships with other investigators at UC Davis, Stanford, UCSF, USC and the Cancer Prevention Institute of California and to translate the findings into prevention and treatment strategies.

Carvajal-Carmona's genomic expertise is also being used to identify genes associated with cancer therapy-related toxicity. In collaboration with Helen Chew, a medical oncologist and leader of the cancer center's clinical breast cancer program, he will be analyzing the genome of an estimated 400 breast cancer patients from UC Davis and its affiliated cancer centers who are being treated with aromatase inhibitors. The hope is to identify genes that will enable physicians to

predict which patients are at higher risk of developing debilitating muscle pain, which can hamper treatment compliance and effectiveness.

"Aromatase inhibitors are very effective in postmenopausal women with hormone-sensitive breast cancers," explains Chew. "However, a significant number of women experience serious joint and muscle aches, which limits compliance. These are drugs that oncologists recommend women take daily for five years. If we can learn more about why some women experience these side effects and why some are spared, we can potentially tailor breast cancer therapy more effectively."

Carvajal-Carmona believes UC Davis has the capability and the technology to find cancer mutations quickly and translate that information into real health gains. "We are optimistic that this work can rapidly contribute to better personalized medicine and global cancer health," he says.

Genetic testing reveals surprising ancestry — and clues to disease

Carvajal-Carmona's study of the genetic makeup of Andean villagers has revealed interesting background on their history and ancestry. Studies of maternal lines through mitochondrial DNA as it is passed from mothers to children show that ancestral mothers were primarily Native American.

More surprising is the paternal lineage. Testing in men found that almost all the genetic makeup of the Y chromosome DNA is European in origin. According to Carvajal-Carmona, it is likely that male Spanish conquistadors settled in the area, taking Native American women as wives. The male Native American population was presumably decimated from disease and conflict. Few European women came to the area, so the European men married the remaining Native American women, each passing on their genetic lines.

The region already is the center of important research into several genetic diseases. A Huntington's disease gene mutation was found in nearby Venezuelan villages. And in the mountains surrounding Medellín, Colombia, where a 5,000-member clan has a very high incidence of early-onset Alzheimer's disease, a large clinical trial is underway for a drug designed to prevent the onset of dementia. The common mutation responsible for the disease can be traced to a single Spanish settler who came to the region in the 1700s.

Carvajal-Carmona is optimistic that cancer research in the region will be as fruitful. In European and North American populations, where people have many different genetic variations, finding a mutation that will likely lead to cancer is like searching for a needle in a haystack. Not so in the Andean villages where there are large families with the same cancers caused by mutations passed down by village ancestors. His group already has screened 191 women with breast cancer in Colombia and identified 19 patients and families with the same genetic

"We are **optimistic** that this work can **rapidly contribute** to better personalized medicine and **global cancer health.**"

~ Luís Carvajal-Carmona

mutation in the BRCA1 gene. Genealogical studies indicate the mutation was likely introduced by a Spanish ancestor who settled in the Huila Province and whose descendants still live in the region.

"These are spectacular numbers," he says. "If we studied 1,000 unselected European-American women, I can almost guarantee you that we would not find even two patients with the same mutation."

Carvajal-Carmona's study of the genetic makeup of Andean villagers has revealed **interesting background** on their history and ancestry.... The **region** already is the **center of important research** into several genetic diseases.

Reducing global health disparities

Carvajal-Carmona expects that his quest for cancer-causing genetic mutations also will help fulfill a personal ambition: to reduce cancer disparities worldwide. He notes that one of science's largest cancer genetics efforts — development of the Cancer Genome Atlas — has involved very few minorities.

"We hope that our studies will produce a body of work that will help fill this research void," he says, adding that his group and collaborative network are leading the world's largest breast and colon cancer genetic and genomic studies in Hispanics, both underway in Latin America.

Cancer is becoming a looming health crisis in Latin America, where rates are rising as the region develops and life expectancy increases. At the same time, few resources have been devoted to cancer screening, prevention and treatment, making death rates from the disease much higher than in Europe and the U.S. Carvajal-Carmona's colon and breast cancer research already has helped affected family members understand the need for regular screening.

The U.S. Hispanic population is also expected to benefit from his research in Latin America, given their shared ancestry. Identification of cancer mutations common in Latin America, for instance, could help in developing rapid screening methods in U.S. Hispanics or more personalized treatments.

Carvajal-Carmona visits Latin America often, maintaining close contact with study families, through their local doctors, hospitals and academic institutions. He also is currently training three doctoral students and four master's level students from Latin America in his UC Davis laboratory.

The scientist looks forward to collaborations with the UC Davis Comprehensive Cancer Center and the School of Medicine on cancer genomics studies in regional populations. He is planning pharmacogenetic studies for breast cancer and the role of DNA repair variation on patterns of cancer susceptibility.

"Now is the most exciting time to conduct cancer research," says Carvajal-Carmona. "We hope that our studies will benefit the people from these remote regions, and also contribute to improving cancer prevention and treatment for people all over the world."

A child's trial and his contributions

Shane Rogers' journey will aid future patients

Years from now, when Shane Rogers' cancer is in the rear-view mirror and he is cancer-free, his mother Kristen says she won't look back on his treatment period in despair, but with gratitude and hope.

"I had been losing my faith in society," Kristen Rogers says of the time before her son's illness. The caring response of her community to her family's ordeal changed that, she says. Now the Rogers family is paying that compassion forward by helping other families — in two very different ways.

First, the family launched a comfort-and-care program to help children diagnosed with cancer. The family also agreed to participate in a clinical trial that tracks Shane's treatment side effects so that oncologists everywhere can learn what works best for children of different ages, ethnicities, genders and with other individual characteristics.

"The reason the childhood cancer survival rate is so good now is because so many families agreed

"The **reason** the childhood cancer survival rate is so good now is because so many families agreed to **participate in clinical trials.** I know how important they are for **bettering society.** It was a no-brainer."

~ Kristen Rogers

to participate in clinical trials," says Kristen Rogers. "I know how important they are for bettering society. It was a no-brainer."

According to the National Cancer Institute, 5-year childhood cancer survival rates increased from 58 percent in the mid 1970s to almost 80 percent today. The improvement is due to significant advances in treatment, resulting in a cure or long-term remission for a substantial proportion of children with cancer. Better treatments are the result of pediatric cancer clinical trials, in which a majority of childhood patients participate.

Because of the Rogers family's participation in a national clinical trial tracking childhood leukemia treatment side effects, Shane's experience will help inform future treatment protocols for other children with the same illness.

Shane, who recently celebrated **his 9th birthday** with more than a dozen friends, will have at least **two more years** of cancer treatment.

"It's because of families like Shane's that we are able to move the knowledge forward," says Jay Balagtas, assistant clinical professor and Shane's oncologist at the UC Davis Comprehensive Cancer Center. As the cancer center's principal investigator of the Children's Oncology Group (COG), Balagtas oversees pediatric clinical trials offered to UC Davis patients. COG trials allow physicians from throughout the nation to track side effects of various treatment regimens, information that contributes to a massive and useful database.

To be sure, Shane has endured many side effects since his 2012 acute lymphatic leukemia diagnosis. In addition to the wrenching bone pain that first sent the 7-year-old to the emergency room, Shane has experienced extreme nausea, hair loss, steroid-induced diabetes, muscle weakness that temporarily confined him to a wheelchair, dehydration, weight loss, confusion and sodium loss.

Shane, who recently celebrated his 9th birthday with more than a dozen friends, will have at least two more years of cancer treatment. Shane lives with his family — mom, Kristen; dad, Sean; and

sister, Reese, 4. Shane is back in school but still beset by treatment side effects, including medication-related diabetes. Kristen Rogers chronicles Shane's journey on a Facebook page called Shanesvillage. In a recent post, she described how she stayed awake with Shane as he struggled with nausea from extremely low blood sugar.

"As I lay here next to Shane while he sleeps, I can't help but listen to his every breath," she wrote. "I want to scream out of frustration, but mostly out of fear... But I am just too tired."

Through the Facebook page and another website called CaringBridge, the Rogers family also shares expressions of hope and gratitude, messages that in some cases have spread far and wide. Their request for followers to post pictures of themselves holding "Shane, you got this" signs spread quickly. People — even strangers — from around the country and beyond posted photos, including a police chief in Mississippi, a SWAT team that made Shane an honorary member, and a boy in Big Bear who wrote "Shane, you got this" in snow.

Shane's father, a former Marine, was particularly moved by the picture of an entire Marine platoon in Afghanistan whose members shaved their heads in solidarity with Shane.

"My husband just broke down in tears," Kristen Rogers says.

The family received a similarly overwhelming response when asking for help moving to a one-story home. Kristen had been carrying Shane up and down stairs to the bathroom and throughout the house because Shane could not walk. She was afraid she would fall and injure him.

Kristen Rogers was stunned when an entire firefighting crew drove up in fire engines, wearing

At Shane's **birthday party** in August, a local **sheriff's squad car** and a **fire truck** — both with sirens blaring — rolled up, offering Shane and his friends some **hands-on thrills.**

"It's because of **families like Shane's** that we are able to **move the knowledge** forward."

~ Jay Balagtas

uniforms and bearing offers to help move furniture.

"Shane said, 'Mom, there are fire trucks here!'" she recalls.

Families from Shane's school, soccer teams, nearby homes and churches stopped by. A stream of visitors carried boxes from the home and helped pack the truck. At Shane's birthday party in August, a local sheriff's squad car and a fire truck — both with sirens blaring — rolled up, offering Shane and his friends some hands-on thrills.

The Rogers family will choose to remember these moments. But Kristen says they won't forget the difficult times, if only to use them to help other families through their journeys. Kristen Rogers says she barely thought about childhood cancer until a few months before Shane's diagnosis, when she began following the Facebook page of a young girl with cancer named Jessie Rees who launched a program distributing jars with little treats and toys for sick children. Jessie, who lost her battle with cancer, called them "joy jars."

"I remember I couldn't even imagine what it was like for her parents," says Kristen Rogers. "But in every picture they were smiling."

Only months later, the Rogers family was facing childhood cancer, too. But through the fear, agony and bewilderment, they endured with the help of the community's kindness. Now they are giving back.

Through their comfort-and-care program, they raise money to buy new comforters and teddy bears for children in cancer treatment at the UC Davis Comprehensive Cancer Center.

"UC Davis Medical Center has done so much for us, and I want to do something to give back," says Kristen Rogers. "It is my life's mission now to be able to tell a family who five minutes ago had been told that their child has cancer that they will smile again."

But through the fear, agony and bewilderment, **they endured** with the help of the **community's kindness.** Now they are **giving back.**

Tailored treatments

Sequencing key to quicker clinical care

Cancer is secretive.

Tumors grow without us knowing, migrate and hide in other organs and resist treatments for reasons we don't fully understand. For years, a major clinical and scientific goal has been to drag cancer into the light. We are almost there.

Clinicians and researchers at UC Davis now have a state-of-the-art genome sequencing tool to expose cancer, technology that can quickly read cancer genomes and tell us which mutations are making it grow and spread; providing, in essence, a shop manual for tumors that clinicians can use to guide treatment.

A genomic revolution

When talking about cancer, clinicians and researchers speak a different language. They use abbreviations like EGFR, KRAS, PI3-kinase and many others, references to the mutated genes and proteins that drive cancer birth, growth and metastasis. Entire generations of scientists have devoted their careers to understanding how these mutations generate disease, but that knowledge hasn't always translated into improved patient outcomes. However, recent advances in genomics — the ability to read the letters in a DNA sequence — will soon allow clinicians to translate this information into better patient care.

"We're creating gene panels that will identify the mutations in each patient's cancer," says Clifford Tepper, technical director of the UC Davis Comprehensive Cancer Center's Genomics Shared Resource. "For any patient that comes in the door, we want to be able to precisely molecularly characterize their tumor."

Though clinicians have been able to profile some cancer mutations,

"**Genetic sequencing** can analyze all the genes **simultaneously** and **do it much faster.**"

~ Jeff Gregg

"For any patient that comes in the door, we want to be able to **precisely molecularly characterize** their tumor."

~ Clifford Tepper

their range has been limited to one or two genes per test, an expensive and time-consuming process. In addition, biopsies haven't always produced enough material to test for all relevant mutations.

"Genetic sequencing can analyze all the genes simultaneously and do it much faster," says Jeff Gregg, professor and senior director of clinical pathology in the Department of Pathology and Laboratory Medicine. "We can then get the results to clinicians, who can start molecularly guided treatment significantly earlier."

The new panels will analyze selected regions of a tumor's genome rapidly, picking out mutations from as many as 400 choices. This approach, called massively parallel

sequencing, will provide the big picture on a tumor and influence a variety of clinical decisions.

"This is a revolution in the way we approach and treat patients," says gastrointestinal oncologist Thomas Semrad. "Patients will receive profiles to tailor the right treatments to their specific needs."

Personalizing treatment

The new gene panels will read mutations that are "clinically actionable." In other words, they will pinpoint genetic variations that directly affect patient care. This could mean finding a mutation that can be targeted by a specific drug, determining whether the cancer is resistant to treatment or precisely classifying a particular tumor.

"Once we get the results, we will create a detailed report," says Tepper. "We'll list and prioritize all the aberrations we find, the impact they have on protein function, which drugs target those specific mutations and whether there are any clinical trials available."

With this genetic report, oncologists will have a powerful new tool to build a treatment plan. For example, a comprehensive list of mutations will tell them whether a given therapy will have any effect against a patient's cancer.

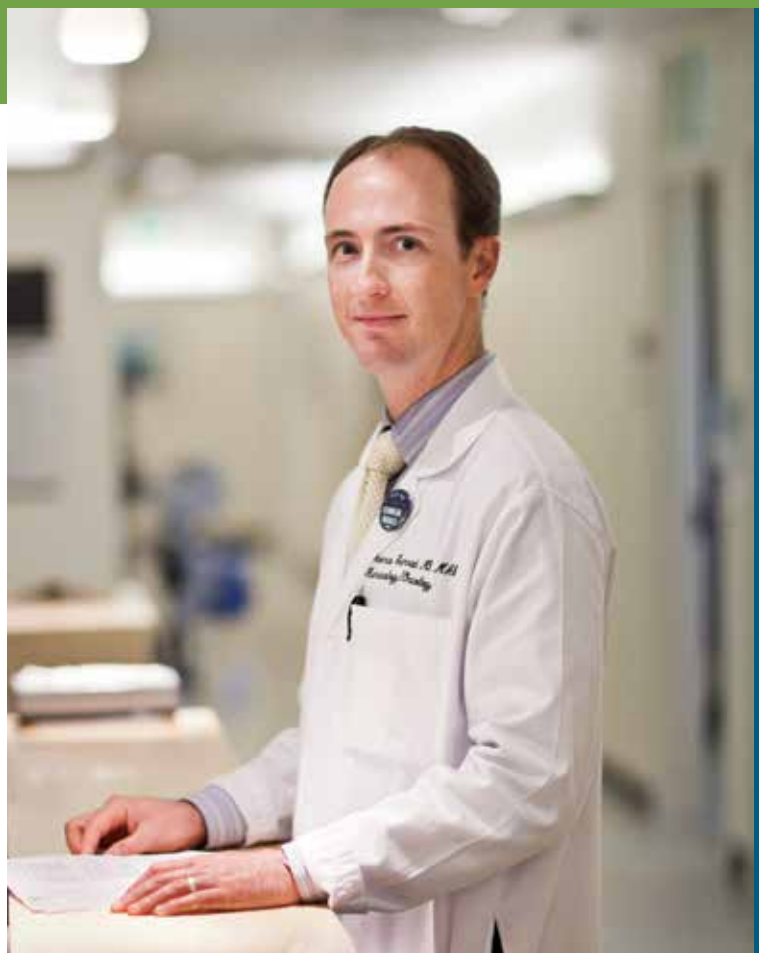
"Certain mutations in the KRAS gene indicate that colon cancer will not respond to a particular antibody drug," says Semrad. "If a patient's cancer has that mutation, we know to administer a different treatment."

Other variations might allow physicians to recommend less toxic treatments. Semrad notes that certain mutations in the EGFR gene in lung tumors allow patients to take an oral medication that is much gentler than traditional chemotherapy.

Equally important, the panels will provide more information than previous methods — like going from a magnifying glass to a microscope. This will expose mutations that are either uncommon or may exist in only a few cells.

"The beauty of the targeted approach is that we're able to sequence at high depth — sequencing each gene a thousand times," says Gregg. "If you have a rare mutation

In addition to investigating cancer, the **new genomic capability** will also help clinicians **better target** cardiovascular disease, seizure disorders, developmental delay and **other conditions with genetic underpinnings.**



"This is **a revolution** in the way we approach and treat patients. Patients will receive profiles to **tailor** the right **treatments** to **their specific needs.**"

~ Thomas Semrad

in a population of cells, the panel will pick that out."

Finding new therapies

Genomic sequencing will also have an enormous impact on clinical trials and drug discovery. Limited genetic information has hampered oncologists' ability to refer patients to trials. It simply does not make sense to test a potentially toxic drug on a patient who may not have the mutation being targeted.

"This gives us a great ability to survey all these genes and then put patients in clinical trials," says Gregg. "We wouldn't have been able to do this in the past because you have to demonstrate the patient has that mutation."

In addition to helping patients, this new approach could boost clinical trial enrollment. Low participation can limit a trial's ability to determine a therapy's effectiveness, short-circuiting the ability to advance new therapies.

"This is going to be really great for patients participating in clinical trials because there are many trials for targeted therapies but, without sequencing, we might not test for that mutation," says Gregg. "Having the additional information will get more patients into trials, and the larger cohorts will tell us more about a drug's effectiveness."

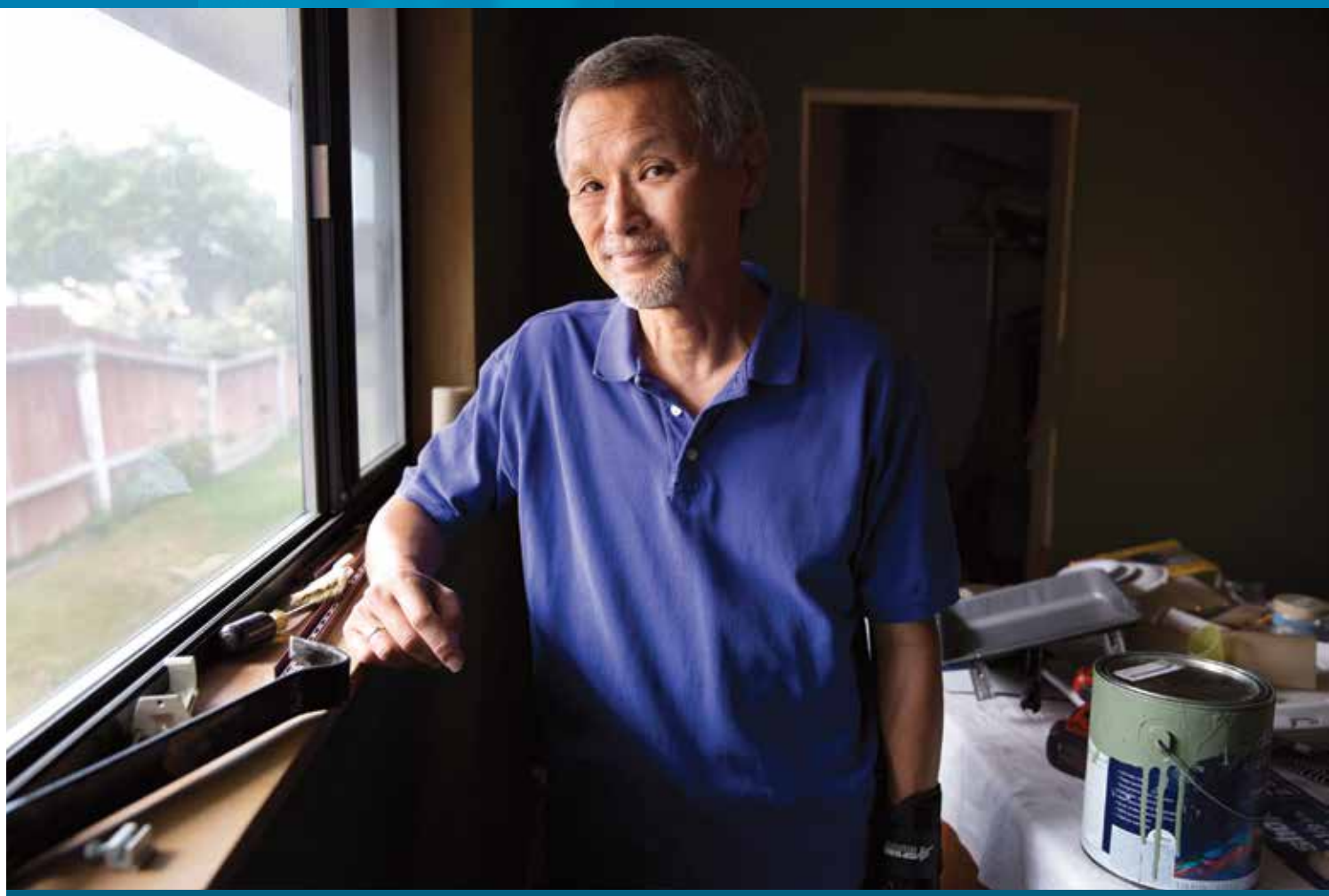
The future is now

The cancer center will start with two panels, a large 400-gene approach that encompasses mutations from multiple cancers and a more targeted, 55-gene panel for melanoma, lung cancer and other conditions. Eventually, new panels will be designed to catalogue mutations from other cancers.

The researchers expect to implement the sequencing program in early 2014. The genomics facility will be housed in the Molecular Diagnostic Laboratory in the Department of Pathology and Laboratory Medicine and will be certified under CLIA, the standards all clinical laboratories must meet before testing patient samples.

In addition to investigating cancer, the new genomic capability will also help clinicians better target cardiovascular disease, seizure disorders, developmental delay and other conditions with genetic underpinnings.

"This is an amazing advance," says Semrad. "We've come from sequencing the first genome for several billion dollars, and taking years to do it, to sequencing individual patients for only a few thousand dollars in less than a day. It's going to change cancer care forever."



Participation through education

Asian-Americans offered clinical trials navigation

When Gary Funamura was diagnosed with prostate cancer in the fall of 2012, his UC Davis oncology team presented him with two choices.

Over the past year, **AANCART's outreach team** at UC Davis has determined that **many Asian-Americans** had no idea **what clinical trials are,** who pays for them, and what sorts of **risks and benefits** are involved.

He could follow a conventional treatment course that included surgery with possible radiation or hormonal therapy down the road. Or he could join a clinical trial testing the use of chemotherapy plus hormone depletion therapy to attack cancer cells before the prostate was removed.

For Funamura, 59, the decision to go with Plan B was a "no-brainer."

"I had done some research, and I knew I would get excellent follow-up care through the trial," he says. "Frankly, I couldn't see a downside."

Regrettably, researchers say that Funamura's enthusiasm about clinical trials is relatively rare — especially among Asian-Americans. Language barriers, mistrust of the medical system, and other cultural dynamics often create misunderstandings about the nature and purpose of cancer trials, discouraging participation and leading to underrepresentation of Asian-Americans.

Troubled by this historic pattern, UC Davis is turning its ongoing campaign to increase awareness of clinical trials into a full-blown patient recruitment program called AACES, or Asian-American Cancer Education Study.

"Asian-Americans are the only racial group for whom cancer is the leading cause of death, so we are highly motivated to increase their involvement in these critical trials," says UC Davis professor Moon Chen, who leads AACES. The program's goal is to demystify clinical trials for eligible Asian-American patients and encourage them to participate, both for their own benefit and to help scientists develop better cancer drugs and protocols for future generations.

Clinical trials evaluate the effectiveness and safety of cancer medications and medical devices by monitoring their effects on large groups of people. Such trials are considered vital to the development of cancer therapies, and inclusion of meaningful numbers from all racial/ethnic populations and both genders is "crucial to ensure the therapies we develop are based on specific characteristics of these populations," Chen says.

"Only 3 percent of adults are enrolled in clinical trials, and only 10 percent of those are minorities," he adds. "So it's essential that we do what we can to overcome the barriers keeping minorities from participating in and benefitting from these trials."

AACES was hatched under the banner of the Asian-American Network for Cancer Awareness, Research and Training (AANCART). Established in 2000 and headquartered at the UC Davis Comprehensive Cancer Center, AANCART is dedicated to reducing cancer health disparities through community education, training and research.

Language — specifically the **imprecise translation** of certain terms and phrases — also **creates confusion** about clinical trials.

Outreach>>

Over the past year, AANCART's outreach team at UC Davis has determined that many Asian-Americans had no idea what clinical trials are, who pays for them, and what sorts of risks and benefits are involved.

Language — specifically the imprecise translation of certain terms and phrases — also creates confusion about clinical trials, according to Julie Dang, AANCART's UC Davis community health educator. When translated literally into some languages, for example, the word "trial" created the misimpression that a legal proceeding was involved, a prospect that stirred anxiety among some Asian-Americans.

"People also suspected that clinical trials were about experimentation, and that they would become guinea pigs," Chen recalls. "So we had to find the right scientific term (in Asian languages) to ensure the meaning was translated accurately for those who don't speak English."

To overcome patient misgivings and provide a base of understanding about clinical trials and biospecimen contribution, the AANCART outreach team created brochures and a five-minute DVD in seven Asian languages, from Cantonese to Tagalog. Starting this fall, every Asian-American cancer patient will have an opportunity to have a one-on-one educational session with bilingual and bicultural staff about cancer research opportunities available to them.

Cancer center urologic oncologist, Marc Dall'Era, told Funamura that his cancer was **particularly aggressive** and **suggested a clinical trial.**

Patients eligible to participate in a trial after discussing it with their doctor are then assigned a bilingual "patient navigator" who helps them through every step of the clinical trial.

"We think the understanding created through the brochures and DVD, combined with the personal help of a navigator who speaks their language, will make the experience more comfortable for patients," Dang says.

While Funamura did not share the reservations many Asian-Americans hold about participating in clinical trials, he understands well the culturally based hesitation. The Lodi lawyer says his parents and other older Japanese-Americans view health-related concerns as "something not discussed outside your close family circle."

"I think with my parents' generation, especially, there is a cultural sense among Japanese-Americans that these are considered private matters," Funamura says. "For me the clinical trial sold itself. But obviously that's not true for everybody. "

For Funamura, participation in the trial has met his expectations, and then some. His cancer center urologic oncologist, Marc Dall'Era,

"We think the **understanding created** through the brochures and DVD, **combined with the personal help** of a **navigator** who speaks their language, will make the **experience more comfortable** for patients."

~ Julie Dang

"I think with my **parents' generation,** especially, there is a **cultural sense** among Japanese-Americans that these are **considered private matters.** For me the **clinical trial sold itself.**"

~ Gary Funamura

told Funamura that his cancer was particularly aggressive and suggested a clinical trial investigating a new treatment protocol.

After discussing the possibility with his fiancée and a cancer center clinical research coordinator, Funamura signed on. A random selection placed him in the active arm of the trial, and treatment began.

First came six rounds of chemotherapy, along with monthly injections of Lupron, a drug that reduces a patient's testosterone levels, thereby inhibiting the growth of prostate cancer cells. Patients in the trial's control group, meanwhile, had the surgery to remove their prostates but no pre-treatment with chemotherapy and Lupron.

In early April, Dall'Era performed a prostatectomy. "A week after the surgery, Dr. Dall'Era called me with the pathology work and said they couldn't find any cancer. It was gone," Funamura says. "It was a miracle. And we are all doing the happy dance."

A biopsy several months later confirmed the results, and aside from "a bit of a hangover from the chemotherapy," Funamura says he couldn't be happier now that he can focus his energies on renovating the home in Lodi where he and his fiancée are settling.

His doctor is also pleased, noting that Funamura's cancer was high-risk, and that 30 to 40 percent of men with that type of cancer will experience a recurrence if their treatment is limited to only surgery or radiation.

"That's too high (a percentage)," Dall'Era says, so the trial aimed to find out if these patients do better if they are treated first with hormone therapy and chemotherapy.

"Mr. Funamura had a phenomenal response," says Dall'Era. "We found no residual cancer in his prostate."

Asked if he hoped his participation in the trial would benefit future patients, Funamura gave an answer likely to please Chen and others seeking to engage more Asian-Americans in such research.

"Someone said they thought it was 'generous' of me to participate, and possibly help other people through the development of new drugs or protocols," he says. "I suppose that's true, and I'm happy to contribute. But honestly, I always saw the clinical trial as a benefit to my treatment.

"And I would not hesitate to do it again."

While Funamura did **not share the reservations** many Asian-Americans hold about participating in **clinical trials**, he **understands** well the **culturally based hesitation.**

Grabbing cancer by the helm

Survivor invests in brain tumor research

Against the San Francisco skyline, Scott Winneker vigorously tacks the jib aboard the *Gemini* just as the warm Bay breeze catches its sails.

"I feel it, I love it," he says, settling back at the helm of his 1970 Ericson 35 sailboat.

Nine years ago, when Winneker was diagnosed with brain cancer, neither he nor his physicians imagined he would still be thrill-seeking on the San Francisco Bay. Now 58, Winneker has not only beaten very grim odds but has become a passionate supporter of causes he cares about, including the work to better understand glioblastoma cell formation at UC Davis Health System and Comprehensive Cancer Center.

"For whatever reason, I'm still here," says Winneker, in happy disbelief.

Winneker's brain cancer journey began when he was working as an air traffic controller and had a routine annual physical as required.

"I had to **tell myself** that **things would be OK.** I had a **lot of people helping me** and giving me good vibes. I've been **very fortunate** with people, with God — it's a **good thing.**"

~ Scott Winneker

At the time, he sensed that something was wrong with his visual perception. Further tests revealed a stage 4 glioblastoma multiforme brain tumor, the most common and most serious malignant brain tumor in adults.

Based on prior medical studies, "doctors gave him a 20 percent chance of surviving two years," says Julie Rader, Winneker's significant other and the UC Davis Health Sciences Development business manager.

The prognosis was devastating, and Winneker feared he would not live to see his two sons graduate from college, get married or buy their first homes.

"I had to tell myself that things would be OK," Winneker recalls. "I had a lot of people helping me and giving me good vibes. I've been very fortunate with people, with God — it's a good thing."

Voyage to survivorship

Winneker underwent a craniotomy, and surgeons removed the tumor. He then had six months of simultaneous chemotherapy and radiation therapy, then more chemotherapy. Winneker's physicians monitored him and, when a small growth appeared at the tumor site, they performed a gamma knife procedure. He recalls his head being placed in a metal harness, then receiving high-energy gamma rays shot directly at the tumor. Winneker light-heartedly relates the procedure to a scene in the science fiction movie *Back to the Future*.

Winneker's humor and positive attitude have been a driving force along his voyage.

"I don't remember getting mad at the situation because, to me, cancer is a part of life and you've got to deal with it the best you can," Winneker says.

Winneker survived some major setbacks. Following an additional surgery at a Bay Area cancer center, he contracted a staph infection, requiring intravenous antibiotics 24 hours a day for six months.

"That was an extremely difficult time for us, but we got through it," Rader says.

The infection ultimately led to removal of his bone flap, which left him with a permanent soft spot on the back of his head. Winneker also developed Parkinson's disease, aphasia (difficulty speaking), short-term memory problems and a loss of peripheral vision — the result of years of cancer treatments.

But he has slowly been weaned off of his monthly chemotherapy, and his medical condition is considered "stable."

And he is happy to report that both his sons graduated from college, got married and have their own homes.

"Scott is an inspiration to everyone who has helped him through this journey," says Rader.

An anchor for giving

Winneker's journey to survivorship sparked his philanthropic activities. He began giving to the UC Davis Health System when he purchased 12 paintings during the Children's Miracle Network's fundraising gala "Painting for Miracles." The works decorate the walls of his home.

When informed of important research into the causes of his own disease, Winneker made a $25,000 gift to Paul Knoepfler, UC Davis associate professor of cell biology and human anatomy. Knoepfler's research aims to understand why glioblastoma forms and to find new ways to treat the disease by killing the cancer cells.

"Any gift to UC Davis is a **meaningful investment** in our **programs** and our **leading-edge research** initiatives."

~ Jeffrey Fischer-Smith

"I was **very blessed** with my career as an air traffic controller, and I **wanted to give back.** I felt **UC Davis** was a **good place** to do that."

~ Scott Winneker

Winneker doesn't plan to stop there.

"I was very blessed with my career as an air traffic controller, and I wanted to give back," he says. "I felt UC Davis was a good place to do that."

Winneker plans to earmark a portion of his estate to support scientific research at UC Davis in perpetuity.

"Any gift to UC Davis is a meaningful investment in our programs and our leading-edge research initiatives," says Jeffrey Fischer-Smith, the cancer center's senior director of development. "A planned gift is the perfect way for a donor to contribute to a specific program or area of research and to receive assistance in the estate planning process to ensure their wishes are carried out."

Riding high on the waves of retirement

Now six years into retirement, Winneker continues his active lifestyle playing Ping-Pong, riding his stationary bicycle and keeping his 1973 Dodge truck in perfect running condition. Winneker and Rader also enjoy spending time at home together, cooking, dining and watching Winneker's beloved Seattle Seahawks.

"I do my own thing for the most part, but I find a way to make things work with the help of my friends," says Winneker.

But his greatest thrill is still behind the helm of the *Gemini* with the San Francisco Bay breeze in his hair and the cool spray of white-capped waves upon his face.

News briefs>>

Pediatric infusion center's new murals are just what the doctor ordered

Local muralist Kent Peterson has transformed the walls of the cancer center's Pediatric Infusion Center into whimsical mysteries of the jungle and vibrant depths of the sea.

"How the kids react when they see it is testimony to what a difference this kind of artwork makes," Peterson said.

The transformation began when Peterson painted the imaginative underwater illustration, which faces the infusion isolation rooms.

Kent Peterson

"Being isolated from the rest of the room can be very difficult, and the mural really helps draw the patients out," said Melinda Beckham, the center's pediatric charge nurse.

Peterson has since carried his talents to the 120-foot-long hallway leading into the Surgery Center of the UC Davis Children's Hospital.

Reducing unnecessary and high-dose pediatric CT scans could cut associated cancers by 62 percent

A study examining trends in X-ray computed tomography (CT) use in children in the United States has found that reducing unnecessary scans and lowering doses for the highest-dose scans could lower the overall lifetime risk of future imaging-related cancers by 62 percent. The research by UC Davis scientist and cancer center member Diana Miglioretti was published in *JAMA Pediatrics*.

Diana Miglioretti

The 4 million CT scans of the most commonly imaged organs conducted in children each year could result in approximately 4,870 future cancers, the study found. Reducing the highest 25 percent of radiation doses could prevent 2,090 — or 43 percent — of these future cancers. **By also eliminating unnecessary imaging, 3,020 — or 62 percent — of cancers could be prevented, said Miglioretti, dean's professor in biostatistics in the Department of Public Health Sciences at UC Davis Health System.**

"There are potential harms from CT, meaning that there is a cancer risk, albeit very small in individual children, so it's important to reduce this risk in two ways," Miglioretti said. "The first is to only do a CT when it's medically necessary, and use alternative imaging when possible. The second is to dose CT appropriately for children."

Miglioretti said that children's organs are at an increased risk of cancer from CT scans because children still are growing and their cells are dividing rapidly.

Radiation oncology chief leads development of new prostate cancer guideline

Based on a major effort co-led by UC Davis prostate cancer expert Richard Valicenti, the nation's leading urological and radiation oncology organizations announced a new guideline for radiation therapy after prostatectomy.

The guideline, released jointly by the American Society for Radiation Oncology (ASTRO) and the American Urological Association, for the first time provides evidence- and consensus-based recommendations about the benefits and risks of additional cancer treatment after prostate-removal surgery.

Valicenti, chair of the UC Davis Department of Radiation Oncology, championed the comprehensive review on behalf of ASTRO. The guideline was based on an analysis of 324 research articles published between 1990 and 2012.

"My hope is that this guideline will lead to higher overall survival rates and better quality of life for men undergoing radical prostatectomy," Valicenti said.

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

Father and son present their respective cancer research at ASCO

Matthew Lara, a Davis High School student and son of UC Davis medical oncologist and researcher Primo (Lucky) Lara, Jr., presented his findings on non-small-cell lung cancer during a poster session in Chicago in June at the annual meeting of the American Society of Clinical Oncology (ASCO).

Matthew's project was born at the dinner table. "We were talking about lung cancer, and I asked my dad if young people get lung cancer and if they do better than older people," Matthew said. "My dad said, 'Well, you can certainly try to find the answer to that yourself!' So we did."

Matthew's poster described his findings that younger people with lung cancer tend to have better survival rates than older patients with lung cancer. His poster represented the largest analysis of age-related survival in lung cancer ever conducted. The work was based on data from the California Cancer Registry.

After Matthew's research poster was accepted at ASCO, he received a $500 grant from the Davis High School Blue and White Foundation to support his trip to Chicago. After high school and college, Matthew hopes to follow in his father's footsteps as an oncologist and cancer researcher.

"There are so many people who still die from cancer," Matthew said. "I want to understand it better — how it works and how we can make it better for people."

UC Davis Comprehensive Cancer Center medical oncologist and researcher Primo (Lucky) Lara, Jr., and son Matthew

UC Davis Cancer Care Network News

Gene Upshaw Memorial Tahoe Forest Cancer Center welcomes new physician

Gene Upshaw Memorial Tahoe Forest Cancer Center, a service of Tahoe Forest Health System, is pleased to announce the addition of hematologist and medical oncologist Melissa Kaime. She comes to the Gene Upshaw Memorial Tahoe Forest Cancer Center from Walter Reed National Military Medical Center, where she was a staff physician in the Department of Hematology/Oncology. Prior to that she was the US Navy Medical Corps Hematology/Oncology Specialty Leader for the chief of the Bureau of Medicine and Surgery. Kaime completed her medical education at the St. Louis University School of Medicine.

Melissa Kaime

AIS Cancer Center director leads book discussion

Oscar E. Streeter, Jr., medical director of the AIS Cancer Center at San Joaquin Community Hospital, moderated a discussion about "The Immortal Life of Henrietta Lacks" at the Kern County Library's "One Book, One Bakersfield, One Kern" reading program at the Bakersfield Museum of Art in October. The book details the story of a young black woman, whose cervical cancer cells were taken from her in 1951 and live on to this day. The real-life story takes on real-life ethical dilemmas, although Lacks' cells directly led to the vaccine for polio and launched a medical revolution into the genome industry.

AIS Cancer Center physicians publish research

Two AIS Cancer Center physicians have published cancer research. Oscar E. Streeter, Jr., medical director, was a co-author of the article, "Curative Treatment of Esophageal Cancer; An Evidence Based Review," published in July in the *Journal of Gastrointestinal Cancer*. The authors examined the role of radiation therapy, chemotherapy and surgery in the curative management of esophageal cancer.

Oscar E. Streeter, Jr. (left), and Vikas Ghai

Vikas Ghai, an AIS Cancer Center oncologist, co-authored an article describing findings that a combination treatment including oral chemotherapy was better tolerated than standard, aggressive and intravenous chemotherapy treatments for elderly patients with acute myeloid leukemia. The paper was published in the May issue of the *Journal of Clinical Oncology*.

News briefs>>

UC Davis endowed chair for clinical cancer research established

Karen Kelly, associate director for clinical research at the cancer center, is the recipient of the university's first endowed chair in cancer clinical research. The appointment was celebrated at a private reception at the cancer center in September.

The Tegley & Harmon Endowed Chair is named in honor of Elizabeth Erica Harmon, who passed away at age 30, and her cousin Jennifer Rene Harmon Tegley, who died at age 18, one year after being diagnosed with a very aggressive throat cancer.

The Harmon family made a $765,000 gift to create the endowed chair to support the work of Kelly, who managed Jennifer's end-of-life care and is building the cancer center's phase I clinical trials program. The Harmon family gift was matched with funds from the UC Davis Health System's Dean's Catalyst Fund.

"As the university's first cancer clinical research chair, I am honored to lead our comprehensive cancer center team in bringing these innovative new treatments to patients," Kelly says.

Cancer essays yield college scholarships

Kimberly Schmidt and her father, Bobby Schmidt

Kimberly Schmidt, a California State University, Sacramento, senior, was awarded a $2,500 college scholarship for an essay detailing her family's experience following her father's brain tumor diagnosis and treatment at the cancer center.

The award was presented by athletes who ran across the country to raise funds for cancer programs — including the scholarship program — that benefit adolescents and young adults. The runners are part of 4K for Cancer, one of several fundraising events of the Ulman Cancer Fund for Young Adults.

"Even though living with a cancer patient presents challenges, I have been successful because I know that every day is a gift to be embraced and lived to the fullest," Kimberly wrote in her scholarship application.

Kimberly will graduate with a double major in English and marketing, and plans to attend law school.

In September, 20-year-old Arianna Lawson-Price of Colfax was presented the John McClean Hero Award scholarship from the Keaton Raphael Memorial (KRM). Lawson-Price, who was treated at the cancer center for stage IV, large B-cell non-Hodgkin's lymphoma in 2008, won the award for her essay about life with the disease.

Arianna Lawson-Price (left) and Teresa Hofhenke, KRM Executive Director

"My experience with childhood cancer has given me wisdom that was achieved at a very early age and, as a result, has made me a better person," Arianna wrote in her award-winning essay.

Lawson-Price is attending California State University, Sacramento. She hopes to become a child-care specialist working with patients with cancer and other life-threatening illnesses.

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

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ADDRESS SERVICE REQUESTED

Radiation oncology resident Lauren Tait is rewarded with a hug and a bouquet from El Dorado Hills resident Gary Cooper days after she assisted him during a medical emergency he suffered onboard a flight to Sacramento.

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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.