

# CITY NEWS

VOL. 31 NO. 2 FALL 2020

## Cancer Can't Wait

Providing care during  
a pandemic



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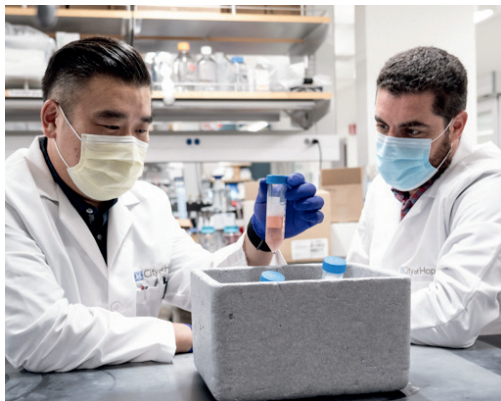


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*Your Thoughts, Your Wishes, Your Community*

Where those touched by cancer can be connected, survive and thrive together.



### LEADERSHIP MESSAGE

## CANCER DOESN'T STOP

Dear Friends,

Cancer does not stop during COVID-19, and neither do we. We continue to be a sanctuary of healing and hope for patients who need us. Through our decades of treating immunocompromised patients, we have developed deep knowledge and expertise in infection prevention and control. While COVID-19 overwhelmed much of the nation's health care system, we have persevered. I am convinced that City of Hope is the safest place in the country for cancer patients to receive lifesaving care and access vital research.

In this issue of City News, you will see how we are uniquely equipped as a National Cancer Institute-designated comprehensive cancer center to provide specialized treatment during the pandemic, why preventive cancer screening is essential and what kinds of treatment should not wait. You also will learn about a breakthrough in pancreatic cancer and read a patient's moving story of participating in a potentially life-changing clinical trial.

We invite you to join us in celebrating the life and work of Arthur Riggs, Ph.D., who is retiring as director of our Diabetes & Metabolism Research Institute. Those of us privileged to call Art a colleague and friend over the 41 years he has been at City of Hope are as impressed with his character as we are with his scientific contributions. In 1979, the National Academy of Sciences published a paper about an innovative discovery at City of Hope that forever changed the treatment of diabetes. Dr. Riggs and Keiichi Itakura, Ph.D., revolutionized diabetes treatment when they used a synthetic DNA chemistry and recombinant DNA technology to make a novel gene, one that coded for human insulin.

The priorities that define us – speed, science and an unwavering commitment to patient care – enable us to meet the ongoing challenges of COVID-19. Adversity reveals character. Our extraordinary team of researchers, doctors, nurses and staff are working together to move breakthrough therapies from laboratories to patients, and we are grateful for your philanthropic partnership.

**ROBERT STONE**  
*President and Chief Executive Officer*  
City of Hope

# newHOPE

NEW FACES · ADVANCING SCIENCE · BEGINNINGS

## Charles Brenner, Ph.D.

Professor and Founding Chair, Department of Diabetes & Cancer Metabolism



Charles Brenner, Ph.D., joined City of Hope on Aug. 17, 2020, as professor and founding chair of the Department of Diabetes & Cancer Metabolism and the Alfred E Mann Family Foundation Chair in Diabetes and Cancer Metabolism. He comes to City of Hope from Carver College of Medicine at University of Iowa, where he was Roy J. Carver Chair & Head of Biochemistry and founding director of the Obesity Research & Education Initiative.

He received his Ph.D. in cancer biology from Stanford University and was a postdoctoral fellow of the Leukemia Society. Prior to joining University of Iowa in 2009, he was a researcher and professor at the Norris Cotton Cancer Center and Dartmouth Medical School.

It was at Dartmouth that he discovered nicotinamide riboside as a vitamin precursor of NAD (nicotinamide adenine dinucleotide) and developed a National Science Foundation-funded program on NAD metabolism, the main focus of his research efforts. He runs internationally recognized research programs in NAD metabolism and the epigenetic silencing of tumor suppressor genes in malignant transformation.

## Alexey Danilov, M.D., Ph.D.

Professor and Associate Director, Toni Stephenson Lymphoma Center



Alexey Danilov, M.D., Ph.D., joined City of Hope in early 2020 as associate director of the Toni Stephenson Lymphoma Center and professor in the Department of Hematology & Hematopoietic Cell Transplantation.

A board-certified clinician and talented researcher, Danilov focuses on blood cancers, including chronic lymphocytic leukemia and many forms of lymphoma. He's published dozens of papers and initiated multiple drug trials and is a Leukemia & Lymphoma Society Scholar in Clinical Research. He is focused on a particular niche of targeted therapy: identifying cell proteins — some that promote cancer growth, some that inhibit it — learning how they deteriorate and finding drugs that can affect the process.

Danilov chose oncology as a career because of its breadth and potential. Oncology, he says, “touches all areas of general medicine” and is a most exciting field because of the many new treatments now emerging.

A native of Russia, Danilov earned his medical degree and Ph.D. at Yaroslavl State Medical Academy. He continued his training with a residency at Brown University in Providence, Rhode Island, and a fellowship at Tufts Medical Center in Boston.

## Ping Wang, M.D.

Professor and Chair, Department of Clinical Diabetes, Endocrinology & Metabolism



Ping H. Wang, M.D., has joined City of Hope as a professor and chair of the Department of Clinical Diabetes, Endocrinology & Metabolism, effective Sept. 16, 2020. As department chair, Wang focuses on delivering state-of-the-art clinical care to our patients with diabetes and endocrine neoplasms, advancing the science to clinical trials in diabetes. Wang is responsible for quality, clinical research and the strategic direction of the department.

In the laboratory, Wang focuses on the mechanisms that lead to diabetes and its complications, with potential for new discoveries in both type 1 and type 2 diabetes.

Prior to joining City of Hope, Wang served as chief of endocrinology at University of California Irvine Medical Center, director of the UC Irvine Diabetes Center and professor of medicine at UC Irvine. He received his M.D. from Kaohsiung Medical College in Kaohsiung, Taiwan, and a master's degree in epidemiology from the Harvard School of Public Health. Wang received endocrinology fellowship training at Harvard Medical School and the Joslin Diabetes Center.

An award-winning clinician, Wang has served as a member of study sections for the National Institutes of Health and UK Medical Research Council.

# cityBUZZ



*On the Duarte campus, City of Hope staff members gather to collectively reaffirm their opposition to discrimination and racial injustice.*

## Standing United

From our main campus in Duarte, California, to City of Hope Orange County and all of our community practice sites, City of Hope physicians and staff gathered in silence for eight minutes, 46 seconds in remembrance and solidarity for George Floyd, Ahmaud Arbery, Breonna Taylor and so many others on June 5. “We stand united with the African American community and steadfastly against racism, discrimination and racial injustice in any form or place,” said Robert Stone, City of Hope president and CEO. City of Hope leadership is strengthening its actions to achieve, sustain and nurture an increasingly diverse, equitable, inclusive and just workplace for all of its people and for the communities it serves. Its strong network of employee resource groups, such as CPAD (Connecting People of African Descent), are important partners in these efforts.

## Feeling Cared For

Dozens of individuals and organizations have risen to the challenge of protecting City of Hope staff and patients with masks, face shields, gloves, gowns and other items. Philanthropic partners and new friends have donated more than 400,000 units of personal protective equipment. These include chambers of commerce; retail, packaging and manufacturing companies; and community and multicultural groups. Apple, The Home Depot and Panda Restaurant

Group witnessed the work of our Heroes of Hope and donated gear to keep our vital mission intact.

In addition, thousands of orchids were donated by Westerlay Orchids to brighten the spirits of those on the frontlines, while



Erminia Massarelli, M.D., Ph.D., M.S., with her donated orchid



Staff enjoyed a free lunch courtesy of Panda Express.

restaurants and individuals have contributed food (Panda Express, King Taco) for staff working onsite.

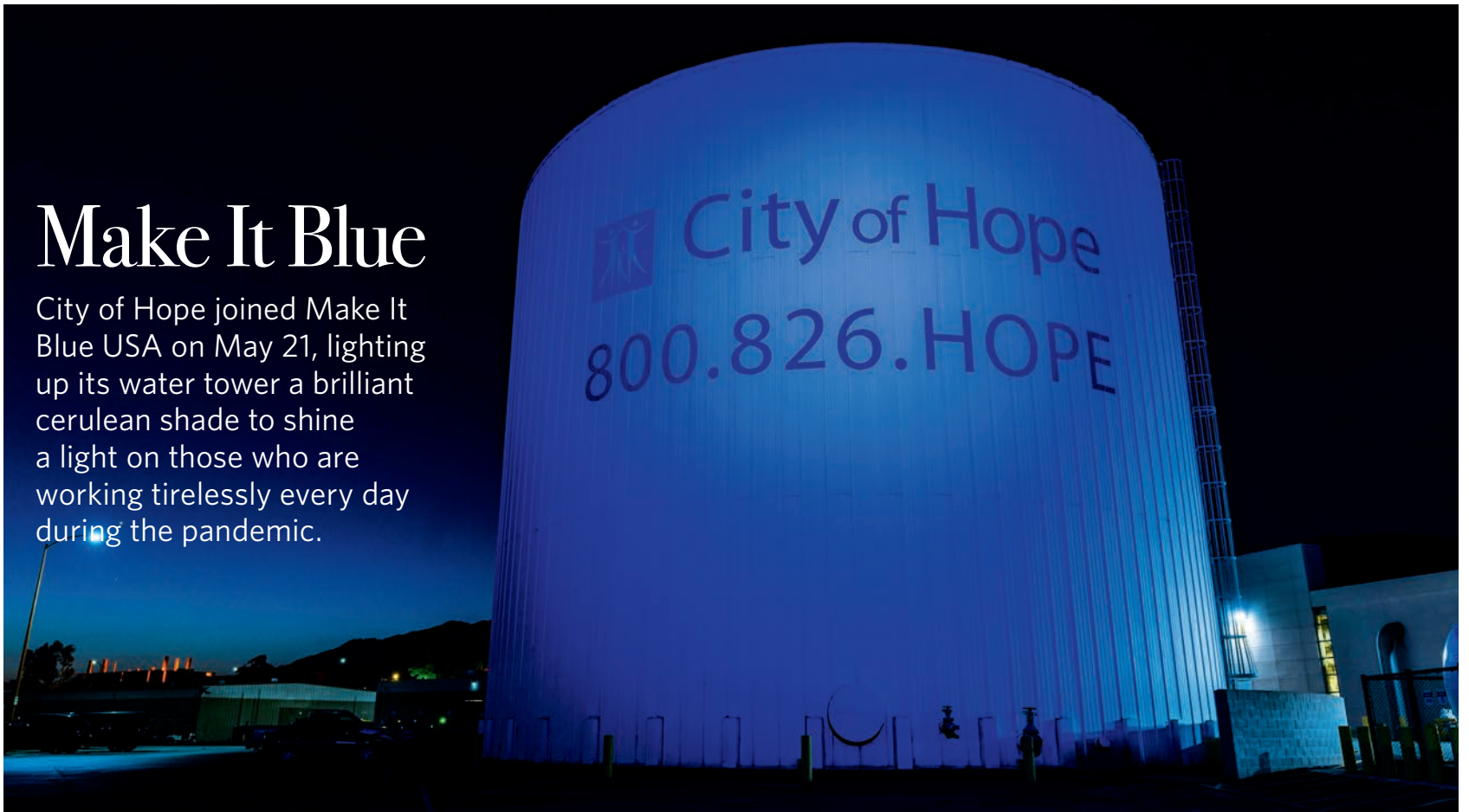
## Memorial Day Honor

On Memorial Day, May 25, the D-Day Squadron — consisting of 18 WWII-era aircraft in formation — flew over the Duarte, California, campus at approximately 12:53 p.m. to salute our nation's military personnel and to honor City of Hope heroes.



## Make It Blue

City of Hope joined Make It Blue USA on May 21, lighting up its water tower a brilliant cerulean shade to shine a light on those who are working tirelessly every day during the pandemic.



## Bleeding for a Cause



Robert Stone, president and CEO; Michael Caligiuri, M.D., president of City of Hope National Medical Center and the Deana and Steve Campbell Physician-in-Chief Distinguished Chair; and other City of Hope leaders rolled up their sleeves to donate blood for our patients during this critical time.

# Remaining Vigilant

Two City of Hope physicians give guidance on what cancer screenings you can and can't put off, plus some you can do at home, at least temporarily.

BY WAYNE LEWIS

**W**ith many Americans staying at home to help flatten the curve of the novel coronavirus' spread, non-urgent medical visits are down dramatically. One report showed that in March 2020, routine screenings for cancer were down as much as 94% compared to the previous average.

Indeed, starting in April, the National Comprehensive Cancer Network, the American Society of Clinical Oncology, Susan G. Komen for the Cure and others issued guidelines suggesting that people postpone cancer screenings that require clinic visits. Meanwhile, the American Cancer Society (ACS) emphasized the importance of consulting with a medical professional about this issue.

As communities in the U.S. reopen in a patchwork fashion, you may be wondering what the best approach is for early detection of cancer. Asked about their recommendations for screening during the COVID-19 pandemic, two City of Hope physicians who treat common cancers echoed the ACS's recommendation, underlining that there is no one-size-fits-all answer.

"It really depends on the patient," said Farah Abdulla, M.D., assistant clinical professor of dermatology. "Every patient is different. I have those conversations with my patients on a case-by-case basis before they come in."

Likewise, Lily Lai, M.D., associate clinical professor of surgical oncology and chair of City of Hope's Clinical Cancer Committee, urges an individualized approach.

"There has to be some risk stratification," said Lai, who treats breast and colon cancers. "Depending on your cancer risk, you have to judge that against the risk of being exposed to COVID-19 by being outside your home."

## WHO NEEDS TO BE SCREENED?

Both Abdulla and Lai noted that healthy people with no symptoms and no factors that increase the chances of developing cancer can safely defer

screening for the time being. However, there are categories of patients who ought to keep to their testing schedule or, at most, space out visits a little bit.

For instance, according to Abdulla, certain circumstances make an in-person trip to the dermatologist too important to put off.

- diagnoses that increase risk for skin cancer such as myelodysplastic syndrome, chronic lymphocytic leukemia or graft-versus-host disease

- excessive sun exposure
- family history of skin cancer

Lai similarly identified factors that should drive a person to keep up their colon cancer screening regimen.

- family history of colon cancer
- risk for polyps that could develop into colon cancer
- conditions that increase risk such as inflammatory bowel disease



Lily Lai, M.D., surgical oncologist





*"I want you to know your own body," said skin cancer specialist Farah Abdulla, M.D. "Be in tune with what's going on and reach out when you need help."*

More broadly, a personal or family history with any type of cancer that's subject to screening is a good reason to visit the doctor's office on schedule, regardless of the pandemic.

## WHAT CAN BE DONE FROM HOME?

The housebound do have early-detection options for certain cancers.

For colon cancer, there are at-home tests — the fecal occult blood test and the fecal DNA test — that involve collecting a stool sample and sending it to a lab.

For skin cancer, you can perform a careful monthly inspection with the help of a partner who checks places that you can't see on your own such as the scalp, the back and behind the ears.

Lai and Abdulla concurred on a general principle that holds true even in less extraordinary times — pay attention to your body and be on the lookout for changes.

"I want you to know your own body," said

Abdulla. "Be in tune with what's going on and reach out when you need help."

## WHICH SYMPTOMS SHOULDN'T BE IGNORED?

Some signs of disease are so significant that, should you notice them, you need to consult with your physician as soon as possible.

**Skin cancer:** new lesions that don't go away or grow in size, changes to existing lesions or extensive rashes

**Breast cancer:** a new lump or breast mass, bloody discharge from the nipple or changes to the skin of the breast such as redness

**Colon cancer:** changes in bowel habits, including blood in the stool

**Lung cancer:** a new cough, an increasingly productive cough, shortness of breath or excessive fatigue (some of the same symptoms associated with COVID-19)

"We do want people to see their physicians," Abdulla said. "If you find something new that's

concerning, follow up with your primary care doctor via video or phone."

## JUST HOW IMPORTANT IS CANCER SCREENING?

The physicians advocate that, when a "new normal" begins to assert itself, people get back on track with their routine cancer screenings.

As the acute phase of the outbreak wanes and more services reopen, you should find out when your primary physician's office is back to offering routine physical exams and screenings such as mammograms and colonoscopies.

Doing so can make a tremendous difference.

"Screening does save lives," said Lai. "Early detection results in cancers that can be treated and patients that can be cured. The data — especially for breast and colon cancers — demonstrates that pretty strongly."

She continued, "The world order can change, but there are some things that remain immutable such as the need to take care of yourself and your body, which includes screening for cancer."



*According to a recent report from Epic, preventive cancer screenings have dipped more than 90% during the pandemic. City of Hope's Chief Medical Officer Vijay Trisal, M.D., explains how cancer risks may be impacted with screenings at historic lows, which screenings we should all be doing at home and symptoms that no one should ignore, even during a national emergency.*

# Cancer Can't Wait



Why City of Hope is uniquely equipped to continue providing cancer care during the COVID-19 pandemic.

BY WAYNE LEWIS

**T**he coronavirus pandemic has dominated the public consciousness in the United States for much of the last several months — and rightly so.

And the outbreak has hampered care for other diseases, including cancer. A recent survey by the American Cancer Society showed that about a quarter of people currently in treatment are experiencing delays in care. And a recent UK study showed that people delaying care are being diagnosed at a later stage. Cancer doesn't go away on its own, so those delays risk worsening patient outcomes.

In a disarrayed medical landscape, one Los Angeles-area institution — ranked as one of the top cancer hospitals in the nation for 14 consecutive years by U.S. News & World Report



City of Hope Chief Medical Officer Vijay Trisal, M.D.

California, campus and in nearly 30 community practice sites around Southern California.

A rallying cry has emerged: Cancer doesn't stop for the coronavirus. And neither does City of Hope.

## SAFETY FIRST

It's well-documented that the coronavirus is particularly dangerous for people with cancer, especially those whose immune systems are compromised. So patient safety is the bedrock for City of Hope's efforts to deliver timely cancer care in the COVID-19 era.

City of Hope has had just a handful of patients infected with the coronavirus, and zero cases of in-hospital transmission. That number is the result of exacting precautions.

The care team wears masks, gloves and eye protection for all patient encounters.

Of the approximately 1,000 asymptomatic City of Hope employees who have been tested, none have tested positive.

"That gives us an indication of how good we are at taking precautions," Trisal said.

Staff and patients are checked for fever through thermal screening.

Coronavirus tests with less than three-hour turnaround are administered to any symptomatic staff or patients, as well as to all patients before admission or treatment.

Potential patients with the coronavirus receive care in an isolation unit.

Physical distancing is observed in waiting rooms and treatment areas.

For the time being, visitors are not allowed for both inpatients and outpatients (with rare exceptions such as for pediatric and end-of-life patients).

That last rule can be tough on patients, but it also safeguards lives.

"We want to decrease those 'shots on goal,'" Trisal said. "If you have five family members coming with the patient, you don't know who might be asymptomatic and can spread the coronavirus not only to that patient, but to others as well."

## THE PERSONAL TOUCH

City of Hope has earned a longtime reputation for compassionate, individualized care. Focused on patients' emotional needs, the institution provides interdisciplinary supportive services, including psychology, social work, palliative care, physical and occupational therapy, and nutritional and financial counseling.

"This is our responsibility," Trisal said. "Our traditional supportive care is at full strength, because in this time people need it more."

Another aspect of City of Hope's cancer care during the pandemic aims to both increase patient safety and ameliorate the effects of isolation: employing video chat and other technology for connecting people remotely.

In this way, hospitalized patients can have virtual

"face-to-face" interactions with loved ones. At the same time, a dramatic expansion of telehealth offerings such as virtual video visits has reduced foot traffic — another method for reducing those COVID-19 "shots on goal."

"Instead of coming to the hospital five times, a patient comes only once, when they need to," Trisal said. "COVID has taught us we can do things better, and I want to make sure that those learnings continue into 2021 and beyond."

## A PIONEERING HISTORY, A COMMITMENT TO THE FUTURE

City of Hope is particularly well-suited to drive extraordinary cancer care through an unprecedented outbreak because the medical team has a substantial track record of experience protecting patients from communicable disease.

Physicians at City of Hope were among the pioneers of the blood stem cell transplant, a treatment for diseases such as leukemia that knocks down the immune system in order to build it back up, starting with healthy cells from the patient or a donor. Forty-plus years and more than 16,000 transplants later, City of Hope has one of the largest and most successful transplant programs in the country.

To see transplant patients through recovery, the institution has had to fine-tune its protocols for thwarting everyday bugs, such as the flu, that prove dangerous to immunosuppressed patients.

"Being particular about infection is ingrained in our DNA," Trisal said. "Our ability to pick up and treat infection early has helped us create a sanctuary where your risk is much lower than going to the grocery store or the park."

"We have continued to do the same number of allogenic transplants during the pandemic," he added.

In the last couple of decades, City of Hope has moved to the forefront of a newer way to fight cancer: CAR T cell therapy, an approach that reengineers patients' own cells to fight cancer.

However, success sometimes brings its own peril. The death of a tumor can arouse a dangerous immune reaction involving an overload of small proteins called cytokines. It happens that "cytokine storms" are a feature of the late, inflammatory stage of COVID-19, and City of Hope has a biologic medication on hand — based on technology developed at City of Hope — that helps calm those storms.

Meanwhile, City of Hope has kept most of its clinical research active despite COVID-19. Beyond their crucial role in turning lab breakthroughs into innovations, these studies offer patients the newest investigational therapies. Sustaining clinical research is part and parcel of City of Hope's dedication to saving lives — today and tomorrow.

"We continue doing the work that we need to do by eliminating the risk of having someone come through our doors who may infect others," Trisal said. "There's a lot of people working tirelessly — day and night, weekends — to prevent interruptions."

— presses on to continue treatment safely.

"At City of Hope, our core mission is to fight life-threatening diseases," said Vijay Trisal, M.D., the organization's chief medical officer and the Dr. Norman & Melinda Payson Professor in Medicine. "Anything that impacts people's overall survival, their symptom management, their families or communities, we are called to do something."

City of Hope is a comprehensive cancer center, the National Cancer Institute's highest designation. That label recognizes excellence in treatment, research and outreach, with expertise to address the many faces of the disease, whether early or late stage, common or rare. Today, despite the pandemic, critical surgeries, chemo and radiation therapy, programs for blood cancers and clinical trials continue on the main Duarte,

# ‘Cancer Can’t Wait’: Aiden’s Story

7-year-old Aiden couldn’t delay his stem cell transplant until after the coronavirus crisis abated.

BY ABE ROSENBERG

**A**iden Anderson, a happy, active, inquisitive and rather talkative 7-year-old, likes to stare into the web camera, closer and closer, until all you see is his left eye. Typical kid.

Ever-smiling, he’s excited about his upcoming birthday. Just not for the reasons you might expect.

“It’s going to be 100 days since my transplant!” he points out.

When he was 5, this normally high-octane kindergartener started feeling tired. His school noticed. A nurse thought Aiden’s belly looked distended. She sent him home. Within hours, Aiden’s father was taking him to the hospital.

Tests quickly revealed the problem. Aiden had a slow-moving case of chronic myeloid leukemia (CML), extremely rare in children — barely 100 cases are reported each year in the U.S.

The news stunned Chris Anderson, Aiden’s father.

“I fainted,” said Chris.

“I couldn’t process it,” recalled Ann Anderson, Aiden’s mom. “I thought they must be wrong.”

Chris stayed in the hospital with Aiden for five days while his symptoms — an inflamed spleen and liver — subsided.

Fortunately, CML treatment is straightforward and generally successful. After taking care of his enlarged spleen and liver (the distended belly), doctors gave Aiden targeted therapy drugs known as tyrosine kinase inhibitors. TKIs are taken in pill form and they do a good job; Aiden got better and eventually was well enough to return to school. For about a year, all seemed normal.

Until everything changed.

CML patients must meet specific milestones to confirm the drugs are still working. Aiden missed a critical 18-month milestone; his disease was becoming resistant. Later, a biopsy discovered evidence of a malignant “blast”: a sudden, rapid growth of cancer cells, mimicking the more dangerous acute lymphoblastic leukemia, but less likely to respond to standard chemotherapy used to treat it. Aiden would need a stem cell transplant. Soon.



Aiden Anderson, 7, displays his certificate of completion and his champion medal after finishing treatment.

“It was just so surreal. I never thought we’d ever be in that situation. I think I cried through that entire meeting,” said Ann, crying as she tells the story. She remembers how Aiden stayed calm, asking only one thing. “He wanted to make sure we’d be there with him,” she said.

You really never know when or how fate may step in, but at this point two utterly stunning things happened. One dramatically increased the odds of a successful transplant. The other might have derailed it entirely.

Aiden’s mom is Chinese; his dad is African-American. It can be nearly impossible for biracial families to find a compatible, unrelated stem cell donor. The Andersons didn’t have to look far. Aiden’s big brother Ian turned out to be a perfect match.

## TRANSPLANT SCHEDULED

First, Aiden went through four weeks of chemotherapy, then another month of immunotherapy to shrink that “blast.” Next would come 11 sessions of radiation and more chemo to eliminate the remaining diseased bone marrow. Everything looked good, with the actual stem cell procedure on track for spring 2020.

Then fate dropped the other shoe.

The COVID-19 pandemic.

Virtually overnight, life at hospitals across the country and around the world flipped upside down. Entire floors were set aside to treat the desperately ill. Overflow wards went up in public parks. And if you weren't ill, it became dangerous to venture anywhere near those places. Priorities changed. Elective surgery? Forget about it.

After all those drugs, Aiden was already immuno-compromised. Would his transplant have to wait?

Not a chance, his doctor insisted.

“We didn't delay anything,” said pediatric hematologist and oncologist Nicole Karras, M.D., assistant clinical professor of pediatrics at City of Hope. “Cancer can't wait. If you delay, there's always a risk the cancer will come back, and the more cells that return, the harder they are to treat.”

But some things would be different from now on.

Aiden's smile vanishes when he remembers the four coronavirus tests he endured — with that long, irritating nasal probe — because it was feared he might have been exposed at different steps along the way. Always brimming with questions for the hospital staff, he now had just one: Why so many tests? “It's not fair,” he lamented. He tested negative all four times.

“He had more COVID-19 tests than anyone I know!” said Karras.

Mom got tested too, as did Dad ... and Ian, who now wouldn't be allowed to visit the kid brother whose life he was saving. All tested negative. As the pandemic grew, City of Hope tightened the rules. Masks on everyone.

Temperature screenings. Only one visitor per patient, Mom or Dad, not both. And you couldn't go home. Not for the entire 45 days Aiden was scheduled to be there. (Some of these rules were later relaxed on a case-by-case basis; ultimately, the hospital permitted Ann and Chris to take turns visiting.)

Adapting to the evolving changes left Mom temporarily “floored.” But how the people at City of Hope handled it all left her permanently impressed.

“It was so calm at City of Hope,” she remembers. “Even though it was so crazy outside. The staff was phenomenal. They were so kind. Even when Dr. Karras explained that Aiden may not be able to have children ...”

The tears are flowing again.

“As an educator [she's an assistant principal, Chris is a math teacher], you want to treat the children as if they're your own. Everyone at City of Hope treated Aiden like he was their son.”

Aiden's experience is being replicated across the City of Hope campus, which, as a self-contained center whose emergency department is exclusively for its own patients, has not received a barrage of coronavirus cases (the handful who do test positive are isolated in a remote area). Cancer treatment has continued uninterrupted, with multiple safety and security enhancements added, making it possibly one of the safest places for a cancer patient to be.

“This is the reality,” asserted Karras. “This virus isn't going away. People shouldn't panic. It's more important for cancer patients to get their proper treatment.”

It was the right call for Aiden, who's headed for that big birthday in very good shape. Karras calls Aiden “a trouper” and says “it was a pleasure to take care of him.” What does Aiden say?

He has a bit of advice for anyone who might be concerned about coming to City of Hope during this challenging time.

“It's gonna be OK,” he says reassuringly. “The nurses and doctors will take very good care of you!”

# Hope for People With the Rarest Cancers

BY JAY FERNANDEZ

Iain Whyte wants you to know that even in the darkest moments of a journey marked by failing health and a string of misdiagnoses, there is still hope.

An athletic type who enjoyed playing soccer and volleyball, Whyte first noticed a knee-centered limp and numbness in his thighs and arms, which led to a partial knee replacement in 2016. He was then treated for a progressive version of a neurological disorder called Guillain-Barré syndrome at one hospital, then another. Meanwhile, his mobility continued to deteriorate, and he was no longer able to stand.

Eventually, neurologist Richard A. Lewis, M.D., an expert in Guillain-Barré at Cedars-Sinai, ordered a VEGF blood test that signaled it could be POEMS syndrome, a rare blood cancer that attacks the bones and neurological system. A whole new battery of tests finally revealed that POEMS was indeed the true culprit. The bad news was that there is so little data about the disease — only 3,000 cases globally have ever been identified — that few doctors knew how to treat it and late diagnosis typically meant a short life expectancy for those afflicted.

Once he was properly diagnosed, Whyte came to City of Hope because of our expertise in treating blood cancers, including rare types like POEMS. Whyte began seeing Amrita Krishnan, M.D., director of the Judy and Bernard Briskin Center for Multiple Myeloma Research, who put Whyte on an enhanced chemo program for six months. In March 2017, he was strong enough to receive a bone marrow transplant.

Recovery was slow and difficult because his nervous system had been severely damaged, but three years later he is in complete remission, has some feeling back in his toes and walks unassisted with leg braces. The



City of Hope patient Iain Whyte with his son Sean, wife Carrie, and daughters Elsa and Chloe

doctors have marveled at his progress, and if the disease comes back, City of Hope has a reserve of his stem cells to provide treatment.

“City of Hope's responsiveness was impressive,” said Whyte. “The first day, I knew I was in good hands. Unlike other hospitals, they only focus on cancer. There was a lot of energy, a huge focus on treating the disease. There was an attitude of ‘let's keep pushing forward.’ I could see that everyone around me was in the same boat, and I felt a brotherhood. I felt like I was home.”



Courtesy of Steve McGrew

*Blacksmith Steve McGrew works in his forge in Spokane, Washington. He doesn't know how or when he was exposed to the asbestos that eventually led to his mesothelioma.*

A blacksmith's workshop with a large window and various tools.

# Forging Ahead

A dire cancer diagnosis of Stage 3 mesothelioma — during a national pandemic — sparks a blacksmith's 1,200-mile journey to City of Hope to join a potentially lifesaving clinical trial.

BY ABE ROSENBERG

Steve McGrew's move from Spokane, Washington, to a neighborhood near City of Hope's Duarte, California, campus is a story that's part karma, part dogged determination. It's a case study in what's possible when individuals and institutions resolve to press forward when a pandemic turns everything upside down.

McGrew moved here temporarily to take part in a potentially life-changing clinical trial to treat his Stage 3 mesothelioma. He might never have come to City of Hope if not for one of his students, who wanted to learn how to make knives.

McGrew built a comfortable career developing tech applications for industry and government; things like security holograms and microbial detection systems. It came naturally to the ever-curious McGrew, who enjoys "making things" and isn't intimidated by complexity.

That was his day job.



Yuman Fong, M.D., first met McGrew as a student in his forge.

On the other hand, his "hobby," now a full-time pursuit, dates back thousands of years. As a blacksmith, he heats and pounds metal into knives, swords, works of art and more. He doesn't take shortcuts. McGrew built his own forge and designed his own anvils. And he teaches the craft to a lucky few who travel to his workshop.

One of those was Yuman Fong, M.D., chair of City of Hope's Department of Surgery and the Sangiacomo Family Chair in Surgical Oncology. A mutual friend brought them together. Fong is a self-described "dabbler" who seeks out master teachers to instruct him in new disciplines. Their relationship yielded some new handcrafted knives for Fong. It would give McGrew much more.

He's not sure how or when exposure to asbestos — the primary cause of mesothelioma — ultimately made him ill. As a child, McGrew crawled through an attic with asbestos insulation. He remembers odd jobs: cutting asbestos boards and inhaling the dust, demolishing an old Army barracks (the military was a heavy user of asbestos). Or perhaps it happened when his dad, a paleontologist, brought home a tool of his trade — plaster laced with the deadly material. It could have been any of the above; mesothelioma has a latency period as long as 50 years.

He was 74 when his chest began to feel strange and he started losing weight. A few months later, he became short of breath and couldn't eat. Tests detected a pool of fluid squeezing his right lung. A CT scan and biopsy revealed so many mesothelioma tumors in the lung's lining that his doctor nearly gave up on McGrew right then and there.

"He said all I had left was palliative care," McGrew remembered. "I didn't like the sound of that, so I started looking for alternatives."

Enter Yuman Fong. Again.

"I heard from our mutual friend that Steve had a 'lung problem,'" Fong said. "In seconds I knew it was mesothelioma." He also knew how rare and deadly this disease can be.

Most important, Fong knew what McGrew's doctors in Spokane didn't. A clinical trial at City of Hope was combining immunotherapy with chemotherapy, followed by surgery, then more

and we were being very cautious," Kim recalled. "It turned out that I wasn't actually exposed, but it was eye-opening and it helped us reevaluate our safety protocols."

McGrew was reevaluating, too. The quarantine delay left him with much less time to reach City of Hope before the trial's enrollment window closed. But with COVID-19 wreaking havoc with air travel, there was no way he'd get on a plane. And all the while Fong was telling him, "Get here now!"

He had just one option.

"We drove," he said. "Myself, my wife and the dog. Twelve-hundred miles in three days. We slept in the car. We ate food out of a cooler."

They made it. Barely.

"We signed up for the trial 30 minutes before the deadline," he said.

When McGrew arrived, he found a campus fully prepared to deal with pandemic issues. From masks to temperature screenings to repeated coronavirus tests, City of Hope built on its long experience with immuno-compromised patients to keep everyone safe without compromising cancer care.

"As a major cancer center, we protect patients really well," Fong pointed out, adding that coronavirus concerns forced other hospitals to cut cancer screenings by as much as 90%.

"Cancer won't wait for the pandemic to be over," added McGrew's oncologist, Marianna Koczywas, M.D. "If the patient waits too long, cancer can recur or worsen."

McGrew's clinical trial consists of four cycles of the checkpoint inhibitor atezolizumab (Tecentriq), plus the chemotherapy drugs pemetrexed and cisplatin. "The goal is to shrink his tumors and make surgery more effective," explained Koczywas, adding that McGrew will keep receiving atezolizumab after surgery for up to a year.

It's working.

"I've improved even more than they expected," said McGrew. "The tumors have shrunk. And I feel great. Almost normal!"

He'll be ready for surgery soon, and it will be extensive, involving removal of the lining around his lung, heart and diaphragm. His surgeon is confident McGrew can handle it. "Steve is a very smart, positive person with a lot of inner strength," said Kim.

None of this is a cure, and McGrew knows it. This blacksmith with the high-tech mind researched his disease and City of Hope's track record as carefully as any project he's ever undertaken. He liked what he saw. And he likes his chances.

"I'm ready for the best- and worst-case scenarios," he said. "Could be five years. Could be one year. And then we'll try something new." And yes, he fully expects to see that "something new," because at City of Hope he's surrounded by "doctors and researchers who always know what's coming."

"There's no better place in the country. I'm in the best possible hands."



Fong crafted this knife from a railroad spike in McGrew's forge.

immunotherapy afterward. The new approach was improving outcomes and extending life expectancy.

Fong urged McGrew to come to California. "We'll get you into that trial," he promised.

But by now it was March 2020 and the rampaging coronavirus was changing everything.

To prepare for the trial, McGrew needed exploratory surgery to make sure his disease hadn't spread further. But before City of Hope thoracic surgeon Jae Kim, M.D., could operate, he was forced into quarantine because of a possible exposure to COVID-19.

"It was early in our experience with the pandemic



# Creating Personal Roadmaps to Treat Kidney Cancer

BY STEVE YOZWIAK

**E**xperts at City of Hope and Translational Genomics Research Institute (TGen) are using one of the world's most comprehensive genomic analysis tools to map out personalized treatment plans for metastatic kidney cancer patients.

While the physician-scientists are at the beginning of this long journey, they believe they're on the right path. They recently published a study in the *Journal of Immunotherapy of Cancer* that suggests mutations in the TERT gene predicts that a patient may not be receptive to immune checkpoint inhibitors such as nivolumab or pembrolizumab.

"The hope is to one day identify patients who will benefit from immunotherapy and those who will not. Eventually we may be able to distinguish which patient is better suited for other treatments, like targeted therapy," said Sumanta Pal, M.D., one of the study's senior authors and co-director of the Kidney Cancer Program at City of Hope. Examples of targeted therapy include vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors like cabozantinib.

Nearly 74,000 new cases of kidney cancer will be diagnosed this year, and about 14,800 people will die from the disease, according to the American Cancer Society. Ironically, experts know patients who have certain genetic mutations are more susceptible to specific drugs, but most doctors are not genetically sequencing each kidney cancer patient's tumors, Pal said.

"It's a paradox: We don't use targeted therapy in a targeted fashion," he added. "At City of Hope, we have begun to provide comprehensive genome and exome sequencing for all patients with Stage 4 cancer, regardless of their cancer site."

City of Hope is on pace to be the only major cancer center in the United States to genetically profile the tumors of every single patient, regardless of cancer type. The goal is to enable patients to receive effective targeted therapies or to enroll people in innovative clinical trials as early as possible so that they can fight their disease.

In the study, Pal and his colleagues sent samples of 91 patients' tumors to TGen's clinical laboratory, Ashion Analytics, so that the specimens could be sequenced by GEM ExTra, a leading-edge tool that features tumor-normal whole exome sequencing and tumor whole transcriptome sequencing. These are molecular-level analyses of each patient's entire protein-coding DNA and RNA.

"The goal was to identify genomic alterations that correlated with therapy response," said Sara Byron, Ph.D., assistant professor in TGen's Integrated Cancer Genomics Division and co-senior author of the study. (Ashion Analytics recently announced that Medicare has approved



*Sumanta Pal, M.D., is using genomic analysis to determine which therapies will be best for individual kidney cancer patients.*

coverage of GEM ExTra, potentially providing 44 million more patients access to this test.)

Kidney cancer treatment regimens involving either targeted therapy or immunotherapy have burgeoned since 2015. Because new treatments sprouted so rapidly, scientists have not yet discovered the ideal strategy to sequence regimens for optimal outcomes. Moreover, the current way treatment risk is assessed tends to be subjective with ingrained bias, the study reported. City of Hope and TGen are working to develop objective laboratory-based biomarkers for kidney cancer.

Only patients whose genomic profiling was performed prior to systemic treatment were included in the study. Patients received either targeted therapy known as VEGF tyrosine kinase inhibitors (sunitinib, cabozantinib, lenvatinib/everolimus) or immunotherapy (nivolumab, ipilimumab, pembrolizumab). They were divided into those who received no clinical benefit, meaning their disease progressed, or those who received clinical benefit, meaning the tumor shrunk or stabilized for more than six months. Some 19,396 genes and nucleic sequences were analyzed to tease out a therapeutic treatment plan that would have best suited each patient based on their specific tumor mutations. More research in larger sample sizes are needed, but the scientists are off to a good start.

"Stage 4 cancer is often considered incurable, but that doesn't always have to be the case," Pal said. "By sequencing all protein-coding DNA, that is by sequencing the whole exome, we may be able to identify new therapeutic targets, and that's a very exciting prospect."

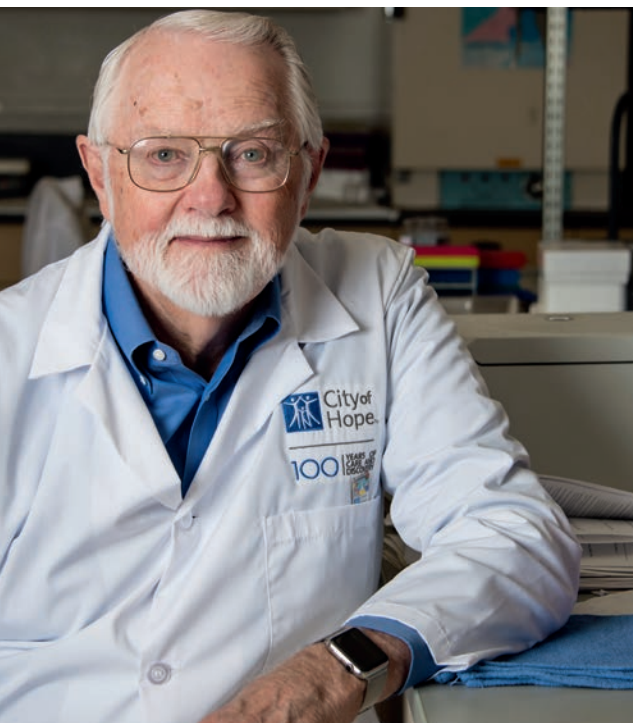
# A Bold New Vision

Debbie Thurmond, Ph.D., becomes the new director of the Diabetes & Metabolism Research Institute after famed diabetes researcher Arthur D. Riggs, Ph.D., steps down

BY SAMANTHA BONAR

**A**fter 41 years at City of Hope, Arthur D. Riggs, Ph.D., is stepping down as director of the Diabetes & Metabolism Research Institute (DMRI), handing the reins to Debbie Thurmond, Ph.D. Riggs will continue doing research.

In addition to pioneering the science leading to the development of some of the most effective immunotherapies for cancer in use today, Riggs' generation of the first synthetic human insulin has improved the lives of millions of people around the world.



Arthur D. Riggs, Ph.D.

"I really enjoy doing science and I really enjoy interacting with and helping my colleagues at work. But around my 80th birthday last year, I realized it was time to develop a succession plan, and I thought Thurmond would be the perfect person for the job," Riggs said. "She has outstanding skills, both scientifically and administratively."

"She's a rising star in her field," he continued. "And she is an excellent mentor. I found that she was just naturally inclined to help others be successful. For me, that's very important.

Finally, I thought she had the appropriate vision for the future of the DMRI and is very good at communicating the big picture."

## THURMOND'S VISION

As for Thurmond, she says she is "absolutely delighted, humbled," to have been chosen to lead the DMRI into the future. "Art has built a phenomenal institute, and I have the great pleasure of facilitating its continued growth and prominence in the diabetes space."

A renowned expert in the biological underpinnings of diabetes, Thurmond, Ruth B. & Robert K. Lanman Chair in Gene Regulation & Drug Discovery Research, joined City of Hope in 2015 as professor and founding chair of the Department of Molecular & Cellular Endocrinology within the DMRI. She became deputy director of the institute last year, and began her new role as director on Sept. 30. Previously, she was a professor of pediatrics and associate director of the Basic Diabetes Research Group within the Herman B. Wells Center for Pediatric Research at Indiana University.

Thurmond received her Ph.D. and postdoctoral training at the University of Iowa. She serves on multiple editorial boards, as well as on national and international grant review panels, including chairing one of the five National Institutes of Health (NIH) metabolism-based panels in the National Institute of Diabetes and Digestive and Kidney Diseases.

In 2018, Thurmond became the first woman to be awarded the Davidson Award in Physiology from the University of Toronto, Canada, as part of the Banting and Best Award in Diabetes.

Thurmond and her team's research efforts include identifying cellular and molecular mechanisms in diabetes development and finding therapies to stop the disease's progression.

Thurmond's work is supported by five research awards from the NIH, the JDRF and the Larry L. Hillblom Foundation. In 2018, Thurmond and her lab team were highlighted in the journal *Diabetes* for their discovery and identification of a new potential target that can keep the immune system stable and islet beta cells healthy, ultimately keeping type 1 diabetes in check.

But a particular interest is the intersection of diabetes and cancer, a connection she feels

warrants much further study. Her goal looking forward is for the DMRI and City of Hope to "corner the market on connecting the dots between diabetes and cancer. We are the only institute that's uniquely designed to focus on how to cure both diseases and to develop treatments to prevent and cure either disease that won't also inadvertently contribute to the cause of the other disease."

Thurmond points out that some cancer treatments can destroy insulin-producing beta cells, causing a type 1 diabetes-like requirement for insulin injection in patients, and that type 2 diabetes puts individuals at significantly higher risk for various forms of cancer.

"We have the ability to prospectively evaluate whether or not we need to be mindful of the individual's susceptibility to metabolic disease with cancer treatment, so if there are more than one cancer treatment strategies available, it helps to say, 'You know what, this individual might be at risk. Therefore, we're going to go with the treatment that we think will be less damaging to their metabolic system.'

"I'm enthusiastic about charting this new territory," she continued. "There's no precedent for this really. So not only are we charting our own course, we're charting the course for future institutions on what this is going to look like. We're doing something that's truly unique. And I don't want it to stay unique. I want us to set the standard for other institutions to pick up on because cancer care and diabetes care can rapidly evolve nationwide to be much more effective."

Other "modest" goals: "We want to cure type 1 diabetes. We want to cure and prevent type 2 diabetes and prevent pre-type 2 diabetes, which also will help with the prevention and treatment of cancer, Alzheimer's and cardiovascular disease," she said.

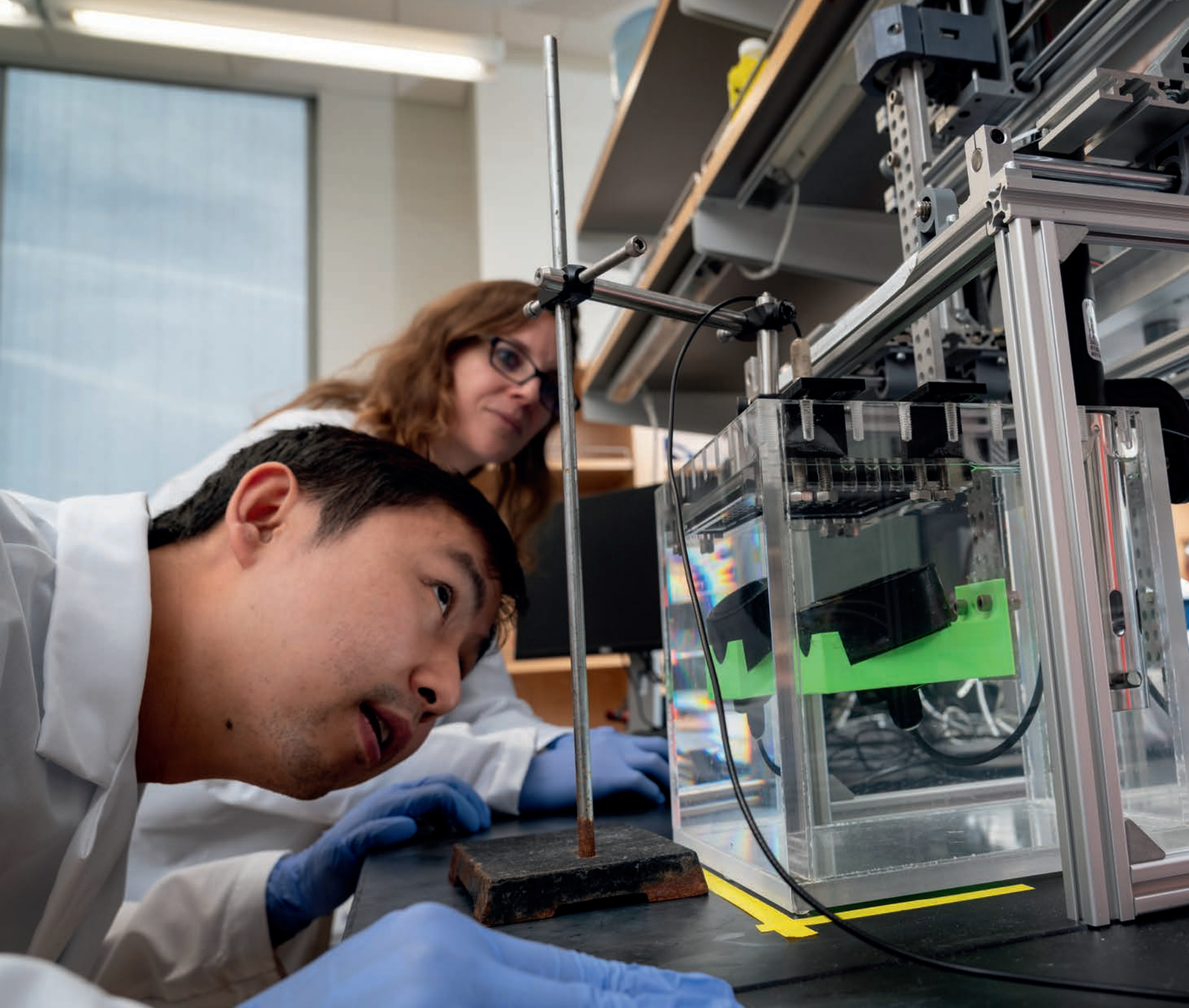
Two substantial new hires are already on board to help with those efforts. On Aug. 17, Charles Brenner, Ph.D., joined the institute as the inaugural Alfred E Mann Family Foundation Chair in Diabetes and Cancer Metabolism and founding chair of the Department of Diabetes & Cancer Metabolism. And on Sept. 16, Ping Wang, M.D., began as chair of the Department of Clinical Diabetes, Endocrinology & Metabolism. (See page 4.)

"I am so excited," Thurmond said. "Every day I get up and I just can't wait to get started."



*Debbie Thurmond, Ph.D., director of the Diabetes & Metabolism Research Institute at City of Hope, discusses how she is tackling both type 1 and type 2 diabetes in her lab.*

*Debbie Thurmond, Ph.D.*



*Jian Ye, Ph.D., and Caroline Hoffmann, M.D., Ph.D., demonstrate how the oncotripsy device works.*

# A One-Two Punch

Oncotripsy uses ultrasound to selectively kill cancer cells

BY MICHAEL EASTERLING

**I**n a collaboration with Caltech, Peter P. Lee, M.D., chair of City of Hope's Department of Immuno-Oncology and co-leader of the Cancer Immunotherapeutics Program, and members of his lab are developing a new way to target cancer and kill it without harming healthy cells: low-intensity pulses of ultrasound.

"The concept is based on the notion that cancer cells have different biophysical properties, (size, shape, stiffness, etc.) from normal healthy cells," said Lee, the Billy and Audrey L. Wilder Professor in Cancer Immunotherapeutics. "If you can hit cancer cells with the right frequency, inducing harmonic resonance, you can selectively kill those cells." Lee said the principle behind

harmonic resonance is not unlike the opera singer who can break a glass with her voice. "What we're doing is finding the harmonic resonance for specific cancer cells, to 'shatter' them so they are destroyed. Since this is a totally new way to target cancer based on biophysical properties, cancer cells cannot mutate to become resistant to this therapy — which is



“What we’re doing is finding the harmonic resonance for specific cancer cells, to ‘shatter’ them ...”

— PETER P. LEE, M.D.

called ‘oncotripsy,’” he said. “And sound waves can be transmitted innocuously through healthy tissue. We can potentially transmit sound waves to the brain and only selectively resonate the cancer cells. It’s a very targeted therapy.”

Lee partnered with Caltech’s Michael Ortiz, Ph.D. Lee’s lab contributed a number of cancer

cell lines, but also many normal cells to advance the research.

To further the research, Lee applied for biomedical research grants that allowed him to secure postdoctoral fellow Jian Ye, Ph.D., and visiting scholar Caroline Hoffmann, M.D., Ph.D., a head and neck surgical oncologist from the Institut Curie in Paris. “Caroline found out about our work and contacted me, interested in helping us move this project forward. She joined us for a year in late 2019,” Lee said.

A pilot instrument was built on the Duarte, California, campus to mirror the one at Caltech, enabling Lee, Ye and Hoffman to test samples right in the lab without having to transport them back and forth between Duarte and Pasadena.

An important element of this approach is how it kills cancer cells, Lee explained. “Cells can die in different ways. Most common is a process called apoptosis, or programmed cell death. It’s also called cell ‘suicide.’ Most cells in our body die in this way, and it is an ordered cell death. The immune system ignores apoptosis, and it is immunologically silent. On the other hand, if a cell is killed by trauma or by a virus (such as the COVID-19 coronavirus), the immune system is triggered — called ‘immunogenic cell death.’”

Lee said his research posits that the kind of low-emitting sound wave they are experimenting with will kill a cancer cell in an immunogenic way.

Over time, Lee and his team expanded the repertoire of cancer cell lines being tested, drawing samples from humans and mice to include colon and breast cancer. They also tested a variety of healthy human cells, including immune cells, to check how the treatment affects these cells.

The hope, Lee says, is that the ultrasound will kill cancer cells in a specific way that will also engage the immune system and arouse it to attack any cancer cells remaining after the treatment. “This is critical because it means that we can combine oncotripsy with immunotherapy to potentially cure patients — even with metastatic cancer.”

If ultrasound can be used to cause cell death in a way that the body’s immune system recognizes as injury, instead of as apoptosis, this could lead to the site of the tumor being flooded with white blood cells that could attack remaining cancer cells. So far, most of the testing has been done in cell cultures in petri dishes, but Lee said his team is now expanding the testing to solid tumors in living animals. Lee said the team hopes to begin a first-in-human clinical trial within the next few years.

“We don’t have to kill every last cancer cell for this to be a successful innovation,” Lee said. “If we can bring the immune system into the equation, your own cells do the rest. Even if we’re able to kill 70-80% via oncotripsy, the patient’s immune system will mop up what’s remaining. My ultimate hope is that this treatment will be combined with immune-based therapy for a one-two punch to beat cancer.”

## A Gift of Trust



Judy Sonney

Judy Sonney first connected with City of Hope’s mission several years ago, after her sister was diagnosed with multiple myeloma. Though her sister was not treated at City of Hope, Judy started to learn more about the groundbreaking work being done here through friends and neighbors who were connected with City of Hope. “The work they do with research and the clinical trials with many types of cancer and other illnesses give so many patients hope and longer lives. I think that is very, very important. My hope is that those clinical trials will become routine treatments and that patients all over the world will benefit.”

Judy’s support for City of Hope became even more personal when her neighbor became ill. “I’ve lived in my neighborhood for over 40 years and know my neighbors well. One of them is a man in his early 50s, with a wonderful family. He’s an amazing husband and father. I’ve seen them grow as a family for many years and when he became sick with cancer, I was just devastated. But he was treated at City of Hope and now he’s doing very well.”

A friend’s gift of real estate to City of Hope gave her the idea to create her own gift with real estate. Judy liked the idea of supporting City of Hope and at the same time, easing the burden of managing an apartment building.

She hopes that other supporters will consider a similar gift: “I would tell others that they don’t have to experience the burden of managing property. While I could have engaged a management company, I was still responsible, and it’s a challenging time to be a small landlord. You can receive income and help City of Hope and their patients. It’s that easy.”

Learn about easy ways to create your legacy of hope at [myplanwithcoh.org](https://myplanwithcoh.org).

# Vision for Campus of the Future Becoming a Reality

Nearly two years after receiving approval from the city to begin construction in earnest, City of Hope's new medical and administrative office building is complete.



*City of Hope's \$1 billion main campus expansion continues during the pandemic. Pictured is the new four-story Medical and Administrative Leadership Pavilion.*

**E**ven in the midst of a pandemic, plans for a cancer campus of the future are speeding ahead at City of Hope. The institution is in a time of tremendous growth, building more facilities and hiring more clinical and research staff — all to support the increasing number of cancer patients seeking high-quality care.

Two years after receiving approval from the city of Duarte to begin the approximately \$1 billion project, City of Hope's new, state-of-the-art, 100,000-square foot Medical and Administrative Leadership Pavilion (or "the Pavilion") is complete.

The Pavilion houses the departments of Surgery, Medical Oncology & Therapeutics Research, Hematology & Hematopoietic Cell Transplantation and Pediatrics.

The opening of the Pavilion marks the first milestone in realizing City of Hope's vision for a patient-friendly, environmentally conscious, technologically advanced campus. The next phase is construction of the new Duarte Outpatient Center (DOC), an eight-story, 350,000-square-foot facility that will double the number of exam rooms and infusion capacity.

The DOC will house the latest, most advanced

equipment, specialty clinics, new radiation oncology and laboratory services, and dedicated clinical trial infusion and monitoring. It will create enclosed walkways and bridges between buildings to provide a safe and more comfortable experience for patient transport, especially for immuno-compromised patients. The DOC is planned to be completed in 2024.

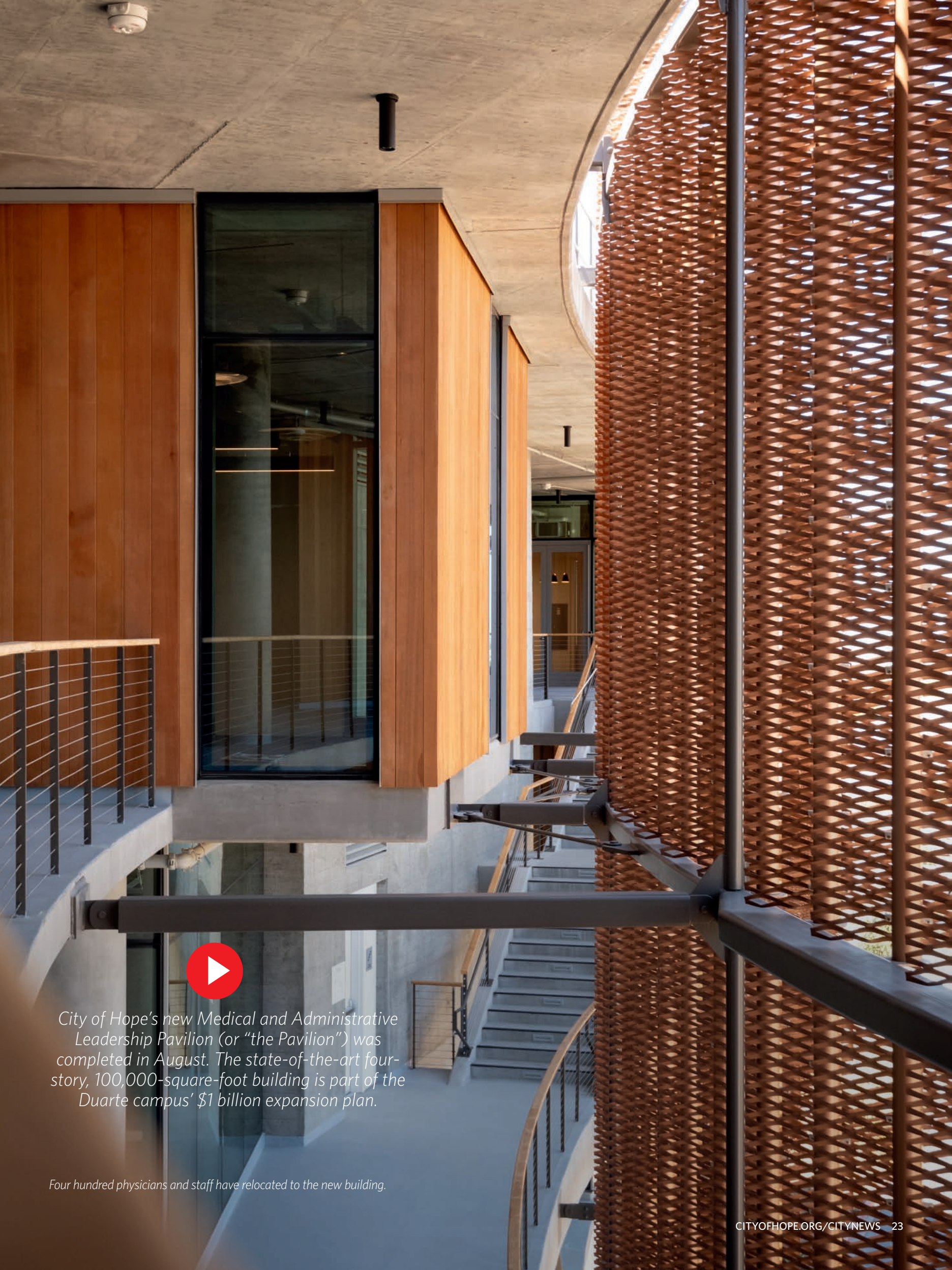
In addition, a new 10,000-square-foot Outpatient Imaging Center was completed in September, nearly doubling imaging technologies and capacity, including new MRI, CT and PET scanners. It houses a PET/MRI machine, a hybrid that produces the most highly detailed images of the body.

Construction is well underway on the new Hope Village, targeted to open in 2021, a five-story, 147-room hospitality and wellness building for patients recuperating or those requiring extended treatment. This will allow patients who need easy access to City of Hope outpatient facilities to stay nearby and receive care in a comfortable, private, home-like setting.

Supporting the expansion plan is a new parking structure consisting of approximately 1,000 spaces for patients and visitors.

The renovated campus will have a strong focus on sustainability and environmental friendliness, and will maintain the features of landscaped walkways and green spaces that have long characterized City of Hope, said Jeff Walker, M.B.A., chief operating officer. "One of the guiding principles of the expansion is that the design of our new buildings and open spaces will contribute to the healing of patients by creating strong relationships with nature."

"We are incredibly excited to celebrate the opening of the Pavilion," said Walker. "This marks the beginning of an exciting transformation of the Duarte campus that will allow us to help more patients and their loved ones who turn to us at a time of great need for our unique care and capabilities."



*City of Hope's new Medical and Administrative Leadership Pavilion (or "the Pavilion") was completed in August. The state-of-the-art four-story, 100,000-square-foot building is part of the Duarte campus' \$1 billion expansion plan.*

*Four hundred physicians and staff have relocated to the new building.*



# A Killer Combo

Scientists combine two powerful immunotherapies to eradicate tumors.

BY LETISIA MARQUEZ

*Saul Priceman, Ph.D., left, and Anthony Park, Ph.D., right, recently published a promising study combining oncolytic viruses with CAR T cell therapy for use on solid tumors, which are difficult to eradicate with CAR T cells alone.*

**C**ity of Hope scientists have combined two potent immunotherapies — an oncolytic virus and chimeric antigen receptor (CAR) T cell therapy — to target and eradicate solid tumors that are otherwise difficult to treat with CAR T therapy alone, according to a new Science Translational Medicine study.

In preclinical research that could lead to a clinical trial for patients with intractable solid tumors, City of Hope scientists genetically engineered an oncolytic virus to enter tumor

cells and force their expression of the CD19 protein on their cell surface. Scientists were then able to use CD19-directed CAR T cells to recognize and attack these solid tumors.

CD19-CAR T cell therapy is approved by the U.S. Food and Drug Administration to treat certain types of blood cancers, namely B cell lymphomas and acute lymphoblastic leukemia. This new research may expand the use of CD19-CAR T cells for the treatment of patients with potentially any solid tumor.

“Our research demonstrates that oncolytic viruses are a powerful and promising approach

that can be combined strategically with CAR T cell therapy to more effectively target solid tumors” said Saul Priceman, Ph.D., the study’s senior author and an assistant professor in City of Hope’s Department of Hematology & Hematopoietic Cell Transplantation.

“In addition, this therapeutic platform addresses two major challenges that make solid tumors so difficult to treat with immunotherapy. There are limited, established solid tumor targets that T cells can be redirected against with CARs,” Priceman added. “Furthermore, solid tumors





*City of Hope scientists have combined two potent immunotherapies — an oncolytic virus and chimeric antigen receptor (CAR) T cell therapy — to target and eradicate solid tumors that are otherwise difficult to treat with CAR T therapy alone, according to a new Science Translational Medicine study.*

are surrounded by a brick wall — a so-called immunosuppressive tumor microenvironment. When a CAR T cell attempts to enter the tumor, survive and kill cancer cells, it can't effectively because of this barrier."

Yuman Fong, M.D., the Sangiacomo Family Chair in Surgical Oncology at City of Hope and a leading scientist who is developing oncolytic viruses for cancer treatment, added that the virus was able to break through that barrier.

"We designed this oncolytic virus to do what it does so well," Fong said. "It entered the cancer cell and used the cell's own machinery to replicate itself, and engineer the cancer cells to express a truncated form of the well-known

CAR T cell target, CD19."

Researchers first created an oncolytic virus (OV19t) in Fong's lab to get into tumor cells and start producing truncated CD19 (CD19t). They did this successfully in triple-negative breast cancer lines, as well as in pancreatic, prostate, ovarian, and head and neck cancer, as well as brain tumor cells. CD19-CAR T cells were then combined with OV19t in vitro and in therapeutic studies in mice.

## SEVERAL KEY FINDINGS

"When we infected tumor cells with the virus, we observed the first signal that this may work. CD19t was being expressed by tumor

cells much sooner than the virus was able to kill them, giving us a window of opportunity to be targeted by CD19-CAR T cells," said Anthony Park, Ph.D., the study's lead author and a postdoctoral fellow in Priceman's lab. "The combination of the two had a powerful, synergistic effect."

Researchers also showed that mice already cured of their cancer with the oncolytic virus and CAR T cell combination demonstrated prolonged protective anti-tumor immunity.

"The immune system built a memory response to the tumor," Park added. "Once it eradicated tumors, following the initial combination treatment, the mice were shielded against tumor recurrences."

**"The combination of the two had a powerful, synergistic effect."**

— ANTHONY PARK, PH.D.

Solid tumors are often immunologically cold, which means they are not typically responsive to therapies that use the body's own immune system to fight cancer, Park said. Introducing the virus reversed the tumor's harsh microenvironment, making it more receptive to receiving CAR T cell therapy.

The research demonstrates City of Hope's collaborative approach to finding better immunotherapy cancer treatments.

A few years ago, Priceman, Fong and Stephen J. Forman, M.D., director of City of Hope's Hematologic Malignancies Research Institute, met to brainstorm how they might combine their expertise, namely oncolytic virus and CAR T cell therapies, to target solid tumors.

"It was a simple concept but one that took many steps to get us to where we are today — we are now designing a clinical trial to test this combination in patients," said Priceman.

The trial will first test the safety of OV19t in patients with solid tumors. If found to be safe and effective, the oncolytic virus and CAR T cell therapy could then be tested in sequence. The trial is anticipated to start in 2022.

# Celebrating the Lives of Two Philanthropic Visionaries Who Changed Hematology

## Toni Stephenson Planted Seeds for the Defeat of Lymphoma

BY WAYNE LEWIS

City of Hope lost an extraordinary friend and steadfast supporter when businesswoman and philanthropist Toni Stephenson died on May 2, 2020. She was 74.

Prolific as both an entrepreneur and a benefactor, Toni is remembered for her deeply kind nature, her unfailing optimism and a smile that brightened any room graced by her presence. Along with her husband, Emmet, and their daughter, Tessa Stephenson Brand, she established the

Toni Stephenson Lymphoma Center at City of Hope in 2014 with a \$10 million gift. This aspect of her legacy fuels the progress of new, potentially lifesaving options for fighting the disease. On City of Hope's campus, Toni's name will continue to inspire hope in patients facing the toughest fight of their lives.

"Toni's vision, exuberance and enormous generosity have touched so many lives," said Robert Stone, City of Hope's president and CEO. "Her commitment encouraged us to dream big and to turn extraordinary science into powerful

treatments. The seeds she planted at City of Hope have grown robustly, into a dynamic research program that will carry her vision for defeating lymphoma far into the future. We were honored to count her as part of our family."

Toni is also survived by her two granddaughters — the passion of her life — as well as four siblings. Outside her business and philanthropic interests, she loved skiing, both on snow and water, as well as bowling. She was an ardent football fan who rooted zealously for the team at her and Emmet's alma mater, Louisiana State University, as well as the NFL's Denver Broncos. She enjoyed traveling with her husband, visiting 112 countries around the world together.

Toni and Emmet Stephenson were partners in business, philanthropy and life. Their love story stretched back to their first meeting as kindergarten classmates in their hometown of Bastrop, Louisiana. It continued with their courtship during college days at LSU and onward through 53 years of marriage.

Together, the Stephensons earned great success in their diverse entrepreneurial pursuits. Among more than 20 enterprises, they founded the online

publishing company Domain.com, the customer-service outsourcing business StarTek and the private equity firm Stephenson Ventures.

Business took a backseat in their lives, however, when Toni was diagnosed with T cell lymphoma in 2013.

After the cancer spread to her central nervous system, she turned to City of Hope. There, treatment from the hematology team drove the disease into remission. Her experience as a patient helped inspire her and her family to make the donation that established the Toni Stephenson Lymphoma Center,

the cornerstone of City of Hope's Hematologic Malignancies Research Institute.

"The Toni Stephenson Lymphoma Center is a testament to Toni's big heart and eagerness to give back so that patients everywhere could benefit," said Steven T. Rosen, M.D., City of Hope's provost and chief scientific officer, Irell & Manella Cancer Center Director's Distinguished Chair and Morgan & Helen Chu Director's Chair of the Beckman Research Institute. "She and her family have made a difference that will echo forward for decades to come."

Dedicated to patient-centered science, the Toni Stephenson Lymphoma Center combines lab

and clinical studies designed to advance the understanding of lymphoma and help patients enjoy longer, healthier lives — with the ultimate goal of finding cures. Research made possible by the Stephensons' contribution is pushing forward new approaches to immunotherapy, which harnesses the body's natural defenses to fight cancer, and personalized medicine, the customization of treatment to the genetic signatures of each patient's disease.

Importantly, the family's investment built up infrastructure at City of Hope that has helped to garner additional support for lymphoma investigations. To date, private donors have augmented the Stephensons' support with over \$19 million through gifts of all sizes. And thanks in part to the momentum created by the Stephensons' giving, the National Cancer Institute renewed a grant for the Specialized Program of Research Excellence for lymphoma at City of Hope in 2018, providing \$12.5 million over five years for leading-edge science.

"It's impossible to overstate the importance of the Stephensons' contribution as a magnet for further support," said Larry W. Kwak, M.D., Ph.D., director of the Toni Stephenson Lymphoma Center, deputy director of City of Hope's comprehensive cancer center and Dr. Michael Friedman Professor in Translational Medicine. "Toni and Emmet put a high priority on encouraging others to give. It takes a special kind of person to rally others to a cause like that, and Toni was a very special person indeed."

The Stephenson family's philanthropy also included substantial gifts for cancer research at USC, Tessa's alma mater, and seven programs at LSU focusing on areas from entrepreneurship to veterinary medicine. Toni was an avid volunteer in charity health care and a member of the Board of Dean's Advisors at Harvard Business School, where she had completed the Owner/President Management Program. The LSU College of Business inducted Toni into its Hall of Distinction in 2013. In 2017, Louisiana Public Broadcasting recognized her and Emmet as Louisiana Legends. "We'll remember Toni for her joy in living, her devotion to her family and her determination to bring better options to patients," said Kristin Bertell, City of Hope's chief philanthropy officer. "She inspired us all."

**"It's impossible to overstate the importance of the Stephensons' contribution as a magnet for further support."**

— LARRY W. KWAK, M.D., PH.D.



*Toni Stephenson with her husband Emmet, daughter Tessa, son-in-law Michael and granddaughter Chloe.*

# Bernard Briskin: Few Have Done More to Realize a Cure

BY WAYNE LEWIS

Bernard “Bernie” Briskin — a beloved figure in the Los Angeles business community, a champion of the local Jewish community and a generous supporter of City of Hope — died on Feb. 29, 2020, at the age of 95.

For decades, Bernie helmed the company behind the popular Gelson’s Markets. Widely admired by everyone from executive peers to frontline grocery workers, he built his career upon the timeless values of hard work, square dealing and creative problem-solving. Bernie was also well-known for his generosity as a donor to charitable causes. He and his wife, Judy, made multimillion-dollar gifts to City of Hope, establishing a multiple myeloma research program and an ultramodern clinical research space that both bear their names.

“To put it simply, Bernie and Judy transformed this institution,” said City of Hope president and CEO Robert Stone. “They targeted their philanthropy to propel City of Hope’s science toward solutions for disease. Bernie’s insightful approach has benefited — and will benefit — a multitude of patients, from the thousands receiving the newest treatments through clinical trials to the countless myeloma survivors of the future.”

Born in New York and transplanted to Los Angeles at a young age, Bernie grew up with a superb role model in the person of his father, Sam, a movie mogul who helped set the foundation for Hollywood as an industry. Among the dozens of films Sam Briskin produced over the course of decades is the Frank Capra classic, “It’s a Wonderful Life,” one of the most-watched movies ever and a fixture of holiday TV viewing.

Bernie would complete undergraduate studies at UCLA and then serve in the U.S. Marine Corps during World War II. After 10 years gaining experience working for others, he built upon his father’s example to cut his own path as an entrepreneur.

In 1963, he acquired Teleautograph, which made a predecessor to the fax machine, and was president of the company until 1978. That year, he took over as owner, president and CEO of the Arden Group, whose holdings included Gelson’s Markets, Mayfair Markets and Farrell’s Ice Cream. The business made a major turnaround under Bernie’s leadership. In 1994, he added the title of chair of the Arden Group, continuing on until his retirement in 2014.

Himself a survivor living with multiple myeloma,

in the 2010s Bernie sought to make a significant contribution to help translate scientific research into new ways to fight the disease, which has no cure — an endeavor that connected him with City of Hope.

“With their great personal warmth, their savvy and their absolute commitment to the well-being of patients, we all came to see Bernie and Judy as members of the City of Hope family,” said Steven Rosen, M.D., provost and chief scientific officer, Irell & Manella Cancer Center Director’s Distinguished Chair and Morgan & Helen Chu Director’s Chair of the Beckman Research Institute at City of Hope. “They made me feel like I was a part of their family as well. I really miss my good friend, Bernie.”

The Briskins were so impressed with the excellence of City of Hope’s myeloma investigations that they directed a substantial gift from their family foundation in 2015 to establish the Judy and Bernard Briskin Center for Multiple Myeloma Research within City of Hope’s Hematologic Malignancies Research Institute.

“With their great personal warmth, their savvy and their absolute commitment to the well-being of patients ...”

— STEVEN ROSEN, M.D.

The center fuels basic and clinical studies, as well as efforts that bridge the two.

“We will always remember Bernie with fondness and gratitude,” said Amrita Krishnan, M.D., director of the Judy and Bernard Briskin Center for Multiple Myeloma Research and professor of hematology and hematopoietic cell

transplantation. “There are few philanthropists — not just at City of Hope, but anywhere — who have done as much as the Briskins have to realize a cure for multiple myeloma.”

In recognition of the Briskins’ generosity, City of Hope named the Judy & Bernard Briskin Imaging Center in their honor, a facility where the latest technology is deployed to diagnose and treat all types of cancers.

Another major gift from the Briskins enabled City of Hope to open a central hub for clinical trials. The state-of-the-art Judy & Bernard Briskin Center for Clinical Research, opened in 2018, doubled City of Hope’s capacity for patient visits related to trials, with a focus on leading-edge technology, comfort and opportunities for social support. The Briskin Center quickly became a model for peer institutions.

“When I think of Bernie, I think of his unwavering dedication to making an impact in the lives of patients and families,” said Marwan Fakih, M.D., inaugural recipient of the Judy & Bernard Briskin Distinguished Director of Clinical Research and medical director of the Briskin Center. “The Briskins established City of Hope’s home for second chances — and third chances, and so on — where people who might’ve thought they were out of options can receive the latest treatment protocols. I’ve always been moved by how their philanthropy helps to renew these patients’ hope while also accelerating progress in science and medicine.”

Additionally, a pair of funds at City of Hope link the Briskins’ legacy with those of two City of Hope advocates who were Bernie’s close friends and longtime business associates: The Kenneth Goldman and Briskin Family Clinical Trials Program has supported tests of emerging treatment approaches for those battling multiple myeloma. The Steven Gordon and Briskin Family Innovation Grant Program has advanced high-risk, high-reward investigations that cultivate potential breakthroughs in the understanding and treatment of myeloma.

Elsewhere, the Briskins made important contributions as donors and volunteers to UCLA, Temple Israel of Hollywood, the Jewish Federation of Greater Los Angeles, the Jewish Home and Cedars-Sinai Medical Center, among others. Cedars-Sinai recognized the Briskins in 2015 with its Humanitarian Award. Bernie also received the UCLA Anderson School of Management’s John E. Anderson Distinguished Alumni Award in 2018.

Bernie is survived by his wife, Judy, eight children, 12 grandchildren and six great-grandchildren. To honor him on campus, City of Hope added his name to the wall at the La Kretz House of Hope, alongside those of his parents; each year, a *yahrzeit* memorial will be lit on the anniversary of his passing. Arrangements have also been made by City of Hope for trees to be planted in Israel in his memory, through the Jewish National Fund.

*Judy & Bernard Briskin Center for Clinical Research*





*Judy and Bernie Briskin*

# Well Said, Fred

BY ABE ROSENBERG



PHOTO BY

Former longtime Dodgers General Manager Fred Claire and his wife Sheryl

When Fred Claire was facing major surgery plus dozens of radiation sessions and multiple rounds of chemotherapy to treat skin cancer that had spread to his jaw, he received some advice from an old friend; someone he'd hired 30 years earlier.

"To get through this," the friend said, "your mind will have to be stronger than your body."

It was Kirk Gibson.

You may recognize the name.

On Oct. 15, 1988, a hobbling, badly injured Gibson rocked the baseball world with a dramatic pinch-hit home run that helped the Los Angeles Dodgers go on to win the World Series. As the Dodgers general manager and executive vice president, Claire had signed the free agent Gibson, one of many key player deals that transformed the squad into champions.

Claire spent 30 years with the Dodgers, more than a decade as general manager. Naturally he's often asked to rate the best teams he's ever seen. He doesn't hesitate.

"City of Hope," he says without even a trace of hyperbole, "is the greatest team of my lifetime!"

Claire's years-long experience with cancer and treatment at City of Hope was challenging. After his initial surgery, radiation and chemotherapy in 2016, the cancer came back aggressively, spreading to his neck. An immunotherapy clinical trial saved his life. But then an infection forced him to undergo even more extensive facial reconstruction surgery, replacing his jawbone with a bone from his leg.

Grueling. But also inspiring.

Because how he was treated at City of Hope so moved Claire, he's become one of the institution's biggest boosters, speaking out at every opportunity and organizing a pair of celebrity golf tournaments that have

raised half a million dollars.

He keeps two goals in mind: financial support of course, but more important, he wants to tell the story. It troubled him that relatively few people knew anything about City of Hope.

He decided to fix that.

The result is "Extra Innings: Fred Claire's Journey to City of Hope and Finding a World Championship Team" (Mascot Books and Amazon). Written by veteran journalist Tim Madigan, it's really multiple books in one. There are plenty of cool fly-on-the-wall stories about that miracle 1988 Dodgers championship season. Mostly though, "Extra Innings" vividly tells the 100-year-old City of Hope story.

Claire adds life to that history with memories of the remarkable people he's encountered through his own cancer journey. The stories will make you smile, make you cry and help everyone understand City of Hope's uniqueness ... which is exactly what Claire wanted more than anything.

"He is more passionate about this mission than any previous pennant race," wrote Madigan.

It shows. When Claire speaks lovingly about his doctors, it's their humanity, even more than their skills and knowledge, that he treasures. He compares them to a baseball pitching coach who once explained his formula for success: "Show them you care," the coach said, "before you tell them what you know."

And whether it's the doctors, nurses, his patient navigator, a valet parking attendant who greets folks with a cheery, "We'll take good care of you," or even the custom-built, patient-centered technology, everyone and everything at City of Hope, Claire says, is totally focused on the patients' well-being, literally "taking them by the hand," so no one ever feels alone.

Net proceeds from "Extra Innings: Fred Claire's Journey to City of Hope and Finding a World Championship Team" will benefit City of Hope.



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Aiden Anderson, a pediatric patient at City of Hope



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800-423-7119

**PATIENT REFERRAL LINE**  
(for patient-referral inquiries)  
800-826-4673

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