

C I T Y O F H O P E

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CITY NEWS


VOL. 29 NO. 1 | SPRING 2018

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BREAKTHROUGHS

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TRAILBLAZER

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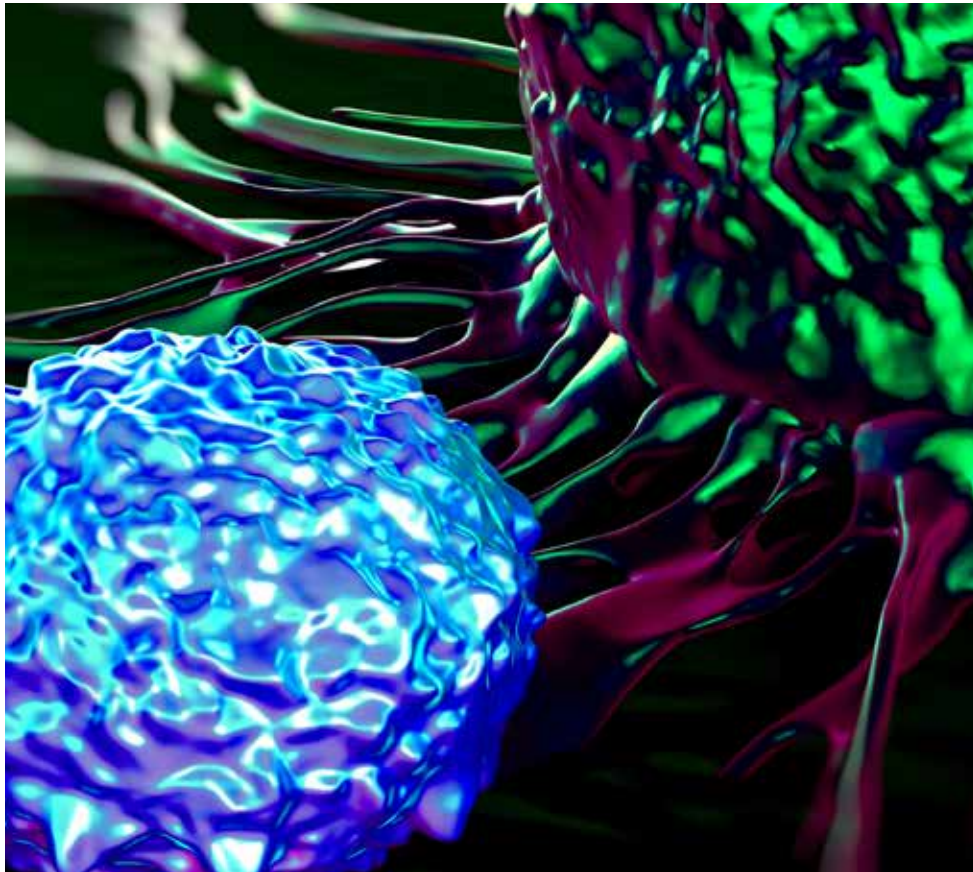
the **MIRACLE** of **SCIENCE** with **SOUL**  City of Hope®

# AN INSIDE JOB

With CAR T cell therapy, City of Hope  
physicians and researchers are enlisting your  
own immune system to fight cancer

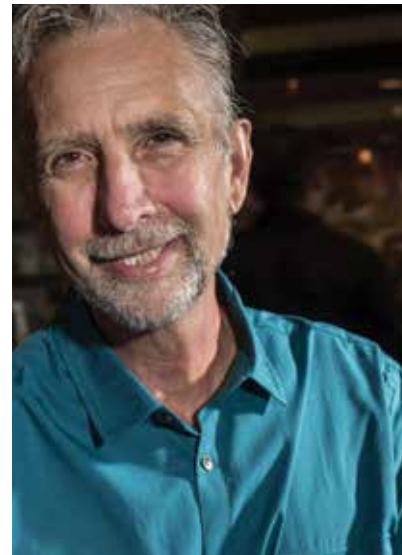
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# City of Hope®

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Associate Vice President,  
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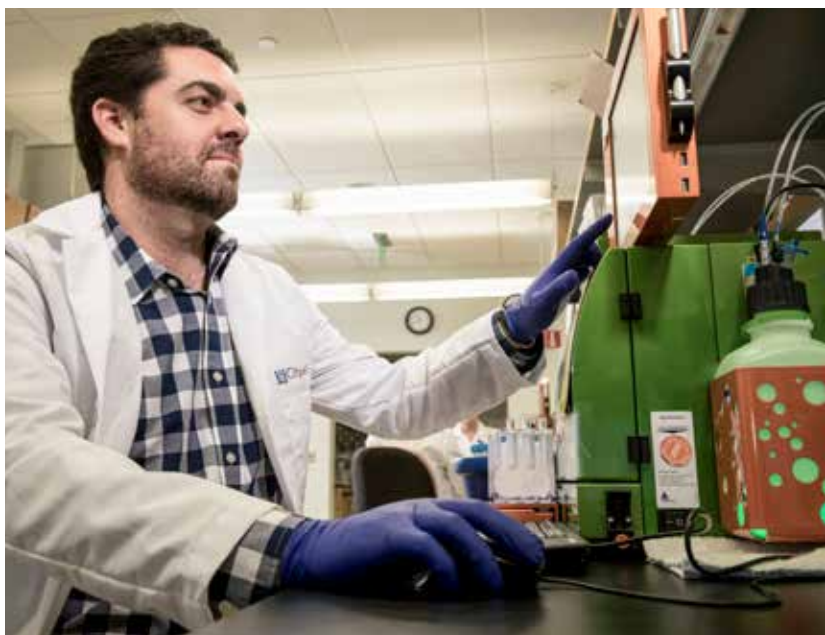
Copy Editor  
**LAURIE BELLMAN**

Printing  
**LITHOGRAPHIX INC.**

Writers  
**SAMANTHA BONAR**  
**PHYLLIS FREEDMAN**  
**DENISE HEADY**  
**WAYNE LEWIS**  
**SARAH MARACCINI**  
**LETISIA MARQUEZ**  
**ABE ROSENBERG**

Photographers  
**THOMAS BROWN**  
**VERN EVANS**  
**CRAIG TAKAHASHI**





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Hopeful.org

*Your Thoughts, Your Wishes, Your Community*

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



# LEADERSHIP MESSAGE

Revolutionary. Game-changing. Lifesaving.

Those are the words physicians and scientists – moderate, careful individuals who are not given to rash pronouncements – are using to describe CAR T cell therapy.

CAR T cell therapy – the science of re-engineering immune cells into potent cancer-killers – is delivering remarkable results. Remissions are happening. Tumors are disappearing. FDA-approved treatments are emerging. Innovative clinical trials are being developed with the potential to cure the previously incurable.

Across City of Hope, we feel the optimism – an example of our commitment to speed tomorrow's discoveries to the people who need them today.

We stand at the center of this transformational advance, thanks to the hard work and inspired genius of our people.

This issue focuses on our CAR T cell journey, from its earliest origins to today's stunning realities. You will see a record of success and seemingly endless potential, as our clinicians and researchers target one disease after another: from blood cancers to glioblastomas to prostate and breast tumors.

We have one of the most comprehensive CAR T cell clinical research programs in the world, and we are a preferred research and production partner for key biopharmaceutical companies working in this field. The FDA recently approved the first CAR T cell therapy for adult patients with certain types of non-Hodgkin lymphoma and we are one of the first authorized centers to provide this treatment.

Like every achievement at City of Hope over the past century, our CAR T cell breakthroughs are made possible by the teamwork of our staff, our volunteers and our community of donors and supporters. We are poised to take steps we will be telling our children about, years from now. I am proud to be taking those steps together with you.

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



# cityBUZZ



*Clockwise from lower-left: Dodgers outfielder Kike Hernández (right) with his father (left) and Stephen J. Forman, M.D.; City of Hope riders with Los Angeles Mayor Eric Garcetti; the final float on parade*

## Hope on Parade

For the 46th year in a row, City of Hope participated in the Tournament of Roses Parade. This year, 10 patients welcomed 2018 atop City of Hope's Rose Parade float, which won the Isabella Coleman Award for "Most outstanding presentation of color and color harmony through floral design." The float riders included 26-year-old Dodgers outfielder Enrique "Kike" Hernández, whose father battled multiple myeloma.





The board of City of Hope's Music, Film and Entertainment Industry Group with Robert W. Stone (top left), Coran Capshaw (center) and Dave Mathews (right of center)



# Spirit of Life®

City of Hope's Music, Film and Entertainment Industry Group presented its 2017 *Spirit of Life*® Award to Coran Capshaw during a November gala in Santa Monica, California. The event raised more than \$4 million for City of Hope.

Focused on management, touring, branding, venues, festivals and record label interests, Capshaw is one of the music industry's most influential and innovative executives.



Joseph, an all-female musical trio



Dave Matthews



Trey Anastasio



The legendary Preservation Hall Jazz Band





Clive Davis



Hans Zimmer

# Songs of Hope

Music industry luminaries were honored at the annual Songs of Hope event, held this year in Sherman Oaks, California. On hand for the festivities were legendary music executive and record producer Clive Davis; Grammy-winning songwriter Max Martin; Academy Award, Golden Globe and Grammy-winning composer Hans Zimmer and EDM-pop duo The Chainsmokers.

Also at the event, representatives of the Horowitz family presented the inaugural Songs of Hope Beverly and Ben Horowitz Legacy Award. The award, which honors a City of Hope researcher with \$100,000 to further his or her research, was given to Saul Priceman, Ph.D.

# Walk for Hope

On a crisp Sunday in November, survivors and supporters — women, men and children — were united in the fight against women's cancers during the annual Walk for Hope, a 2K/5K walk on the City of Hope main campus. This year's event raised more than \$1 million for City of Hope.

City of Hope President and CEO Robert W. Stone (left) receives a check from Dunson Cheng of Cathay Bank. Cathay Bank employees raised \$260,000 for City of Hope.



Participants in Walk for Hope raised more than \$1 million for City of Hope.





# Q & A with Michael Caligiuri, M.D.



## We sit down with the new president of City of Hope National Medical Center and the Deana and Steve Campbell Physician-in-Chief Distinguished Chair

**City News:** Let's start with the question we're all most curious about: Why did you decide to come to City of Hope? What makes City of Hope special?

Michael Caligiuri: I think first and foremost I was extremely attracted by the senior leadership team at City of Hope, the culture of City of Hope and the organizational structure at City of Hope. I feel strongly that at City of Hope, the patient comes first.

The other thing that was very attractive to me was the huge entrepreneurial effort, spirit and culture that is City of Hope.

**CN:** Can you identify one or two things that you're most excited about at City of Hope?

Michael Caligiuri: I would say it's the focus on the patient from every dimension at City of Hope — all the way from basic and population science right to the bedside. It's the leadership that's in place. You know, you're inspired by leaders, and I really was really impressed during my first meeting with Robert [Stone]. I described him as 'true north,' fully committed to the cause. He's a wonderful human being, and very, very inspirational, and I'm going to enjoy working for him.

**CN:** What's your vision for City of Hope — and cancer care — in the 21st century?

Michael Caligiuri: As you know, the whole delivery of care is coming down to the individual patient. It's about using molecular biology, population science [and] computational biology to determine what's good for a particular patient. And as I see it, City of Hope is poised to be a leader in that particular arena, especially given the alliance with TGen.

**CN:** Tell us a little bit about how TGen (Translational Genomics Research Institute) fits in.

Michael Caligiuri: As you are likely aware, no two tumors are the same. If everybody in this room has lung cancer, the likelihood that a single treatment would work for everyone is zero. The reason for that is that while under the microscope a tumor looks like lung cancer, at the molecular level it doesn't. So having our own assets, our own pool of talent to elucidate the genetic and the molecular makeup of cancer is going to be critically important to the rapid turnaround that's required when someone is diagnosed with cancer.

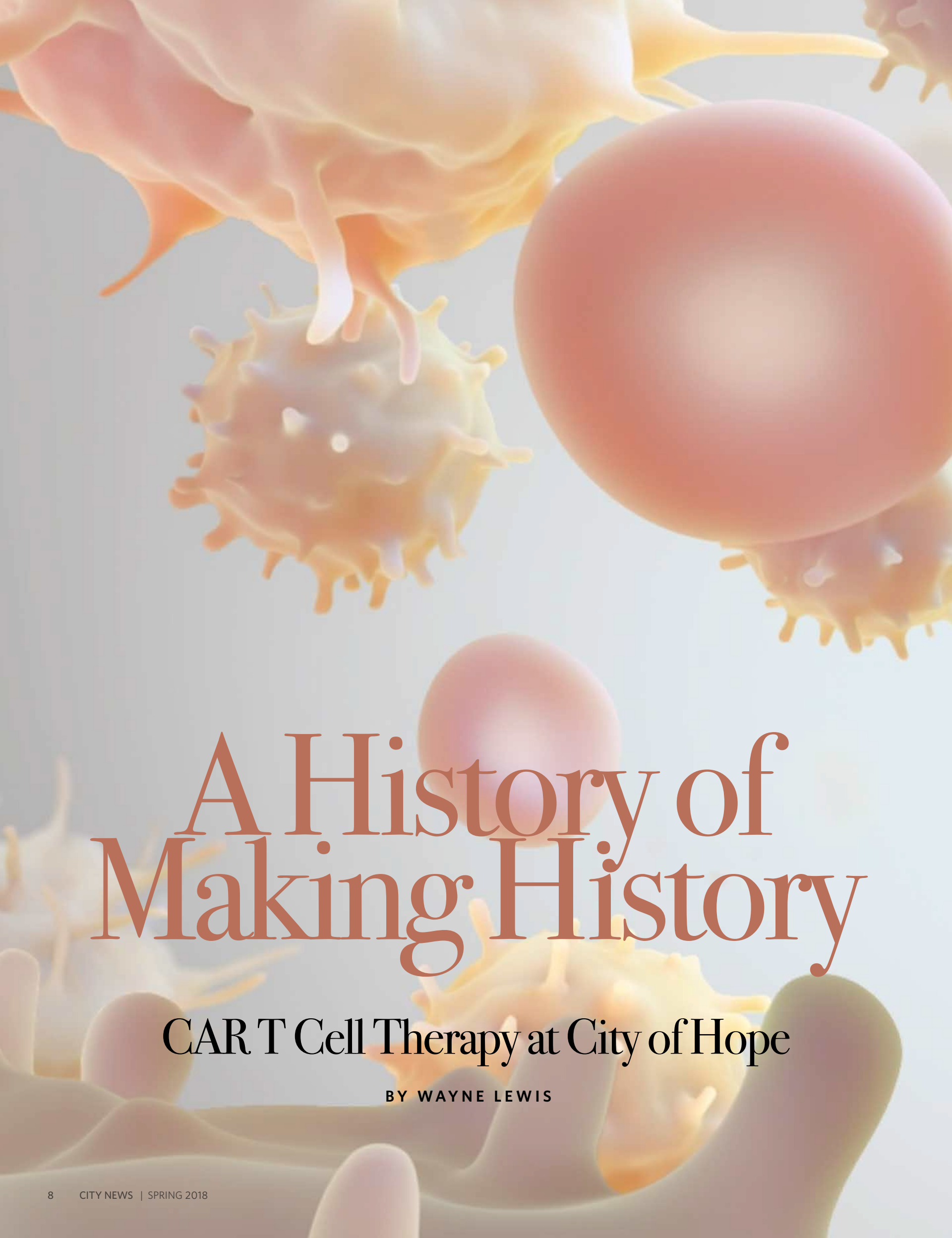
It's going to be really important to practice predictive medicine, which is where City of Hope is going. It's no longer about reacting to cancer. It's about being preemptive, predictive. And understanding the genetic basis of cancer, having access to the world's best minds and tools to look at the genetic predisposition of cancer, is going to be critically important. This is where TGen fits in.

**CN:** We're really excited — for obvious reasons — about immunotherapy, and CAR T in particular. Do you share that enthusiasm?

Michael Caligiuri: Oh, absolutely. My whole area of expertise is immunoncology. I've been working in natural killer cell biology for 27 years, and I also work in hematologic malignancy. So, for me, the time and the place is the perfect storm: City of Hope is a world leader in cancer immunotherapy. It couldn't be any better. It's the perfect opportunity for me to contribute to what is already an amazing effort by Steve Forman, Guido Marcucci, Christine Brown and many others.

**CN:** And you'll be joining some old friends here to accelerate our impact?

Michael Caligiuri: Yes, you know, I've been good friends with Steve Forman for three decades. And then there's Steve Rosen, who I've known for two decades as cancer center directors. In fact, I've been on Steve's board at Northwestern, so I was able to see his genius at work there. And Guido Marcucci trained in my lab more than 20 years ago, and I had the pleasure of working side-by-side with him as co-authors and collaborators on grants for 15 years. And folks like Kim Margolin, Vicky Seewaldt, Lisa Yee, Linda Bosserman, Larry Kwak are people I've had the pleasure of working with in my career. So I'm very, very excited about getting back together with good friends, continuing to work as colleagues and seeing if we can move the needle even quicker.



# A History of Making History

CAR T Cell Therapy at City of Hope

BY WAYNE LEWIS



A microscopic view of various cells, including a large, irregularly shaped cell with a prominent nucleus and several smaller, round cells, all set against a light, warm-toned background.

Biomedical history was made in 2017.

It was the year in which gene therapies first gained approval from the Food and Drug Administration (FDA). And the first two such treatments to be approved had something in common: They were cancer-fighting immunotherapies known as CAR T cell therapy. The basic idea? Retrain a patient's own cells to attack the disease.

This watershed moment for medical science meant a lot more than new treatments on the market. It could usher in an age of safer and more effective ways to combat cancer and other life-threatening diseases. The triumph carried particular resonance at City of Hope. After all, researchers here have been at the forefront of the science behind CAR T cell therapy for decades.



The search for better, more effective therapies comes naturally to City of Hope. So says CAR T cell therapy pioneer Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation.

“City of Hope has accepted the challenge to try to develop a therapy that can be used for patients with many different types of cancers,” said Forman, who leads the Hematologic Malignancies and Stem Cell Transplantation Institute. “Our CAR T program here is focused not only on leukemia, lymphoma and myeloma, but also on solid tumors including breast cancer, liver cancer, brain cancer, prostate cancer and ovarian cancer, as a way to offer effective immunotherapy options for difficult-to-treat cancers.”

## SOLDIERS OF THE IMMUNE SYSTEM

Many understand the immune response as pitting the body against invading germs. But our natural defenses also take care of menaces that arise from within. One such menace might be abnormal tissue that threatens to grow out of control.

Cancer takes hold when such aberrant cells evade the immune response. CAR T cell therapy aims to re-arm that response.

“T cells are like soldiers of the immune system,” said Christine Brown, Ph.D., the Heritage Provider Network Professor in Immunotherapy and associate director of the T Cell Therapeutics Research Laboratory at City of Hope. “They’re white blood cells, and their normal job in the body is to eradicate unwanted cells. So the goal is to use the immune system and T cells to help eradicate cancer.”

In this approach, the medical team starts with T cells drawn from a patient. They augment this raw material with lab-made chimeric antigen receptors — the “CAR” in “CAR T cell.” The enhancement

enables cells to identify a specific cancer by its signature protein. The therapeutic cells are expanded in the lab to a population in the billions and then reinfused into the patient. Back in the theater of immune combat, they do their cancer-fighting work without hurting healthy tissue.

## A POSITION OF LEADERSHIP

Studies into modifying T cells for attacking cancer began at City of Hope in the late 1990s. This early work, spearheaded by Michael Jensen, M.D., and Forman, led to a number of milestones that have helped to move CAR T cell therapy forward.

City of Hope initiated some of the first clinical trials anywhere testing CAR T cell therapy against lymphoma, neuroblastoma, glioblastoma and glioma. In 2013, Forman’s team would become the first ever to integrate CAR T cells into a stem cell transplant for malignant lymphoma, in an approach unique to City of Hope. The following year, City of Hope became the first institution where patients with a blood cancer called acute myelogenous leukemia could receive CAR T cell therapy through a clinical trial.

On multiple occasions, City of Hope clinicians have reported that CAR T therapy enabled patients with few choices to achieve full remission. One such case study, of a patient who faced glioblastoma, appeared in 2016 in the *New England Journal of Medicine*.

City of Hope, with its clinical care, research and production facilities all on one campus, is uniquely positioned to lead this work. Few institutions are capable of harnessing the same comprehensive “bench to bedside” resources necessary for the discovery, translational research, clinical development, manufacturing, quality assurance and delivery of leading-edge treatments for our patients. City of Hope has the ability to harvest, reprogram, multiply and deliver T cells all on the same campus.

“Without the support of our manufacturing colleagues, none of our CAR T successes would be possible,” said Forman. “It’s people like [regulatory operations manager] Jamie Wagner and [leader of the CAR T cell manufacturing team] Araceli Naranjo who enable us to get these lifesaving treatments to patients.”

## BUILDING FUTURE CURES

Today, City of Hope leads more than a dozen studies offering CAR T cell therapy to patients confronted with cancers that resist treatment. Within the next year, numerous clinical trials will open for solid tumor cancers. City of Hope also will be one of the first medical centers where patients can receive axicabtagene ciloleucel, one of the first FDA-approved CAR T cell therapies for lymphoma (*see sidebar below*).

Grant makers have taken note of City of Hope’s influential position. In October 2017, the California Institute for Regenerative Medicine, the state’s stem cell agency, awarded City of Hope scientists Brown and Behnam Badie, M.D., \$13 million. That grant supports an early-stage trial for glioma patients. In this study, City of Hope researchers are enhancing memory T cells, a specific immune cell that provides the body with a lasting archive of defenses against the diseases it has faced.

Building on early successes against cancers of the blood and brain, City of Hope researchers continue to explore ways to improve the performance of CAR T cell therapy and to broaden its scope to attack more types of tumors, as well as HIV/AIDS.

“There are a lot of challenges, but we think we have a good strategy,” said Xiuli Wang, Ph.D., research professor of hematology and hematopoietic cell transplantation. “The current treatment cannot cure HIV/AIDS, and CAR T cells have a better chance to find and kill the virus.”

### LIFELINE:

## First FDA-approved CAR T Cell Therapy for Certain B Cell Lymphomas Available at City of Hope

It’s a breakthrough treatment for one of the most common cancers in the United States — and it’s now available at City of Hope.

City of Hope is one of the first authorized centers in the nation to provide axicabtagene ciloleucel, which the U.S. Food and Drug Administration (FDA) announced is the first approved CAR T cell therapy for adult patients with certain types of B cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment. This is the second CAR T therapy approved by the FDA and the first for certain types of non-Hodgkin lymphoma (NHL).

CAR T cell therapy is one of the most promising areas of cancer research and treatment. Using this approach, immune cells are taken from a patient’s bloodstream, reprogrammed to recognize and attack a specific protein found in cancer cells, then reintroduced into the patient’s system, where they get to work destroying targeted tumor cells.

With axicabtagene ciloleucel, a Gilead therapy, a patient’s T cells are engineered to express a chimeric antigen receptor (CAR) to target the antigen CD19, a protein found on the cell surface of NHL, as well as other lymphoma and leukemia cells.

“City of Hope has been a pioneer in CAR T therapy for nearly two decades. CAR T therapy research is part of our deep commitment to advancing the most innovative treatments for cancer patients worldwide,” said Steven T. Rosen, M.D., City of Hope’s provost and chief scientific officer, and the Irell and Manella Cancer Center Director’s Distinguished Chair. “The FDA’s approval of axicabtagene ciloleucel marks an important milestone and advance in cell-based therapy for NHL patients. City of Hope is uniquely positioned to begin offering treatment immediately to those patients who desperately need new treatment options.”



#### STEP 5:

### TARGET AND DESTROY

They multiply inside the patient's body and, with guidance from their engineered receptors, are able to recognize and then kill cancer cells.

#### STEP 1:

### ISOLATE

T cells are isolated from the patient by way of a specialized blood draw.

#### STEP 2:

### REPROGRAM

The T cells are then reprogrammed to produce special receptors on their surface called chimeric antigen receptors, or CARs. This enables the T cells to better recognize tumor cells.

## How Does CART Cell Therapy Work?

#### STEP 4:

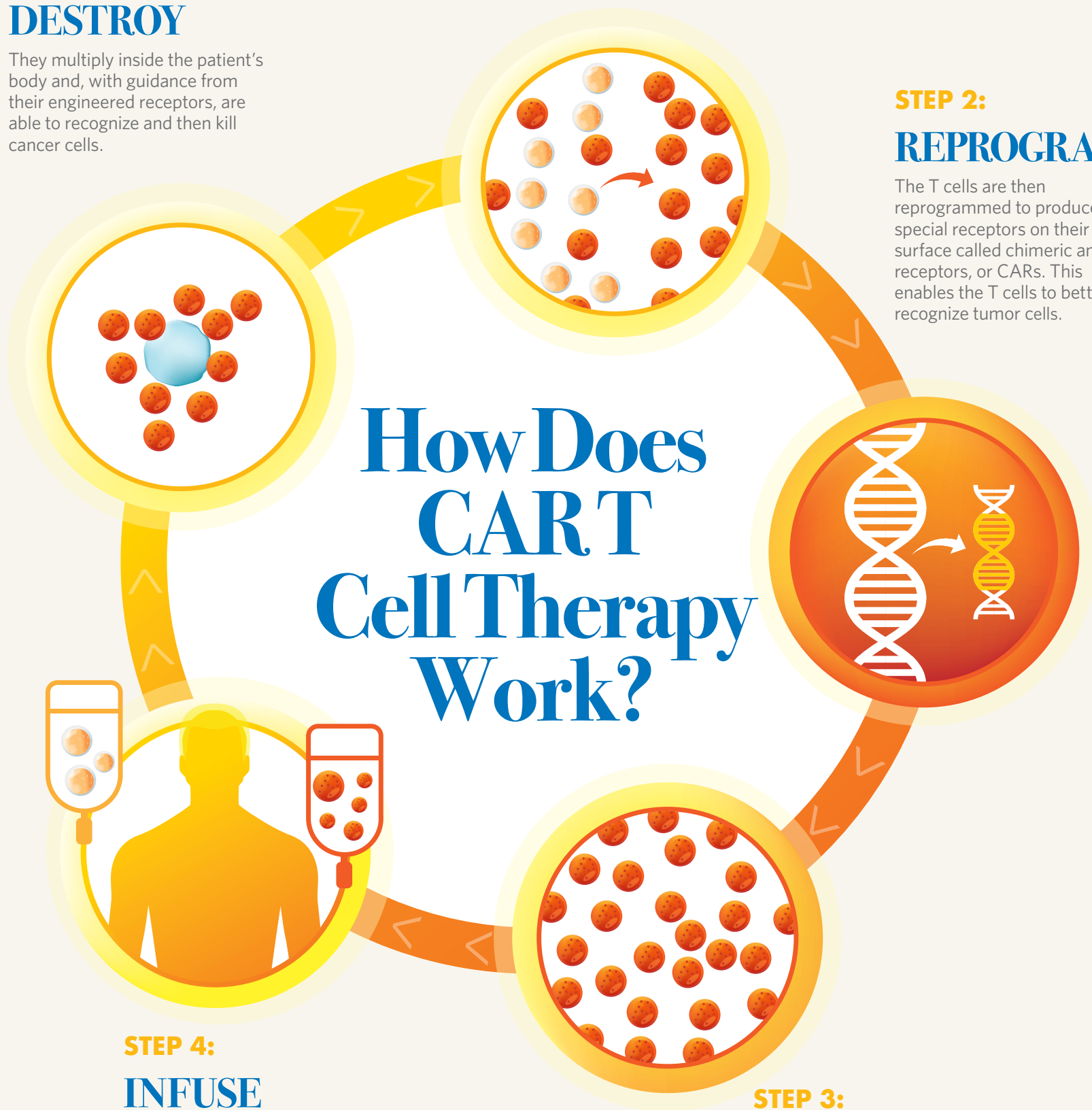
### INFUSE

CAR T cells are infused back into the patient.

#### STEP 3:

### EXPAND

The engineered CAR T cells are then grown in the laboratory until they number in the billions.








# ‘I Am Happy for Every Single Day I Have’

HOW CAR T CELL THERAPY  
SAVED CHUCK FATA’S LIFE

BY LETISIA MARQUEZ

Chuck Fata had tried every treatment possible for the aggressive blood cancer he was fighting — diffuse large B cell lymphoma — by the time he turned his hopes to an innovative treatment he had never heard of: chimeric antigen receptor (CAR) T cell therapy.





Fata's treatment journey began in February 2014 when he was diagnosed with DLBCL, a type of non-Hodgkin lymphoma which attacks the immune system's B cells. He received intensive chemotherapy and went into remission for several months.

But in the winter of 2015, a PET scan showed a little spot of the cancer close to Fata's stomach. He subsequently underwent an autologous bone marrow stem cell transplant (using his own stem cells) in May 2015 and spent 17 days in a local hospital recovering from the transplant.

On one of those days, he watched a livestream of his oldest daughter, Chloe, receiving a master's degree in education from USC. Later in the day, she visited him, dressed in her cap and gown. It reminded Fata of all he had to fight for.

## MAN ON A MISSION

Fata, 60, the owner of the popular Charlie's Trio restaurants in Los Angeles and Alhambra, felt fine for a few months until doctors found another stomach tumor. He started bleeding internally. A surgeon wanted to remove his entire stomach, but Fata joked that "you can't be a restaurant owner without a stomach."

Half of Fata's stomach, the tail of his pancreas and spleen were removed in a seven-hour surgery. He started recovering and was scheduled to start radiation to target other remaining cancer spots in his stomach, but by then the cancer had spread to the lymph nodes in Fata's neck and other areas.

That's when Fata's doctors suggested CAR T cell therapy, a type of immunotherapy that harnesses the power of a patient's own immune system by genetically engineering the patient's T cells, a type of white blood cell, to recognize and attack cancer cells. He received the experimental treatment at City of Hope in February 2016 as part of the ZUMA-1 phase 1 clinical trial sponsored by Kite Pharma Inc. A month after the CAR T treatment, Fata achieved complete remission, and has been in remission since then.

"I am happy for every single day I have, and I credit CAR T therapy and City of Hope for that," he said.

The ZUMA-1 clinical trial that Fata participated in was pivotal in the Oct. 18 Food and Drug Administration's approval of axicabtagene ciloleucel (axi-cel) for adult patients with certain types of large B cell lymphoma.

City of Hope was one of the first four sites worldwide to enroll patients in this trial.

"I'm extremely thankful for what I have now," Fata said. "I'm glad it's getting approved and that people are going to get this opportunity. I hope they are as lucky as I am. I never thought I would end up feeling this great."

## FAMILY BUSINESS

Fata was 14 years old when he helped his father, Charles Jr., start a small pizza restaurant — Charlie's Trio, named after Fata's grandfather, father and himself — in the El Sereno neighborhood of Los

Angeles. By 20, Fata owned the restaurant, which he later expanded with his brother, Mike, to a full-scale Italian restaurant and bar, which now includes a second location in downtown Alhambra. Fata also co-owns the 38 Degrees Ale House & Grill in Alhambra and Monrovia.

In early 2014, Fata thought the pain he felt was just a back problem, perhaps due to a busy schedule that included keeping tabs on the four restaurants and running six miles several times a week.

The first doctor Fata saw thought the same.

"He assumed I was hurting myself from all the activity," Fata said during a recent interview at one of his restaurants. "There wasn't anything significant that suggested I had cancer."

But the back pain worsened and three months later, an MRI found four tumors, including two that were "a pretty good size" on lymph nodes near his heart.

"It was just a shock," he said. "I had just finished running a half marathon in Las Vegas."

Because Fata's cancer resisted chemotherapy and an autologous stem cell transplant, he was eligible for the CD19 CAR T therapy trial at City of Hope.

"Things weren't looking too good at that point," Fata said. "I was running out of options."

## THE COMEBACK

Fata had also lost weight and his hair, and he felt weak.

He read a lot about the therapy before putting his faith in City of Hope, including Fata's hematologist/ oncologist and City of Hope principal investigator of the ZUMA-1 phase 1 trial, Tanya Siddiqi, M.D.

Fata knew he would experience side effects as the infusion of T cells ramped up their immunological power and fought off cancer cells.

"It was harder on my family than on me because they had to see it," Fata said. "I felt so weak after the CAR T. My body had been through almost two years of treatment. I was so tired and beat up."

Despite all that, Fata never lost his positive attitude.

"He has a great sense of humor," Siddiqi said. "He was very brave and positive despite having relapsed after so many treatments when I first saw him."

On the day he was going to find out if the CAR T therapy worked, Fata was emotionally drained.

"When Dr. Siddiqi told me I was in remission, it was like, 'All right, back on the comeback trail one more time,'" Fata said. "I got my miracle."

Today, Fata is back to managing four restaurants. He is playing racquetball again with friends and running as much as three miles a day.

"He is an inspiration to many of us at City of Hope," Siddiqi said.

For his part, Fata said he appreciates each and every day.

"I feel great. All of this didn't seem possible before CAR T," Fata said. "Every day is a blessing. Every day is overtime. I'm gonna make the most of it."

*Chuck Fata*





*Elizabeth Budde, M.D., Ph.D.*



*Samer Khaled, M.D.*

# Cell Mates



*Alex Herrera, M.D.*



*Tanya Siddiqi, M.D.*

**BY LETISIA MARQUEZ**



# New immunotherapy breakthroughs — including several involving CAR T cell therapy — were recently announced by City of Hope physicians.

Among the announcements, City of Hope doctors revealed that patients whose acute myeloid leukemia (AML) was no longer responding to standard therapies, along with a patient with a rare blood cancer called blastic plasmacytoid dendritic cell neoplasm (BPDCN), achieved a complete response after undergoing treatment with CAR T cell therapy.

Of note, the City of Hope BPDCN patient is the first to achieve a complete response to a CAR T cell therapy. This is also the first in-human trial for AML and BPDCN patients using a CD123 CAR T cell therapy.

The therapy, which was developed at City of Hope, was also safe and well-tolerated in patients enrolled in the phase 1 clinical trial.

“This is a very promising CAR T cell therapy for AML and BPDCN patients and furthermore, the side effects they experienced from the therapy were treatable and manageable,” said Elizabeth Budde, M.D., Ph.D., an assistant professor in the City of Hope Department of Hematology & Hematopoietic Cell Transplantation.

## CAR T CELL THERAPY FOR NON-HODGKIN LYMPHOMA

Tanya Siddiqi, M.D., assistant clinical professor in City of Hope’s Department of Hematology & Hematopoietic Cell Transplantation, reported on the first multicenter phase 1 trial of JCAR017, a Juno Therapeutics CAR T cell therapy that targets CD19 cells in refractory/relapsed aggressive B cell non-Hodgkin lymphoma.

JCAR017 (lisocabtagene maraleucel/liso-cel) is a CAR T cell product administered at precise doses. The trial hypothesized that the lack of product variability may better enable the identification of patient factors that are associated with clinical outcomes.

To that end, Siddiqi and fellow researchers performed exploratory analyses that show that baseline patient characteristics like a high tumor burden (a high number of cancer cells or tumors), high LDH (a metabolic enzyme in cancer cells) and elevated levels of inflammatory markers, such as ferritin, are associated with higher CAR T cell expansion and increased rates of cytokine release syndrome and neurotoxicity.

“However, it may be possible to plan trials in the future around strategies to reduce risk of toxicity in patients with higher baseline burden of disease, higher LDH and inflammatory state,” Siddiqi said. “Such patients also have higher expansion of CAR T cells in their blood but durability of responses seem to be lower in them at the three-month mark post-CAR T cells, possibly due to rapid T cell exhaustion.”

Preliminary modeling efforts suggest that a therapeutic window may exist for CAR T cell expansion that could limit toxicity and optimize efficacy, Siddiqi added.

## CAR T CELL THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

As a translational researcher, Samer Khaled, M.D., plays a vital role on City of Hope’s CAR T cell team, linking basic science to clinical protocol and vice versa. He helped develop a clinical trial testing the immunotherapy against acute lymphoblastic leukemia (ALL). The medical director of hematology/hematopoietic cell transplantation clinical operations, he also is part of a group that is drawing up policies that will govern treatment using CAR T cells.

Of this task connecting research innovation with compassionate care — two key focuses at City of Hope — Khaled said: “We want to streamline the process, from patient selection to treatment to follow-up.”

The stakes are high, both for the protection of patients and the future of a potential cure.

It is appropriate, Khaled pointed out, that City of Hope should be advancing a potentially groundbreaking investigational treatment that empowers the body’s natural defenses. After all, in the 1970s City of Hope was among the first biomedical centers anywhere to perform a successful blood stem cell transplant — as Khaled calls it, “the mother of all immunotherapies.”

In CAR T cell therapy, Khaled sees the chance one day to replace the transplant and chemotherapy. One clinical trial for patients with persistent ALL is showing tremendous early success.

“There is huge potential right now that we can actually control disease that we never thought we could before,” he said. “As long as you know the right target, you can use CAR T cell therapy.”

## CLINICAL TRIAL OUTCOMES FOR COMBINATION IMMUNOTHERAPY SHOW PROMISE

Alex Herrera, M.D., assistant professor in City of Hope’s Department of Hematology & Hematopoietic Cell Transplantation, recently presented positive results from a clinical trial using a combination of two immunotherapy drugs — brentuximab vedotin and nivolumab.

The study, led by Herrera and involving cancer researchers from around the country, tested the combination therapy in patients with classical Hodgkin lymphoma whose cancer had relapsed or was resistant to traditional therapies. This population accounts for 10 to 30 percent of Hodgkin lymphoma patients, who are typically treated with traditional and often harsh chemotherapies followed by an autologous stem cell transplant, which uses a patient’s own stem cells. Sixty-two patients were enrolled to test whether brentuximab vedotin and nivolumab might be a more tolerable way for patients to fight the disease before a transplant.

Participants received brentuximab vedotin and nivolumab as an outpatient regimen in three-week cycles for up to 12 weeks. The complete response rate among all treated patients was 61 percent, while the overall response rate, which includes those participants who had a partial response, was 82 percent. For those patients who did not have a complete response, most were able to respond to subsequent therapies and proceed with a stem cell transplant.

“The combination was a safe, well-tolerated and highly effective bridge to transplantation,” Herrera said. The study results were also published in the latest version of the journal *Blood*.

Brentuximab vedotin is an antibody-based treatment that targets delivery of chemotherapy only to Hodgkin lymphoma cells; nivolumab works by blocking the PD-1 immune checkpoint pathway, which tumors often hijack to evade the immune system.

“Now we have shown that the combination is an effective second-line treatment for Hodgkin lymphoma and future trials could explore the role of this regimen in comparison to traditional second-line chemotherapy,” Herrera said.



Christine Brown, Ph.D.

# CART Crusader

BY ABE ROSENBERG

PHOTO BY VERN EVANS



"I guess my timing was lucky."

Christine Brown, Ph.D., the Heritage Provider Network Professor in Immunotherapy, is explaining how, 15 years ago, she happened to join a City of Hope research team that's rewriting the book on brain cancer — literally one cell at a time.

Luck had little to do with it.

"She's smart. She's fearless. She asked the right questions," said Michael Barish, Ph.D., chair and professor in the Department of Developmental and Stem Cell Biology, recalling their first meeting. An early mentor, he saw Brown's potential immediately.

"She thinks widely and deeply," he added. "She willingly entertains out-of-the-box ideas."

Perfect qualities, you might say, for addressing a uniquely out-of-the-box idea: extracting a patient's immune cells, engineering them into living, anti-cancer CAR T cells, multiplying those super-cells by the billions, then injecting them back into the patient.

And watching tumors disappear.

"Back in 2002 when I came aboard," Brown recalled, "CAR T cell therapy was in the early stages of clinical optimization. We didn't know at the time how successful it would be, progressing to where it is today, an actual commercial product that's helping people." (Note: the Food and Drug Administration (FDA) has recently approved two forms of CAR T cell therapy for treating blood cancers.)

Brown reflects back on those early days and is amazed at the progress. Along with Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, Brown runs the T Cell Therapeutic Research Laboratory, which to date has treated more than 100 patients in seven clinical trials, with aggressive goals of opening four new clinical studies within the year.

## 'I STILL GET CHILLS'

Brown knows that extending CAR T cells to solid tumors is going to be particularly challenging, and her research has been focused on developing CAR T cells for the treatment of malignant brain cancers, some of the most lethal and difficult-to-treat solid tumors.

Working together with a clinical team led by neurosurgeon Behnam Badie, M.D., Brown and her fellow researchers are unleashing CAR T cells on these historically stubborn tumors. The project is still in phase 1 clinical trials but researchers already know it works ... often with breathtaking speed.

"I still get chills when I look at the scans," Brown said, remembering one case: "21 days and the disease was disappearing!"

More and bigger chills may be coming, courtesy of the California Institute for Regenerative Medicine. CIRM has awarded a \$12.8 million grant to Brown, Badie and their teams to take CAR T cell therapy for brain cancer to the next level. Clearly, CIRM believes in CAR T's potential and in City of Hope's ability to maximize it.

"City of Hope was the first to try CAR T cells on brain tumors," said Brown, adding that the decision required a certain "audacity."

"We were the first to inject those cells directly into the brain, right into the tumor, as opposed to the bloodstream. And now we're the first to introduce CAR T cells into the cerebrospinal fluid (found in the brain's lateral ventricles, the large cavities in each cerebral hemisphere).

"We're looking for the best method and location" to provide maximum benefit and safety.

Their learning curve was aided immensely by the exceptional contributions of one patient, Richard Grady, M.D., a pediatric urologist who came to City of Hope in 2015 with recurring brain tumors. The CAR T cell trial was his last hope.

## AN INSPIRING FRIENDSHIP

It worked, up to a point. Grady lived another 20 months.

"Rich's response to the CAR T cell therapy was nothing less than remarkable, miraculous even," wrote Badie shortly after Grady's death. "His glioblastoma had gone into remission and history

'I'm so  
excited about  
where we're  
headed.  
We're on the  
cusp of such  
tremendous  
potential.'

was made. His largest removed tumor, where the CAR T cells were infused, never returned."

Other tumors, however, away from the CAR T cell infusion site continued to grow. So Brown and Badie and their colleagues took the steps necessary to receive approval from the FDA to inject the cells into the cerebrospinal fluid, hoping the therapeutic cells would better distribute throughout the brain to target his other tumors. Delivery into the cerebrospinal fluid had never been done before. After several CAR T cell infusions Grady's disease was eliminated and his life extended. His tumors eventually returned in different parts of his brain, even more aggressively than before. While the team had extended his life, they were unable to keep up with the rapid spread of his disease.

During treatment, Brown developed a deep friendship with Grady and his wife, Laura Hart, M.D.

"On the first day Rich and I met her," Hart recalled, "I said to myself, 'This is a caring person.' We saw how well-spoken she was, how excited she was about Rich's treatment. We toured her lab. We talked at length about the scientific challenges. And always, she showed such aplomb and graciousness. She's confident, collected, with a

kindness and generosity of spirit you don't typically find in basic scientists who never see actual patients.

"She's just a lovely human being."

It simply isn't Brown's style to maintain distance and separation from patients who will benefit from her work. On the contrary, they motivate her.

"Sure, as a scientist I'm shielded a bit," admitted Brown. "But you know, we do talk about the patients, and when you hear their stories, what they've gone through ... it makes me want to do better."

It's not her only motivation. Brown personally understands the shock and fear that accompany a cancer diagnosis. In 2012, she was diagnosed with Stage 2 breast cancer.

Now, after treatment, she remains cancer-free. But she remembers.

"It felt so surreal," she recalled. "I couldn't believe it was happening to me. I was healthy. I'd gone for regular checkups, done all the right things to take care of myself. Nobody in my family had ever had breast cancer. And still. It really drove home the reality that cancer can strike anybody."

It did more than that.

"Before, I thought of my work as the study of populations with cancer. Not anymore. Cancer is a personal disease that strikes people. People just like me. It's been a defining, life-changing experience for me. And I truly want to make a difference!"

Making a difference — and making it personal — appear to run in the family. Brown's father plays in a charity golf tournament that supports his daughter's work. When Brown's 19-year-old nephew, Nick, lost his grandmother to brain cancer, he organized a fundraising hike of the 2,659-mile Pacific Crest Trail and wrote a \$1,500 check to Aunt Christine. "I couldn't think of a better place to make a donation," he said.

At home, "Aunt Christine" is married to biotech executive John Desjarlais ("We compete," she laughed, "in a fun way.") They have a 13-year-old daughter and 15-year-old son. Brown's downtime generally involves yoga ("keeps me sane").

Not that there's very much downtime to speak of.

"She's always strategizing for the future," said Hart, "looking for new ways to replace darkness with light."

## LOOKING AHEAD

"She is excellent at identifying the critical missing experiments that will complete a story," added Barish.

And she can't wait to put those missing pieces into play.

"I'm so excited about where we're headed," said Brown. We're on the cusp of such tremendous potential. Yes, there are plenty of obstacles still out there, but we have so many ideas for overcoming them. We are not out of ideas. Whatever problems remain, I think we're going to solve them."

Are we talking "cures?"

"Knocking on wood!" she smiled.



# Passion & Persistence: Meet CAR T Researcher Xiuli Wang, Ph.D.

At six in the morning, and even on Saturdays, you'll often find Xiuli Wang, Ph.D., at her laboratory at City of Hope. Her work is so compelling, she just can't stay away.

"All my passion," she said, "is focused on finding a cure for hematological malignancies."

It's a quest she's pursued across three continents, from China to Norway to the U.S. and City of Hope, where her search is finally paying off.

Wang, a research professor in the Department of Hematology & Hematopoietic Cell Transplantation at City of Hope, is at the forefront of one of the most exciting breakthroughs in cancer treatment: chimeric antigen receptor (CAR) T cell therapy.

CAR T is a process in which the T cells from a patient's own immune system are extracted, multiplied in the laboratory, engineered to target specific cancers, then infused back into the patient.

CAR T therapy appears particularly promising with blood cancers. In one recent trial, Wang partnered with Samer Khaled, M.D., assistant professor in the Department of Hematology & Hematopoietic Cell Transplantation. The trial, designed for B cell leukemia patients, was an extraordinary success.

After 11 years dedicated to CAR T research at City of Hope, Wang couldn't be more thrilled with the results. "It's amazing," she said, "just amazing."

## A PHYSICIAN TURNS TO RESEARCH

Wang's career began in her native China, where she was a physician specializing in hematology, but each day she faced the heartbreaking reality of what her patients — often children, young adults and new mothers with leukemia — had to endure.

"I saw that they suffered a lot, with bleeding, fever, infections," she said. "Many of them died. It was a nightmare."

As a physician, Wang had no way to help them, so she decided to pursue a career in research to find an effective therapy for blood cancers.

From China, she set off for Oslo, where she got a Ph.D. in hematology, then moved on to the U.S. for postdoctoral work at Children's Hospital Los Angeles. Then she heard about City of Hope and their groundbreaking research in CAR T cell therapy for leukemia and lymphoma. That was the work she'd been searching for.

## PERSISTENCE PAYS OFF

Wang joined the research team at City of Hope in 2006, and the first problem she tackled led to a crucial breakthrough.





"At that time, no one knew if CAR would work or not, because the CAR T cells did not persist and disappeared in the body rapidly," she said. "So at the beginning, my research focused on how to make them persist after infusion."

First, Wang found the source of the problem — the cells they were infusing were a mix of old and young. The old cells died off quickly, but the young cells had long lives.

The next step was figuring out how to isolate the long-lived T cells, and Wang discovered a marker, CD62L, found only on young cells. Now, they could isolate and extract only the T cells that would last in the body.

In 2013, phase 1/phase 2 clinical trials began to test the endurance of CAR T cells after infusion. Three years later, Wang published the results. The next step was maximizing their efficacy as cancer fighters.

Wang and her colleagues then began experimenting with new vectors — modifications of the T cells that might more effectively target blood cancers. The cells were so long lasting — and continued to reproduce so effectively in the body — that only a single infusion was needed to maintain them.

## ADVANTAGES OF CAR T OVER OTHER CANCER THERAPIES

The excitement CAR T therapy is generating is due to some significant



Xiuli Wang, Ph.D.

advantages over traditional cancer therapies, such as chemotherapy.

CAR T might also be preferable to other targeted approaches like antibody therapy.

"With antibodies, you need to continuously infuse them because they clear from the body very quickly," she said. "But CAR T cells can persist in the patient for years. A single CAR T cell infusion can clear the tumor, and when a new tumor comes, the CAR T cells can 'conquer' it."

Wang is also working on CAR technology to fight other types of cancers.

Her latest publication, the cover story in the latest issue of *Clinical Cancer Research*, focuses on multiple myeloma, a cancer of the plasma cells that produce antibodies in the blood. Wang and her colleagues developed a novel therapy that reprograms a patient's T cells to recognize a specific protein found on the surface of myeloma cells — and then destroys those cells. This form of CAR T cell therapy is currently in preparation for submission to the Food and Drug Administration, with clinical trials expected to begin in 2018.

For Wang, whose driving passion is to end to the suffering she saw as a physician, her long hours in the lab are truly a joy.

"Every day, I have a new discovery," she said. "And I just feel amazing when I see a patient have complete remission. That's the best thing for me."





# Arresting Development

BY DENISE HEADY



Patients with HER2-positive breast cancer need more treatment options — today, it is estimated that about half of all women with HER2-positive breast cancer will eventually develop brain metastases, and current therapies for these patients are limited.

“Patients with breast cancer are living longer in general and so the incidence of brain metastatic disease is increasing because they’re presenting with metastases years after being considered cancer-free,” said scientist Saul Priceman, Ph.D., assistant research professor in a T cell therapy program at City of Hope.

At City of Hope, scientists and researchers have many active experimental therapies for brain metastatic disease in the works, including investigations into CAR-based T cell immunotherapy, which uses patients’ own modified T cells, a specialized ‘soldier’ of the immune system, to fight the disease.

City of Hope researchers, who were the first to use intraventricular delivery of CAR T cells, have already found that injecting re-engineered CAR T cells locally into the brain or regionally through infusion in the ventricular system has the potential to be dramatically effective in glioblastoma, one of the deadliest brain tumors. And now, these researchers are expanding this type of immunotherapy as a way to treat patients with HER2-positive breast cancer that has spread to the brain.

With  
intraventricular  
delivery, you  
can bathe  
the central  
nervous system  
with  
CAR T cells

“We are actually using the same route of CAR T cell delivery that we developed for our glioblastoma trial,” said Priceman. “The CAR is now targeting the overexpressed protein HER2, so the target is different, but the hope of treating brain cancer is very similar.”

In a study recently published in *Clinical Cancer Research*, Priceman and his research team found that regional intraventricular delivery of HER2-CAR T cells is effective in preclinical models of HER2-positive brain metastases.

Previous research has shown that intravenous delivery of CAR T cells isn’t as effective in treating brain disease. Whether it’s glioblastoma

or brain metastatic breast cancer, the T cells don’t traffic in high enough frequency through the blood-brain barrier to get to the brain.

But, with intraventricular delivery, you can bathe the central nervous system (CNS) with CAR T cells that are then able traffic to multiple sites of CNS disease, said Priceman.

“We found that we could inject CAR T cells in the ventricle in mice with multifocal brain metastases, and those T cells actually traffic out of the ventricles and into tumor sites, generating a robust anti-tumor response.”

To study HER2-positive breast cancer tumors, Priceman and his team used tumors that were originally grown out from a former patient who had brain metastatic breast cancer, harvested from the lab of neurosurgeon and scientist Rahul Jandial, M.D., Ph.D.

“There’s something to be said about getting a tumor directly from a patient,” said Priceman. “Not having it grow for an extended period of time in culture before you implanted it resembles the clinical scenario better. This tumor had high HER2 expression, and that patient may resemble a patient who will be on the trial later this year.”

This first-in-human clinical trial is set to launch in 2018 and is open to all HER2-positive brain metastatic patients. The clinical principal investigator for this trial is Jana Portnow, M.D., along with key investigators including Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation; Christine Brown, Ph.D., the Heritage Provider Network Professor in Immunotherapy; and Behnam Badie, M.D.

Saul Priceman, Ph.D.

# Laboratory Research Yields Promising Prostate Cancer Results

BY LETISIA MARQUEZ

City of Hope physicians have successfully treated blood cancers with chimeric antigen receptor (CAR) T cell therapy, and they are working to expand that therapy to patients with solid tumors.

But in order to make that happen, research needs to take place in a laboratory to test the effectiveness of new CAR T therapies and also the CAR design, which consists of the different components of a CAR T cell. The treatment involves taking immune cells known as T cells from a patient’s bloodstream, reprogramming them in a laboratory to recognize and attack a specific protein found in cancer cells, then reintroducing them into a patient’s system, where they get to work destroying targeted tumor cells.

“Developing a CAR T cell therapy for solid tumors is particularly challenging because they need to first reach the solid tumor and then survive in a harsh microenvironment that is filled with cancer cells and other cells that make up the tumor mass,” said Saul Priceman, Ph.D., assistant research professor in City of Hope’s Department of Hematology & Hematopoietic Cell Transplantation.

Priceman and his research team compared different CAR designs that would critically impact the T cell’s ability to fight prostate cancer that has metastasized to the bone. Their research, which used preclinical animal models, was published in a recent edition of *Oncoimmunology*.

The research ultimately identified a specific CAR design that allowed for optimal cytokine production (chemical messengers that help enhance the antitumor activity of a CAR T cell) and destruction of prostate stem cell antigen (PSCA)-positive prostate cancers by the CAR T cells.

“These CAR T cells homed to prostate cancer cells in the bone, expanded there and demonstrated robust antitumor responses,” said Priceman, the study’s lead author.

The therapy also allowed these T cells to persist for a longer period of time and kill multiple tumor cells, compared with other therapies.

“T cells, once they kill, can also die. We like to equate it to a bee sting — if a bee stings, it then dies. But a CAR T cell has to be able to kill multiple tumor cells and survive a period of time in order to control the tumor,” Priceman said.

The research laid the groundwork for a CAR T cell clinical trial for patients with bone metastatic prostate cancer to start in 2018 at City of Hope; the institution would be one of the first cancer centers in the nation to offer a CAR T cell trial for advanced prostate cancer.

“It helped us generate evidence that our CAR T cell may be therapeutically effective in these patients,” Priceman said.

The Prostate Cancer Foundation funded the study.



# Cheryl's Story

BY LETISIA MARQUEZ



In the almost two years since Cheryl Wiers was diagnosed with cancer, the Redlands, California, mother of two young children has given a lot of thought to the question of why.

"Something as big as cancer doesn't happen for no reason," she reflected. "I think there is a greater purpose for it."

Wiers believes one purpose is her participation in a clinical trial using what is arguably the most promising cancer treatment — chimeric antigen receptor (CAR) T cell therapy. Such therapies reprogram one type of the body's immune cells — T cells, which are white blood cells — to recognize and destroy cancer cells by adding a CAR to those cells.

In Wiers's case, CAR T cells were genetically engineered to target the antigen CD19, a protein found on the surface of non-Hodgkin lymphoma (NHL) and other cancer cells.

Starting in the late 1990s, in an effort led by Stephen Forman, M.D., and Michael Jensen, M.D., City of Hope was one of the first cancer hospitals in the nation to use CAR T therapies in preclinical trials for blood cancers. Wiers is one of 165 patients who have taken part in CAR T cell therapy trials at City of Hope. In Wiers's case, she was part of a trial in which patients received CAR T cell therapy to help build an immune response against cancer cells.

So far, the treatment combining stem cell transplant with CAR T therapy has worked for Wiers and other patients, and it is hoped that this will help preserve the remission and improve the results of transplant, and possibly become a way of improving the cure rate for both transplant and CAR T cell therapy. The approach has kept Wiers's cancer — NHL of the breast — from returning a third time.

"I'm extremely grateful for the treatment I've received at City of Hope, and it's exciting feeling like you are going through this to help other people," said Wiers, 43, the mother of a 6-year-old boy and an 8-year-old girl.

Wiers, a speech therapist, was first diagnosed with NHL in January 2016.

"I felt a lump in my breast but assumed it was a cyst because I had already had one removed before," she said. "I didn't have any other symptoms — that was the only thing I could feel."

Wiers recalls her primary care doctor called her at work to tell her the lump was cancerous. For the rest of the work day, she found it difficult to concentrate, the diagnosis clouding her thoughts.

Primary NHL of the breast is a rare type of cancer that occurs in a breast's lymph nodes and can initially be mistaken for breast cancer. Chemotherapy, radiation and stem cell transplants are standard treatments that are used to combat lymphoma, but CAR T therapy is also emerging as a promising option.

Wiers received chemotherapy at a local hospital when she first learned she had lymphoma. She received six rounds of chemotherapy, which prevented the

cancer from spreading to her brain.

"At times, I was really nervous about it returning, but I just tried to stay positive," she said. "It helps that we are surrounded by a group of wonderful family and friends who have rallied around us."

A relative of her husband, Matt, had already told her that she should get a second opinion from Forman, the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, leader of City of Hope's Hematologic Malignancies and Stem Cell Transplantation Institute and an internationally-renowned expert in the treatment of blood cancers. Forman also leads City of Hope's CAR T cell research, including its clinical trials, and was one of the first doctors in the nation to oversee the therapy in lymphoma patients.

Wiers knew that because her lymphoma had relapsed, she would need a stem cell transplant. And once she met Forman, also a pioneer in the field of bone marrow stem cell transplantation, she knew he had found the right doctor to guide her treatment.

"I liked Dr. Forman's thoroughness and his expertise," Wiers said. "He explained everything so well."

Forman recommended the transplant and Wiers's participation in the phase 1 clinical trial for NHL and some leukemia patients who had already received chemotherapy; the CAR T therapy would be an additional boost against the lymphoma.

Wiers's T cells were collected almost two weeks prior to the stem cells for her transplant. Her T cells were isolated from a sample of her blood, then genetically engineered to target her cancer.

Wiers then received high-dose chemotherapy to kill off cancer cells, a routine treatment for transplant patients, that also prepared her body to receive new, healthy cells. A few days later, she received her own stem cells to produce new, healthy blood cells. Two days after that, the CAR T cells were then infused back into Wiers's blood stream and redirected to attack cancer cells.

Family and friends pitched in to help care for Wiers's kids, including her mother and mother-in-law, who traveled from out-of-state.

Throughout her treatments, Wiers and her husband, have made an effort to keep the children's routine as normal as possible. That means keeping them in school and participating in activities such as soccer, play dates and their friends' birthday parties.

"The kids have dealt with everything remarkably well," Wiers said. "My son, who was 4 when this started, recently told me: 'I don't even know what you look like with long hair.'"

Wiers's lymphoma hasn't returned, and she's hopeful about the future.

"I'm ready to go back to work and to a new normal," she said. "I want to put all this behind me."



*Wiers, pictured here with her children, made an effort during treatment to keep their lives as normal as possible.*

**‘It helps that we are surrounded by a group of wonderful family and friends who have rallied around us.’**

*- Cheryl Wiers*

# The Journey Is Everything

BY ABE ROSENBERG

Suzette Hodnett is many things.

She's a trained therapist, a tai chi instructor in considerable demand and an artist known for bold, fanciful, oversized, uber-metallic creations.

She's a Stage 4 cancer survivor who captivated every medical professional who operated on her, medicated her, irradiated her or rehabbed her.

She was the inspiration for and beneficiary of TeamSuzette, a grassroots support community numbering in the hundreds and assembled by family and friends.

And Hodnett is the author of "The Journey is Everything: Saying Yes to Cancer" (available on Amazon), a thoughtful, emotional, spiritual and decidedly outward-reaching "how-to-get-through-it" book. It's her way, she says, of "giving back."

## THE JOURNEY BEGINS

At Hodnett's home in Whittier, California, there's a palpable feeling of calm, stability and continuity. A baby grand piano — her mother's — occupies one corner. Artworks — not hers, but by her artist friends — cover the walls. As for Hodnett herself, she is slim and serene in a turtleneck, jeans and stylish curly hair.

Only when you look closer do you begin to understand.

Hodnett's smile is a half-smile. The right corner of her mouth does not move and her right eye does not blink, both the result of surgery that severed facial nerves. There are long scars. Her right ear is missing.

Seated in her garden, carefully positioned under an SPF-50 umbrella, she explains:

"Back in 2013, while doing tai chi, I noticed what felt like an enlarged lymph node. It turned out to be Stage 3 follicular lymphoma, slow growing but incurable."

A year later, more tumors appeared all over Hodnett's head, neck and the base of her skull — and they were growing rapidly. What doctors had thought was a particularly aggressive form of lymphoma, instead was advanced metastasized squamous cell cancer, Stage 4.

Thankfully, Hodnett was able to have her care transferred to City of Hope.

City of Hope's tumor board felt that surgery offered the best chance for recovery. But it wasn't going to be easy. And time was running out.

## 'WE WERE QUITE CONCERNED'

"We were quite concerned at the aggressive nature of her tumor," said Robert S. Kang, M.D., M.P.H. "It had grown quite large in a very short time, to the point that her facial nerve was paralyzed between the time we saw her in clinic and the day of surgery."

A team of three surgeons including Kang and Ellie Maghami, M.D., the Norman and Sadie Lee Foundation Endowed Professor in Head and Neck Cancer, labored for 14 hours to remove the cancer and reconstruct the damaged areas as best they could. After surgery, when Kang stopped by to see her, Hodnett silently

reached out with her one good arm, and pulled him close.

She kissed him.

"It felt great!" recalls Kang. "It put a big smile on all our faces!"

## HERE AND NOW

Hodnett's cancer journey was far from over. Over the next year, she endured long stretches of radiation, chemotherapy, often-excruciating physical and occupational therapy, and a skin graft to raise her lower eye lid.

For Hodnett, the way forward was rooted in the here and now. She resolved to live in the present: to extract meaning, peace and gratitude out of every single moment of every single day, no matter how challenging that might be.

"It doesn't mean you're never scared, never sad, frustrated or confused," she insists. "Those are normal emotions. But they are part of the journey. They don't define us. I would never tell myself, 'Don't be scared.' Instead I ask, 'What can I get from this moment? What's true about this moment?' If I'm in pain right now, fine. I don't project it forward. Tomorrow, I'll be in a different place. If I can barely move my arm today, OK. That's today. Tomorrow, we'll see. That's how you embrace the here and now, give your body positive cues, and turn baby steps into leaps!"

## SPREADING THE WORD

Hodnett's insights impressed — and inspired — even her own caregivers.

"Her attitude is memorable to me," said Kang. "She has a positive energy, and is full of gratitude and peace, and it is contagious."

"Suzette's attitude toward her cancer care was one of the strongest I've ever seen," said her radiation oncologist, Sagus Sampath, M.D. "Head/neck radiation is one of the most difficult cancer treatments there is. Her confidence in me is an inspiration that I will never forget."

A year after her treatment for the squamous cell cancer, the slow-growing lymphoma did transform into a highly advanced and aggressive form of the disease. But thankfully, under the care of Auayporn Nademanee, M.D., the Jan & Mace Siegel Professor in Hematology & Hematopoietic Cell Transplantation, she is again cancer-free.

These days, Hodnett is growing stronger and resuming much of her teaching schedule. Despite her severed spinal accessory nerve, she has been able, with physical therapy and adaptations, to return to her life as a professional artist, now with added heart and soul. She recently exhibited the art created during her healing journey in a one-woman gallery show entitled, "The Journey is Everything."

She continues to visit City of Hope for follow-up visits every few months. She can't say enough about the people there.

"Their incredible compassion and expertise played a big role in my healing," she said. "I wouldn't be alive without them."



Suzette Hodnett at home with her art





# TGEN BRINGS GREATER PRECISION TO CAR T THERAPIES

*Michael Berens, Ph.D., professor and head of the Glioma Research Unit, as well as deputy director of research resources, at TGen*

For the past 15 years, scientists at the Translational Genomics Research Institute (TGen) in Phoenix have studied patients' individual DNA blueprints to identify the most effective treatments for cancer and other complex diseases.

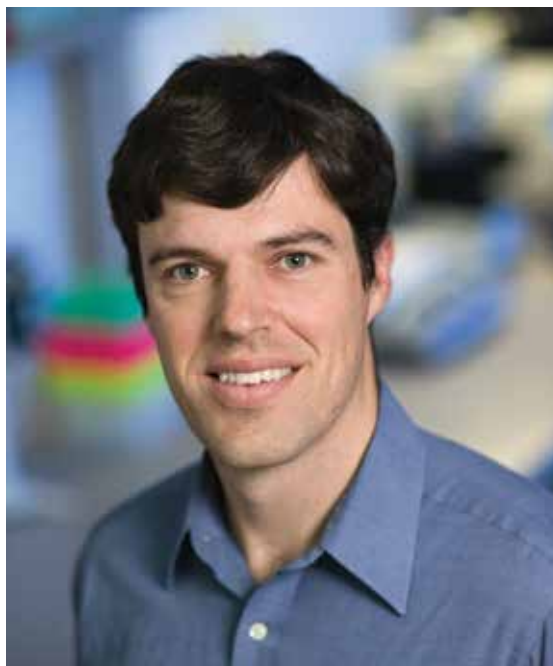
As an affiliate of City of Hope, TGen will use this expertise to chart a path to greater precision in CAR T therapies for cancer patients.

"We are going to add additional experience and techniques to what they do," explained TGen professor Michael Berens, Ph.D., head of the Glioma Research Unit. "Our genomics platforms can look at both the weapon — the CAR T cells and their effectiveness — as well as the targets, or the cancer cells, and how they're shifting and changing."

CAR T cells are genetically engineered to target tumor-specific, surface protein markers, which stimulate a strong immune response to attack the cancer. The challenge is identifying the most effective markers to target among the thousands that may be present on a tumor.

TGen's genomics technology can accelerate the identification of these targets. Traditionally, CAR T cells are aimed at proteins that are found at high levels on the surface of tumor cells, but are at low levels or absent on healthy cells. In addition to identifying additional targets of this kind, TGen scientists are working on a new assay that allows them to identify a different class of targets — known as neoantigens.

"Neoantigens are exciting because they are found only in tumor cells and nowhere else in the body, making them highly specific targets for an immune



*John Altin, Ph.D., assistant professor, divisions of Pathogen and Microbiome, and Integrated Cancer Genomics*

response with less potential for side effects," explained John Altin, Ph.D., an assistant professor in the Pathogen and Microbiome, and Integrated Cancer Genomics divisions at TGen, who helped to invent the new assay.

Immune responses against neoantigens may be either targeted by the CAR T cells directly, or may be a beneficial side effect of CAR T therapy. Ultimately, these approaches promise to generate a more successful immune response for cancer patients at City of Hope.

TGen President and Research Director Jeffrey Trent, Ph.D., is collaborating with Christine Brown, Ph.D., the Heritage Provider Network Professor in Immunotherapy, at City of Hope to use the new assay for CAR T therapies against HER2 breast cancer. The TGen team is also investigating the effectiveness of CAR T against pancreatic cancer, the third-leading cause of cancer death. Pancreatic cancer has proven resistant to other immunotherapy approaches because it has a near-impenetrable physical barrier and an inhospitable environment that thwarts T cells.

In addition to the neoantigen assay, Berens is eager to deploy TGen's single-cell sequencing technologies to study RNA and the epigenome in CAR T therapy and brain tumors. RNA carries out the instructions coded in the DNA blueprint. The epigenome is the machinery on the DNA helix that turns genes on and off, depending on a cell's specific function and location in the body.

With single-cell RNA sequencing, "we can now watch how the engineered T cells behave," Berens explained. "Is it only the CAR T cells that control the tumor, or are they showing the rest of the patient's immune system what to do?"

The epigenome of a cancer stem cell can convert a cell from being quiet and acquiescent to one that is actively invading the surrounding tissue, even though the DNA does not change, Berens said, which can help oncologists understand how brain tumors escape immunotherapy.

"This is another area where TGen's genomics can really add value to City of Hope's CAR T programs," he said.

# supporting HOPE

PHILANTHROPY NEWS AND EVENTS



Left to right: Robert W. Stone, president and CEO of City of Hope, Spirit of Life® honoree Coran Capshaw and musician Dave Matthews

## Special Friendship Drives Gift from Music Industry

On Nov. 2, performers and luminaries of the music industry gathered at the annual *Spirit of Life*® Celebration Dinner. Musicians, producers and executives who attended have more than music in common. They also want to use their influence and talent to further hope.

This year's dinner honored friendship and shared vision in a special way. *Spirit of Life* honoree Coran Capshaw, owner of Red Light Management, announced a \$500,000 gift to establish The Chip Hooper Memorial Fund, named in honor of the successful industry colleague and his dear friend.

Capshaw was joined in this special effort by Dave Matthews, whose band he has managed for more than 25 years.

This new fund honors Chip Hooper, former head of music of Paradigm Talent Agency and agent for Matthews' band. Hooper battled a rare form of neuroendocrine cancer and died in 2016.

Now, through The Chip Hooper Memorial Fund at City of Hope, research into better treatments and earlier diagnosis will help many more patients whose lives and livelihood are threatened by the disease.

The night boasted an incredible show of support, raising some \$4.8 million and adding to the more than \$113 million the Music, Film and Entertainment Industry Group has rallied over its 44-year history at City of Hope.

## When Making Decisions About Philanthropy, Long-held Values Directed Family to City of Hope



David and Natalie Roberts

In 2017, Natalie Roberts established the Natalie and David Roberts Fellowship in Liver Cancer as a memorial to her late husband David, who succumbed to liver cancer in 2012. Although David was not treated at City of Hope, the Roberts family felt confident in the institution's efforts to diagnose the disease earlier and treat it more powerfully.

The Roberts' connection with City of Hope began many years ago when she supported an auxiliary group dedicated to raising funds for cancer research and patient care. Along with contributions over the years to many organizations, the Roberts always included City of Hope in their charitable giving, a value which was passed down to their five children.

City of Hope's Office of Philanthropy worked with Roberts to craft a gift that would honor her husband's life and meet the family's philanthropic goals. The result was the creation of the Natalie and David Roberts Fellowship in Liver Cancer.

The fellowship is designed to attract bright young scientists working on the development of better therapies and a cure for liver cancer. The fund also allows them to be mentored early in their careers by nationally renowned experts in their fields, Yuman Fong, M.D., and Suzanne Warner, M.D., two stand-out physician-researchers.

An endowed fund, the Roberts Fellowship will exist for the life of the institution, which means that Roberts impact will continue for generations to come.



# Gateway to the Future

Members of the Gateway Foundation for Cancer Research gathered on City of Hope's campus to meet with investigators and learn more about transformational advances and breakthroughs in CAR T cell therapy.

Gateway's generous support helps drive the research of Christine Brown, Ph.D., the Heritage Provider Network Professor in Immunotherapy, and Behnam Badie, M.D., who initiated a first-in-human clinical trial using CAR T cells for the treatment of recurrent glioblastoma, the most aggressive and fatal type of primary brain tumor and one of the most lethal of human cancers. Their study provides evidence of the potential therapeutic benefits of CAR T cell therapy against glioblastoma.

The Gateway Foundation for Cancer Research has a vision to shape a world in which a cancer diagnosis is no longer feared. The Foundation's philanthropic grants are accelerating City of Hope's efforts to implement personalized medicine, improve patient quality of life and support researchers in developing new treatments for those suffering from glioblastoma.

Thanks to the support from the Gateway Foundation, City of Hope researchers have been able to provide an important study for the therapeutic potential of promising T cell therapy. Initial results thus far show a potential breakthrough treatment that may have a remarkable impact on patients with malignant brain tumors.



*Pictured from left to right, back row: Teresa Bartels, president and director, Gateway for Cancer Research; Jerian Dixon-Evans, Gateway; Kim Saulsberry, Gateway. Pictured from left to right, front row: Denzi Razon, Gateway director; Mary Lou Smith, J.D., M.B.A., Gateway director; Eveline Mumenthaler, former director of research, Gateway; Anthony Festa, C.F.A., director, Gateway; Domarina Oshana, Ph.D., director of research and grants, Gateway.*

## A CURE WITHIN SIX YEARS

How one family was inspired to support an ambitious goal

Living with diabetes can be challenging at any age, but 12-year-old Grady Sterling has been living — and thriving — with type 1 diabetes since he was just 5. With the help of his parents, Julie and Devin, Grady has tackled his disease head-on and lives a happy and healthy life. But the Sterlings are also working toward a future where Grady no longer needs injections or blood glucose checks — and they're looking to City of Hope to help make it happen.

It was an article in *City News* that first led the Sterlings to City of Hope. Devin Sterling was inspired by the statement he read in last year's spring issue: "City of Hope is committed to developing a cure for type 1 diabetes within six years." He decided to learn more. "For City of Hope to make a concrete statement like that — we knew that our support would make an impact."

They visited the City of Hope campus in Duarte, California, spoke to diabetes researchers and toured the labs where breakthrough discoveries are happening. The trip was inspiring. "We're helping Grady manage his care," Julie Sterling said. "But to see the work going on to make his life better was so moving for all of us. It gave us a lot of hope."

The Sterlings set up an ourHope personal fundraising page and have already raised over \$10,000 — double their goal — to support The Wanek Family Project for Type 1 Diabetes. They are committed to continuing that work in the years to come, as City of Hope sets its sights on a future without diabetes. To start your own personal fundraising page on ourHope, visit [CityofHope.org/ourHope](http://CityofHope.org/ourHope).



*Grady Sterling (right) with his family*



# Gratitude for the Gift of Time: Meet Chuck and Eileen O'Shea

"City of Hope is a place that saves lives," said Chuck O'Shea. "I know, because I'm one of the people whose life they've saved. The instant we met 'Dr. Nadee,' we knew we had met my doctor. She recommended immunotherapy. City of Hope doctors don't settle for standard treatment. They conduct leading-edge research that helps patients do more than survive; they want us to thrive."

In remission since 2010, O'Shea is now a City of Hope volunteer. "During my treatment, I swore that if I had the chance, I would become a volunteer, too," he said. He is also a member of the Patient and Family Advisory Council, which helps improve the experience of patients and their families throughout the institution.

O'Shea and his wife Eileen are grateful for the gift of time they've been given. To demonstrate their gratitude, they recently decided to leave a gift in their trust to City of Hope. "The kind of immunotherapy that saved my life, and the recently approved CAR T cell therapy, which City of Hope is one of the first centers in the nation to offer, is changing the face of cancer treatment," explained O'Shea. "We want our gift to help drive research that will continue to deliver leading-edge therapies."

One thing they've learned, his wife added, is that "every contribution makes a difference. We just want to do whatever we can to help find cures."

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



*Eileen and Chuck O'Shea with their dog, Maggie*

## Celebrating Support in Orange County

Generous individuals from across Orange County in California gathered for the fourth annual Let's Be Frank About Cancer gala on March 3. This inspiring event, chaired by its founder and City of Hope donor Frank Di Bella, raises critical funds and awareness for City of Hope's research.

The gala has also grown to celebrate the generosity of donors and the victories of patients in Orange County. More than 400 individuals attended this year's dinner. That number included honoree and patient Donna Porter, who was directed to City of Hope for treatment by Di Bella.

"I was introduced to some amazing doctors," Porter noted of the life-changing relationships that began with her first appointment. Now, Porter is rallying friends, family and colleagues in Orange County to join City of Hope's network of advocates and philanthropists.

Past honorees of the celebration include Di Bella, S. Paul Musco and His Excellency Milan Panic, former prime minister of Yugoslavia, each of whom helped to drive this effort to spotlight City of Hope's work.

"What I've learned through this experience is the importance of not waiting until you get a diagnosis to help," said Porter. Fueling research with philanthropic support is the key to outpacing cancer and its impact on the lives of those we love.



*From left: Milan Panic, S. Paul Musco, Donna Porter and Frank Di Bella*

Inspired by the care Di Bella received at City of Hope, Let's Be Frank About Cancer was created to honor Sumanta Pal, M.D., and rally support for cancer

research. The event was held at the Balboa Bay Resort in Newport Beach, with live music by Matt Mauser and the Pete Jacobs Big Band.



# HOROWITZ FAMILY CREATES FUND TO ADVANCE INNOVATIVE CAR T THERAPY RESEARCH



*Jody Horowitz Marsh, Stephen Meringoff (center) and Zach Horowitz*

In memory of Ben and Beverly Horowitz, longtime CEO and “first lady” of City of Hope, their family has donated \$1 million to City of Hope to promote groundbreaking CAR T cell research to combat cancer.

The Horowitz’s son, Zach Horowitz, and daughter, Jody Horowitz Marsh, together with their spouses Barbara Horowitz and Gary Marsh, and their cousin Stephen Meringoff via his Meringoff Family Foundation, have created the Beverly and Ben Horowitz Fund for Immunotherapy Research. The fund will advance chimeric antigen receptor (CAR) T cell therapy research at City of Hope and clinical immunotherapy trials in breast, brain and prostate cancer.

The gift was announced by music industry veteran Zach Horowitz, former president and COO of Universal Music Group and chairman and CEO of Universal Music Publishing Group, and his sister, Jody Horowitz Marsh, chair of the board of directors of Beckman Research Institute of City of Hope, at the 13th annual Songs of Hope event sponsored by City of Hope’s Music, Film and Entertainment Industry Group. An additional \$100,000 raised at that event will also be contributed to the Horowitz Fund.

For nearly 40 years, beginning in 1952, Ben Horowitz was the CEO at City of Hope, leading the institution during a time of exponential growth and scientific and clinical advances. He first met Beverly when she ran the Southwest Region for the institution. Under Horowitz’s leadership, City of Hope was transformed from a small hospital that was focused on tuberculosis into a world leader in the treatment of cancer, diabetes and other devastating diseases. Believing that City of Hope’s mission required it to do more than simply provide treatments at its hospital in Duarte, California, Horowitz established City of Hope as a major research center dedicated to finding cures that could help patients around the world. In fact, it was Horowitz

who established Beckman Research Institute of City of Hope. Under Horowitz’s leadership, research was conducted that resulted in the development of synthetic human insulin and four primary drugs used to treat cancer today.

Ben and Beverly Horowitz’s passion for City of Hope has inspired their family’s dedication to the cause. In addition to chairing the Beckman board, Jody Horowitz, Marsh is a member of City of Hope’s national board. Zach Horowitz is a longtime leader of its Music, Film and Entertainment Industry Group, which has raised over \$100 million for the organization. Jody’s husband Gary, president and chief creative officer of Disney Channels Worldwide, was a co-founder of “Concerts for Hope,” which raised over \$2 million for City of Hope. Barbara and Zach’s son, Charles, interned at the Eugene and Ruth Roberts Summer Student Academy at City of Hope. Their cousin, Stephen Meringoff, was also a member of City of Hope’s Board of Trustees. He has a long history of philanthropic activity, primarily in support of public education and leading-edge medical research through the Meringoff Family Foundation.

The generous gift will enable City of Hope researchers, pioneers in the use of immunotherapy, to deepen their investigation of CAR T cell therapy. City of Hope’s CAR T program has become one of the most comprehensive in the world and the institution is one of the only cancer centers in the United States offering clinical studies in this area.

“Our father always considered his establishing City of Hope as a world-renowned research center to be one of his greatest achievements,” said Zach Horowitz. “It gives us great pride to continue his legacy in that area by supporting City of Hope’s scientists in their cutting-edge work in immunotherapy. The trailblazing CAR T cell immunotherapy research at City of Hope has the potential to transform the treatment of disease everywhere.”

# CITY NEWS

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# *the* PAST



## A LEGACY OF RESEARCH BEGINS

In 1952, Ben Horowitz and Samuel Golter's dream of starting a research institute was realized when City of Hope announced that it would combine forces with the fledgling University of California Los Angeles medical school to launch the Cancer Research Institute. The inaugural staff included many promising young scientists, including geneticist Susumu Ohno, D.V.M., Ph.D. (second row, center).

PHOTO COURTESY OF CITY OF HOPE ARCHIVES



# CELEBRATE DOCTORS' DAY

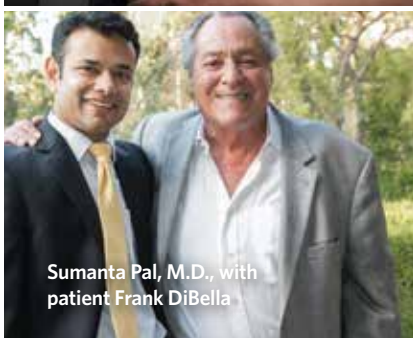
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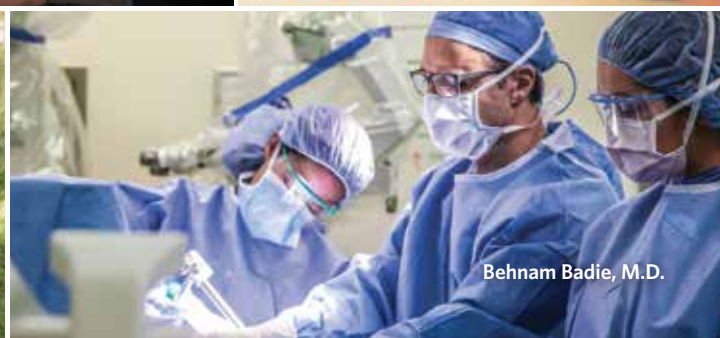
Yuman Fong, M.D.



Arti Hurria, M.D.



Sumanta Pal, M.D., with  
patient Frank DiBella



Behnam Badie, M.D.

Every year, our doctors and researchers help submit applications for dozens of new drugs, conduct more than 500 clinical trials and treat the thousands of patients who walk through our doors.

City of Hope's doctors are both researchers and clinicians, meaning they don't just heal their own patients with breakthrough treatments — they contribute to the worldwide fight against cancer and diabetes by helping patients around the world who benefit from the medical advances made in our clinics and labs.

We are so proud to have them on our team. Please join us in saying thank you to our heroes on **National Doctors' Day** by submitting a note of gratitude.

TO GET STARTED, GO TO  
[CityofHope.org/national-doctors-day](http://CityofHope.org/national-doctors-day)

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800-423-7119

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

## TO MAKE A GIFT

Or to speak with someone about the impact of philanthropic support at City of Hope, contact our

**PHILANTHROPY OFFICE**  
800-667-5310

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# Just Published!

If you or someone you know has been diagnosed with cancer, the days, weeks and even months ahead can be challenging. City of Hope's new publication, *Coping with Cancer*, can help.

The guide includes tips for: staying connected; fighting cancer-related fatigue; ensuring good nutrition; managing work, school and home; sound financial planning; and coping as a cancer survivor.

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